Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

COVID-19 in dialysis patients: adding a few more pieces to the puzzle

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Maintenance hemodialysis (MHD) patients are at increased risk for coronavirus disease 2019 (COVID-19) and its complications, owing to the presence of multiple comorbid conditions. The logistical aspects within a dialysis facility further increase the risk of disease transmission.[1] Despite these obvious concerns, early reports from the epicenter of the disease—Wuhan, Hubei Province in China—suggested that the incidence of COVID-19 was lower than expected, with potentially a milder course and outcomes in MHD patients. With the expansion of the pandemic to Western Europe, more data are emerging regarding the impact of this disease on MHD patients. In this issue, 3 special reports from the UK, Italy, and Spain provide preliminary information offering some clues to the puzzle.

In a letter to the editor, Dudreuilh *et al.*[2] provide the results of serial severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) swab testing performed 7 days after a confirmed COVID-19 diagnosis in 34 MHD patients. Only 5 patients cleared the virus in less than 11 days, and by day 15, a total of 14 patients (41%) had not cleared the virus. The authors noted that it is not known whether detection of viral RNA represents the ability to transmit the virus in these patients, but there is clear precedent to continue to isolate them in the dialysis facility.

In an editorial: special report, Alberici *et al.*[3] describe their clinical experience with MHD patients cared for at 4 outpatient dialysis facilities that are part of the Brescia Renal COVID Task Force. Although 3 units tested only symptomatic patients, one unit tested all patients. In a period of 1 month, viral positivity was detected in 94 of their 643 MHD patients (15%). The positivity rates were not substantially different between the 2 screening approaches (14% vs. 16%, respectively). Patients who tested positive were either managed as outpatients (39%) or hospitalized (61%), based on disease severity as assessed by a clinician. Prominent findings in the study were the mild form of symptomatology at presentation, the high rate of overall mortality (29%), and emergence of usual risk factors for mortality and acute respiratory distress syndrome in SARS-CoV-2–positive MHD patients. In addition, although certain patients were deemed more stable and were managed in the outpatient facility, 3 of those subsequently died, and a substantial portion had significant worsening of their symptoms.

In another editorial: special report, Goicoechea *et al.*[4] describe the clinical course and outcomes of 36 patients from 2 dialysis facilities caring for 282 patients that were admitted to a tertiary hospital in Madrid based on positive reverse transcription polymerase chain reaction for SARS-CoV-2. They report a mortality rate of 30.5%, and 33% of their patients required mechanical ventilation. Although the patients were identified by a variety of symptoms on admission, the ones who had a worsening of their respiratory status, clinically or radiologically, had a much worse outcome. They further note that high lactate dehydrogenase and C-reactive protein concentrations on day 7 after admission were observed in nonsurvivors. Patients were treated with a wide range of

Editor's Note

The information about the impact of coronavirus disease 2019 (COVID-19) on maintenance hemodialysis (MHD) patients is evolving. The Editors recommend that the readers also view the letter to the editor by Dudreuilh *et al.* (see page 236) reporting the results of serial SARS-CoV-2 swabs testing performed 7 days after a confirmed COVID-19 diagnosis in 34 MHD patients. Two other special reports by Alberici *et al.* (see page 20) and Goicoechea *et al.* (see page 27) provide important information about their clinical presentation and mortality rates in MHD patients diagnosed with COVID-19. Generalizability of these preliminary data needs to be confirmed in more comprehensive studies.

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medications. Although the authors note a signal suggesting that treatment with azithromycin and corticosteroids might be associated with reduced mortality, multiple confounders, along with changes in management protocol during the observation period, preclude any firm conclusions.

Taken together, these 3 early reports provide important information regarding the clinical course of COVID-19 in MHD patients. First and foremost, although MHD patients might present with a wide range of symptom severity, the clinical outcomes, especially mortality rates, are dramatically high in this vulnerable patient population, reaching almost 30%. In the report by Alberici *et al.*[3], it is noteworthy that even in MHD patients deemed to be stable and managed as outpatients, there were those whose clinical condition abruptly worsened, leading to subsequent death. This high mortality rate is far greater than that published this year and is more consistent with what would be expected in a cohort with underlying comorbidities that are associated with poor outcomes. MHD patients also had significant pulmonary complications, with high percentages of acute respiratory distress syndrome and mechanical ventilation, suggesting that MHD patients are at very high risk of COVID-19 complications and should be managed accordingly.

