

## COVID-19 Pandemic and Hemodialysis: Disease Parameters and Outcome: Single Center Study

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### ABSTRACT

**Background:** Coronavirus disease 2019 (COVID-19) has significantly affected the provision of medical services. The hemodialysis (HD) facilities together with other medical facilities faced challenges in safely providing clinical care to patients and staff during the pandemic.

**Objective:** To describe our experience during the COVID-19 pandemic as regard infection, mortality rate, clinical manifestations, illness duration and the efficacy of our local infection control measures in our Hemodialysis Unit, Ain Shams University Hospital, Cairo, Egypt.

**Patients and Methods:** followed the interim guidance provided by the US Centers for Disease Control and Prevention (CDC) together with the European Renal Association– European Dialysis Transplantation Association (ERA-EDTA) for dealing with the emerging COVID19 pandemic in HD centers. The study included 238 patients on regular HD from Dialysis Unit in Ain Shams University Hospitals. We monitored all patients and staff members for any symptoms or signs of respiratory tract infection and those confirmed to have COVID-19 infection were followed up through their illness.

**Results:** 42 out of total 238 patients were diagnosed to have COVID19 infection by combination of symptoms, chest imaging and SARS COV PCR. Their mean age was  $49.8 \pm 8.9$  years, 19 were males, the mean  $\pm$  SD total illness duration for all COVID-19 positive patients was  $17 \pm 8.7$ . Patients were further subdivided based on survival into cure group (34 patients) and death group (8 patients). CRP and D-dimer were all significantly higher in death group while  $O_2\%$  were significantly lower in death group compared to cure group.

**Conclusion:** COVID 19 pandemic still a major health problem worldwide with significant morbidity and mortality among hemodialysis patients.

**Keywords:** Ain Shams University Hospital, COVID-19 pandemic, Hemodialysis.

### INTRODUCTION

The SARS-CoV-2 virus causes novel coronavirus disease (COVID-19), which predominantly manifests as an acute upper and lower respiratory tract sickness that can be exacerbated by interstitial and alveolar pneumonia. Multiple additional tissues, including the heart, digestive tract, kidneys, blood, and neurological system, may be affected <sup>(1)</sup>.

The clinical course varies greatly, ranging from asymptomatic or very mild (up to 80%), to severe involvement with unilateral or bilateral pneumonia (approximately 15%), to a very serious course with bilateral pneumonia and respiratory distress requiring ventilatory support in the intensive care unit (ICU; 3%–5%). In extreme circumstances, an immune response can cause a significant inflammatory response, as well as a cytokine storm, which can exacerbate respiratory symptoms and even lead to death <sup>(2)</sup>.

Until July 2021, the COVID-19 pandemic in Egypt had a steadily increasing curve of 283k verified cases with 16,403 death reports. In Egyptian hospitals, however, restrictions have been developed to limit elective hospitalizations and stop needless procedures, although not hemodialysis therapy, of course <sup>(3)</sup>.

For a variety of reasons, patients on maintenance hemodialysis (MHD) are more susceptible to COVID-19 infection and accompanying consequences. Many

MHD patients are older and have concomitant diseases including cardiovascular disease, hypertension, diabetes, and lung disease, as well as an underlying immune-compromised state, all of which are linked to worse outcomes in COVID-19 infection patients <sup>(4)</sup>. The logistical features of MHD, such as recurring physical presence at health care facilities and physical closeness of patients during hemodialysis, enhance the risk of disease transmission. As a result, it's critical to implement suitable preventative tactics as soon as possible in outpatient hemodialysis centres <sup>(4)</sup>.

Estimates of mortality in the general population range from 1.4 percent to 8%, with the risk of death rising dramatically if the patient necessitates hospitalization <sup>(1)</sup>. The impact of this virus on individuals with chronic renal disease, on the other hand, remains unknown. Given these patients' advanced age and comorbidities, mortality may be greater than in the normal population, particularly among dialysis patients <sup>(5)</sup>. We still do not know the specific characteristics of the disease in this population. To date, only isolated observations or small case series on prevalence and mortality rate have been reported <sup>(6)</sup>.

“Interim Guidance for Infection Prevention and Control Recommendations for Patients with Suspected or Confirmed COVID-19 in Outpatient Hemodialysis Facilities” official guidance can be freely accessed at



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the CDC website. In addition, several dialysis organizations have developed their own guidance documents that are distributed to physicians who are related to these entities. Importantly, these documents are considered “interim” and are expected to evolve as more information is gathered<sup>(6)</sup>.

The objective of this observational study is to describe our experience during the COVID-19 pandemic as regard infection/ mortality rate, clinical manifestations, illness duration and the efficacy of our local infection control measures in our Hemodialysis Unit, Ain Shams University Hospital, Cairo, Egypt.

**PATIENTS AND METHODS**

Our Ain Shams University Hospital Hemodialysis Unit serves 238 ESRD patients who dialyze thrice per week. The study was an observational, analytical, retrospective, single-center study.

Patients confirmed, highly suspected and patients hospitalized due to COVID-19 infection, whether by SARS-CoV-2 virus PCR, intermediate to high probability in A high-resolution CT (HRCT) study according to the COVID-19 Reporting and Data System (CO-RADS) criteria<sup>(7)</sup>, or the new onset of symptoms suggestive of COVID-19 infection from 1<sup>st</sup> of March 2020 to 30<sup>th</sup> June 2020 were included.

**Dialysis scheme:**

During admission, all patients received 4-hour dialysis sessions thrice per week using F4008 dialysis monitors, bicarbonate dialysate solution was used, dialyzer surface area 1.6 to 2.2 m<sup>2</sup> and heparin as an anticoagulant. The dialysis prescription was individualized according to previous patient regimes and evaluation during admission.

Patients’ different presentations, progression of their clinical condition, laboratory and radiological results, their illness duration and mortality rate were all analyzed and presented.

**Our hemodialysis unit during the COVID-19 pandemic:**

Our hemodialysis facility serves total of 238 hemodialysis patients, located in the internal medicine hospital, Ain Shams University Hospital, Cairo, Egypt. Since the COVID-19 outbreak started, being among the largest tertiary hospital in Egypt, our hospital was involved in the management of patients with COVID-19.

To provide information on how to best protect these patients from COVID-19, we examined and followed the guidance provided by the US Centers for Disease Control and Prevention (CDC), the European Renal Association– European Dialysis Transplantation association (ERA-EDTA) (Figure 1)<sup>(8)</sup>.




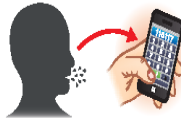


**How can we reduce transmission of COVID-19 in haemodialysis centres?**

This review from the Eudial Working Group of ERA–EDTA provides recommendations for the prevention, mitigation and containment of the emerging SARS-CoV-2 (COVID-19) pandemic in haemodialysis centres

**Recommendations for the healthcare team**

-  Be trained in use of personal protective equipment
-  Inform your team leader if symptomatic or in contact with a case
-  Stay home if unwell
-  Use full personal protective equipment when caring for confirmed cases

**Recommendations for dialysis patients**

-  Be provided with clear instructions on appropriate hand and respiratory hygiene
-  Should perform hand hygiene on arrival and departure from the dialysis unit
-  Body temperature should be checked before the start and end of dialysis sessions
-  Should inform staff of symptoms in advance of arrival at the dialysis unit
-  Should be instructed to self-isolate
-  Symptomatic patients should be dialyzed in a separate isolation room

**Figure (1):** ERA-EDTA recommendations for the prevention, mitigation, and containment of the emerging SARS-CoV-2 pandemic in hemodialysis centers<sup>(8)</sup>.

Among multidisciplinary approaches taken to face such a pandemic in our University Hospital, a small,

dedicated dialysis ward, separated from the main dialysis ward, was set up to deal with the emergency. A

management, isolation and follow up plans were set to ensure the easiness of the dialysis process during the infection time.

Dialysis unit sterilization was performed thrice per day after each hemodialysis shift using concentrated chlorine. Isolation room was sterilized between each patient. Regular trainings were performed by the infection control team in our hospital on the proper infection control measures and the proper use of PPEs to both nursing staff and attending physicians in the dialysis unit.

**Laboratory and radiological assessment:**

On the first suspension, full blood picture with differential count was sent for the patient, chemistry including CRP, D-dimer and ferritin, and SARS-CoV-2 virus PCR.

HRCT chest was ordered for all our patients, COVID-19 infection probability was made based on the CO-RADS Score to low, intermediate, high, and very high probability for infection based on the presence, distribution and severity of the ground glass opacities present in the CT<sup>(1)</sup>.