The report by Dudreuilh *et al.*[2] highlights another aspect of the disease spectrum in MHD patients, namely the prolonged viremia. As noted astutely by the authors, although it is not known yet whether the persistent viremia represents the ability to transmit the virus, it does reemphasize the need for stringent oversight in management of MHD patients with COVID-19 until the relationship between presence of viral RNA in swabs and risk for transmission is further clarified.

The future implications of these preliminary reports are multiple. Given the severe course of disease and poor outcomes, it seems prudent that MHD patients be included in the high-risk populations that are continuously and repetitively tested for screening purposes, such as those that reside in nursing homes. Currently, the capability to screen subjects either with or without symptoms differs among countries and regions. However, allocating screening resources to dialysis patients is a potential opportunity to utilize these resources wisely. This approach will allow early isolation of patients with positive tests, improve staff and patient protection by minimizing potential transmission within a dialysis facility, and direct precious resources to individuals in most need.

Another interesting aspect of these reports is the wide range of symptoms in MHD patients who tested positive for SARS-CoV-2, with a significant portion being asymptomatic. It is yet unclear whether this range reflects the disease spectrum itself or a phenomenon related to underlying advanced kidney disease. The uremic state is well known to be associated with impaired immune response, which could lead to reduced fever occurrence during infection. However, other symptoms of COVID-19, such as cough, shortness of breath, and fatigue, are inherently present in MHD patients and could be underreported by most patients, potentially leading to misdiagnosis. Given the grave nature of disease in these patients, reliance on symptoms for diagnosis and management of COVID-19 could be detrimental, further highlighting the absolute need for universal testing for screening purposes in MHD patients.

Despite their informative nature, these reports must be interpreted with (some significant) caution. Most importantly, these data are descriptive and lack appropriate controls for precise estimations. For example, one cannot draw any conclusions about whether prolonged detection of viral RNA is characteristic of advanced kidney disease or merely a reflection of other patient-specific factors. It is also premature to conclude that MHD patients have a milder clinical presentation compared to individuals of the population at large who have similar clinical and demographic features.[5] Presumably, widespread universal testing in the general population and high-risk patient populations would be able to determine more reliably if such a difference exists. Despite the consistently high mortality rate and disease progression observed in the 2 studies from Italy and Spain, the actual prevalence of the disease and its diagnostic and prognostic predictors are still to be determined. It is also important to recognize that certain logistical issues might have driven a higher than expected mortality rate, such as overwhelmed healthcare systems as observed in Italy and Spain. Future, more comprehensive studies from different geographically diverse cohorts will surely provide more complete data. Finally, these studies suggest that a gunshot approach to treatment of COVID-19 was used in MHD patients. Given the small sample size, lack of appropriate control groups, and the inconsistency and

changes in treatment protocols, any conclusion about effectiveness of any of the treatment regimens should be avoided. It is also crucial to underline that these treatments should be used with great caution in MHD patients, due to their altered pharmacokinetics and toxicity.[6] On the other hand, this approach could lead to an unintended systemic exclusion of MHD patients from ongoing or future randomized trials despite the obvious urgency to include them due to the reasons mentioned above.

Overall, the authors of these early reports must be commended for their diligent and heroic work during a devastating pandemic. These data provide early clues to prevention and management strategies in MHD patients during the COVID-19 pandemic and potentially for future healthcare crises. In order to improve our responsiveness to emerging threats in the future, we undoubtedly need reliable and comprehensive scientific data on a timely basis.

DISCLOSURE

TAI is a member of American Society of Nephrology COVID-19 Response Team and chairs the Nephrologists Transforming Dialysis Safety (NTDS) Current Emerging Threats Subcommittee. TAI reports receiving honorarium from Fresenius Kabi, GmbH, Abbott Renal Care, and the International Society of Nephrology for consulting work.

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