Patients deemed positive/high probability by any of the above-mentioned criteria were further managed according to their condition: (a) Patients with hypoxia  $SO_2\% \leq 90$ , any degree of respiratory distress, intractable symptoms (fever, vomiting/diarrhea ...etc.) that did not improve on home isolation with symptomatic treatment, were hospitalized. (b) Patients with none of these criteria received their dialysis sessions on an outpatient basis in our isolation hemodialysis unit, with taking all the proper infection control measures during session, in patients' transportation and safe paths in and out of the hemodialysis facility.

**Isolation duration:**

Hospitalized patients were isolated until their 1<sup>st</sup> negative PCR for those admitted with positive PCR or 14 days after the onset of their symptoms/HRCT provided the last 3 days were symptoms free. The same criteria applied to those outpatient-based dialysis patients. Both groups, when returned, were further isolated in small, dedicated dialysis ward, set up to deal with the emergency, separated from the main dialysis ward for further 10 days, with a specific nursing personnel before they were able to join the rest in the main hemodialysis ward according to their usual schedule.

**Ethical consent:**

An approval of the study was obtained from Ain Shams University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of sharing in the study. This work was carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

**Treatment scheme:**

**Statistical Analysis**

The collected data was revised, coded, tabulated and introduced to a PC using Statistical Package for the Social Sciences (SPSS 20). Data were presented as mean, standard deviation ( $\pm$ SD) and range for numerical data and as frequency and percentage for non-numerical data.

Student t-test was used to assess the statistical significance of the difference between two study group means. Fisher's exact test was used to examine the relationship between two qualitative variables. P value  $< 0.05$  was considered significant.

**RESULTS**

42 out of total 238 patients were diagnosed to have COVID19 infection by combination of symptoms, chest imaging and SARS COV PCR. Their mean age was  $49.8 \pm 8.9$  years, 19 were males, the mean total illness duration for all COVID-19 positive patients was  $17 \pm 8.7$  (SD). Patients were further subdivided based on survival into cure group (34 patients) and death group (8 patients).

The basic demographic data comparison between both groups are illustrated in table 1. Illness duration was significantly more prolonged in the cure group. Also 100% of death group were PCR positive compared to only 50% in the cure group. Clinical manifestations were comparable except respiratory distress (RD) which was more significant in the death group.

**Table (1):** Basic demographic and clinical features

	Cure (34)	Death (8)	P-value
	M $\pm$ SD N (%)	M $\pm$ SD N (%)	
Age (years)	49.2 $\pm$ 9.5	52.1 $\pm$ 5.1	0.411
Illness duration (days)	19.4 $\pm$ 7.9	6.8 $\pm$ 1.8	<0.001
Sex (males)	17 (50%)	2 (25%)	0.258
PCR (positive)	17(50%)	8(100%)	0.013
Hypertension	21 (61.8%)	7 (87.5%)	0.233
Diabetes Mellitus	6 (17.6%)	1 (12.5%)	1
Ischemic heart diseases	7 (20.6%)	2 (25.0%)	1
Bronchial asthma	6 (17.6%)	1 (12.5%)	1
Collagen disease	1 (2.9%)	0 (0.0%)	1
AA amyloid	2 (5.9%)	0 (0.0%)	1
Hepatitis C virus	2 (5.9%)	1 (12.5%)	1
<b>Clinical manifestations:</b>			
Fever	22 (64.7%)	8 (100 %)	0.080
Respiratory distress	3 (8.8%)	5 (62.5%)	0.003
Cough	15 (44.1%)	5 (62.5%)	0.445
Dyspnea	12 (35.3%)	3 (37.5%)	1
Body aches	8 (23.5%)	4 (50.0%)	0.195
GIT symptoms	1 (2.9%)	1 (12.5%)	0.348
Asymptomatic	3 (8.8%)	0 (0.0%)	1

All patients received standard of care management (including hydroxychloroquine); their

antihypertensive medications, their calcium and vitamin D supplementation as indicated. 23.5% of patient in cure group (8/34) vs 75% of death group (6/8) received steroids therapy (Methylprednisolone), on the other hand Tocilizumab (Actemra®) was used in only one patient in the cure group and two patients in the death

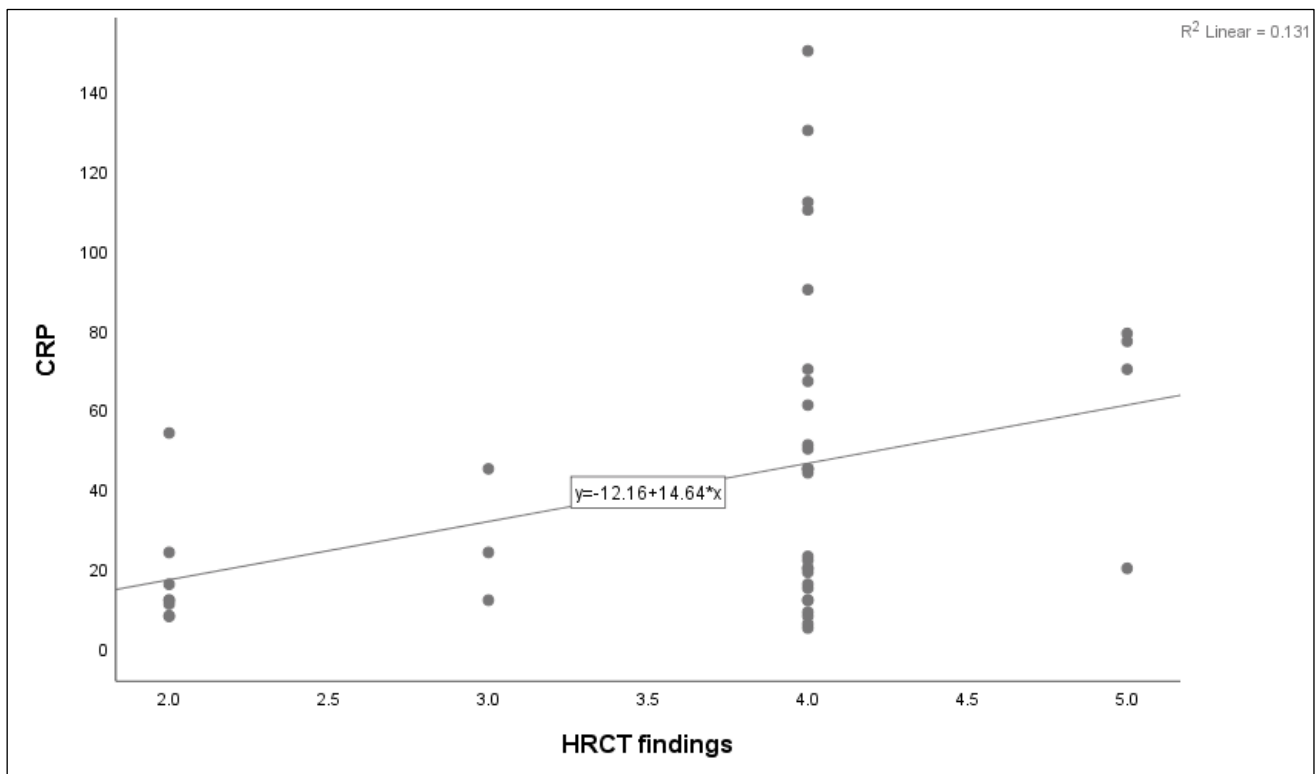
group, that was in addition to symptomatic therapy and O<sub>2</sub> therapy as needed.

As shown in table 2, ferritin, CRP and D-dimer were all significantly higher in death group while O<sub>2</sub>% were significantly lower in death group compared to cure group. There was no significant difference as regard chest imaging.

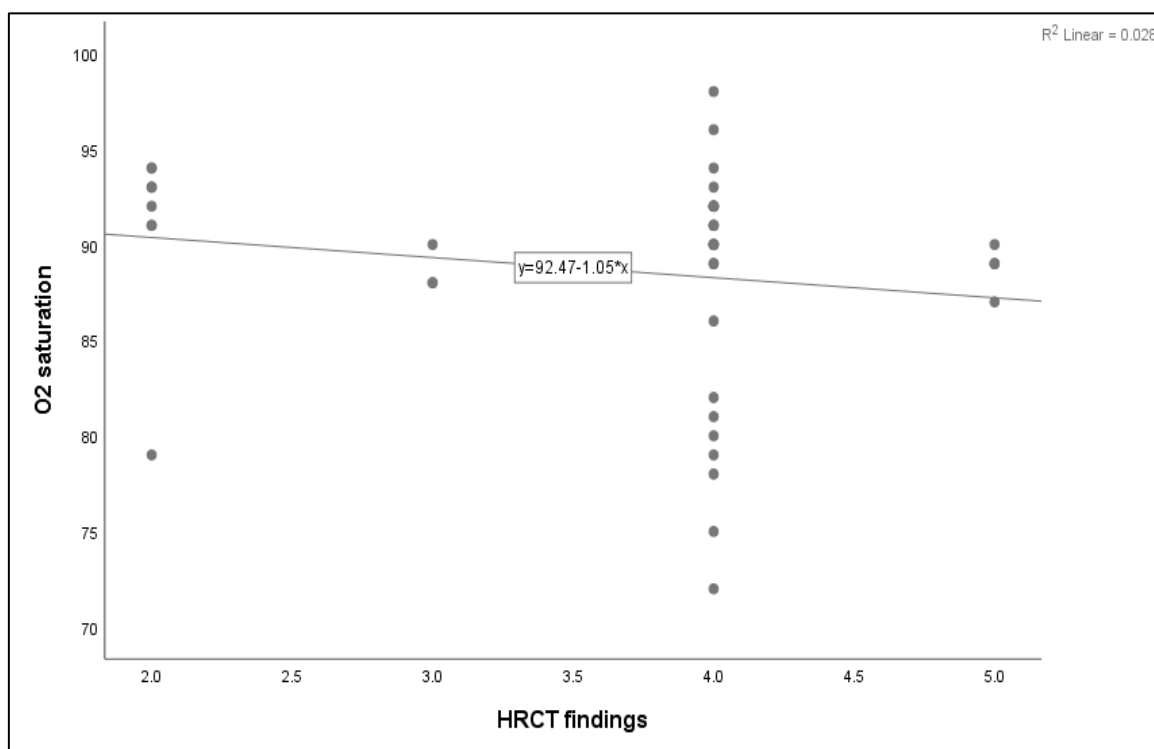
**Table (2):** Laboratory and imaging features of Covid patients

	Cure (32)	Death (8)	P-value
	Mean ±SD N (%)	Mean ± SD N (%)	
<b>Lymphopenia (mcL )</b>	19 (55.9%)	7 (87.5%)	0.127
<b>Lymphocytic count (cells/mcL)</b>	1.28 ± 0.56	0.90 ±0.26	0.008
<b>D-dimer (ng/mL)</b>	665.00 ± 46.49	1212.50 ±64.26	0.012
<b>Ferritin (ng/mL)</b>	1011.68 ± 75.34	1501.25 ± 44.14	0.002
<b>CRP (mg/L)</b>	28.00 ± 2.80	97.13 ± 3.26	0.001
<b>O<sub>2</sub> saturation</b>	90.68± 4.02	80.00 ± 3.21	<0.001
<b>HRCT (CO-RADS)</b>			0.707
Low (2)	7 (20.6%)	1 (12.5%)	
Intermediate (3)	3 (8.8%)	0 (0.0%)	
High (4)	20 (58.8%)	7 (87.5%)	
Very high (5)	4 (11.8%)	0 (0.0%)	

The grade of severity of lung affection in CT scan (CO=RADS SCORE) was positively correlated with CRP levels (r =0.402, P= 0.008) and negatively correlated with O<sub>2</sub>% saturation (r= -0.277, P= 0.076) (Figures 2 and 3).



**Figure (2):** Correlation of HRCT findings with CRP



**Figure (3):** Correlation of HRCT findings with O<sub>2</sub> saturation

During the COVID-19 pandemic, health-care workers' adherence to infection prevention and control guidelines becomes were followed. The infection rate among the medical and auxiliary staff (nursing and general service) was 12 out of 50 personnel, all diagnosed with SARS-CoV-2 PCR, no one needed hospitalization, all were home isolated till 1 negative PCR before they were allowed back to the work.

## DISCUSSION

Until now, there have been very few reports of SARS-CoV-2 outbreaks in dialysis units to allow us to better manage this situation. In the current study, we presented patients' different clinical presentations, progression of their clinical condition, laboratory and radiological results, their illness duration and outcome during the SARS-CoV-2 infection in the period from March 2020 to July 2020 in the Hemodialysis Unit, Ain Shams University Hospitals, Cairo, Egypt. Infection affected 17.6 % of the total patients served by the hemodialysis unit (42/238 patients). 19 % (8 patients) were hospitalized, among those who presented with respiratory distress, only 1 (2.4 %) patient required ICU admission. Mortality was 19 % (8 patients). A close figure was declared by a hemodialysis center in China that used a computed tomography-based screening algorithm for SARS-CoV-2. They reported a prevalence of 17% among patients. Moreover, a large dialysis center in the United Kingdom reported that 19.6% of patients developed COVID-19 over a 6-week period<sup>(9,10)</sup>.

**Yau et al.**<sup>(11)</sup> observed different outcomes in their study where among the 11 of 237 (4.6%) hemodialysis patients with COVID-19, median age was 66 years, 6 (55%) were men. 2 (18%) patients required admission to the intensive care unit. At a median of 30 days' follow-up, no patients required mechanical ventilation or had died. **Zou et al.**<sup>(12)</sup> shared their experience during the COVID-19

pandemic from December 2019 till March 2020. They stated that the incidence of coronavirus infection in their center was 11.0% (66/602), the mortality rate 27.3% (18/66), which was much higher than the general population, even in Wuhan City (nearly 5.1%, 2574/50008).

Among patients described in our study, 28 patients (66%) had hypertension, 7(16.7 %) were diabetics, 9 (21.4 %) had ischemic heart disease, while 3 patients (7%) were tested positive for HCV Ab, with no statistically significant difference between cure and death groups. Comorbid conditions in the COVID-19 positive patients described in the study by **Zou et al.**<sup>(12)</sup>, ten of the 66 patients (15.2%) had chronic obstructive pulmonary disease, 20 (30.3%) had coronary heart disease, 9 (13.6%) had cerebrovascular diseases, 4 (6.1%) had cancer, and 4 (6.1%) had chronic liver disease.

Neither demographic data nor associated comorbid conditions were related to the outcome of the patients in the current study, unlike the laboratory results which varied significantly with the patients' outcome. This agreed in part with the results by **Rincón et al.**<sup>(13)</sup>, where they inferred that neither demographic nor lab data were associated with increased risk for SARS-CoV-2 infection.

In our study, fever, cough and dyspnea were the most common presenting symptoms (71.4, 47.6 and 35.7 % respectively) among studied patients. Other symptoms were body aches (28.6 %), and GIT

symptoms (4.8 %). On the other hand, **Zou et al.** <sup>(12)</sup> showed in their study that cough (69.7%) and fever (37.9%) were still the most common symptoms in hemodialysis patients with COVID-19. Other symptoms were fatigue (34.8%), dyspnea (16.7%), sputum production (10.6%), and diarrhea (7.6%) among others.

In the current observation, asymptomatic patients represented 7.1% (3 patients). A close figure was reported in a large study to trace close contacts of confirmed cases (206 confirmed cases) in two centers from China, the prevalence of the silent infection of COVID-19 was 5.8 % and was more likely to occur in young adults without chronic diseases <sup>(14)</sup>. Differently, a much higher percent was observed by **Rincón et al.** <sup>(13)</sup>, where 25% of patients on dialysis were asymptomatic carriers of SARS-CoV-2. 13

Age did not differ significantly between the cure and death groups, unlike sex where 75 % of the death group were females, however such a result was statistically insignificant. Clinical presentations did not differ significantly between the 2 subgroups except for respiratory distress that was significantly higher in the death group, unlike laboratory results as patients in the death group had significantly lower lymphocytic count and O<sub>2</sub> saturation on admission, in addition to a significantly higher levels of D-dimer, ferritin and CRP.

Similarly, in a study by **Zou et al.** <sup>(12)</sup>, they observed that compared with the survival group, patients in the death group had a significantly higher incidence of fever and dyspnea (37.9% vs 22.9%,  $p < .001$ ; 16.7% vs. 8.3%,  $p < .001$ , respectively). Moreover, patients in the death group had more prominent laboratory abnormalities than those in the survival group, such as leukocytosis, lymphopenia, elevated C-reactive protein levels, extended PT time, and elevated D-dimer level (all  $p < .05$ ).

All the presented patients in the current observation had characteristic HRCT finding of COVID-19 based on the CORAD classification, with most of them exhibiting findings consistent with high to very high probability compared to the cure group. This agrees with **Zou et al.** <sup>(12)</sup>, they stated that almost all hemodialysis patients with COVID-19 had characteristic CT features in the disease process, such as different degrees of ground-glass opacities, multifocal organizing pneumonia, and architectural distortion in a peripheral distribution, but the positive chest CT findings in the death group were more severe than that in the survival group at the beginning of disease.

Time from diagnosis to death was  $6.8 \pm 1.8$  days in the current study, a figure close to that by **Zou et al.** <sup>(12)</sup>.

## CONCLUSION

COVID-19 pandemic still a major health problem worldwide with significant morbidity and mortality among hemodialysis patients.

## Study limitations:

Being a retrospective study of course limited the availability of some of the patients' laboratory results if they were not performed at the time of infection. Also, not all our patients were hospitalized, so the clinical progression of the outpatient dialyzing patients was majorly obtained only during the session or over the phone.

**Conflict of interests:** The authors have no conflict of interests to declare.

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