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Understanding the Burden of the COVID-19 Pandemic for People With Kidney Disease

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Health authorities worldwide began to recognize the enormity of the coronavirus disease 2019 (COVID-19) pandemic late in the first quarter of 2020. The daunting public health implications of the pandemic for people with kidney disease has since become increasingly clear. Indeed, reports on the impact of COVID-19 in people with kidney disease have appeared at a rate unprecedented in the history of nephrology.

Related Article, p. 804

In this issue of *AJKD*, the report by Chung et al[1] provides important insights into 2 questions of supreme importance: *What is the incidence of COVID-19 in people with kidney disease?* and *What is the association between COVID-19 and death in people with kidney disease?* The investigators found that the incidence of COVID-19 in patients with chronic kidney disease (CKD) treated with dialysis was 105 per 10,000 person-weeks; in patients with CKD not requiring kidney replacement therapy (KRT), 16 per 10,000 person-weeks; and in kidney transplant recipients (KTRs), 23 per 10,000 person-weeks. Compared with patients with CKD without KRT, therefore, incidence of COVID-19 is roughly 6 times higher in maintenance dialysis patients and roughly one-and-a-half times higher in KTRs. Regarding the issue of risk of death associated with COVID-19 among people with kidney disease, the authors report that, compared with patients receiving dialysis who did not have COVID-19, the incidence rate ratio (IRR) for death in affected dialysis patients was approximately 8. Analogously, KTRs with COVID-19 had an IRR for death of 42 compared with KTRs who did not have COVID-19. (Owing to a lack of suitable studies, IRRs for CKD without KRT could not be estimated.)

Quantifying the incidence of COVID-19 and COVID-19–related death is obviously of crucial importance, yet generating insights into the relationship between kidney disease and risk of these outcomes is more complex than it first appears. If the goal is to determine the additional risks for COVID-19 and COVID-19–related death associated with kidney disease, merely comparing rates among people with kidney disease to rates in the general population may be inadequate. This is because people with kidney disease have high rates of accompanying comorbid conditions such as diabetes, atherosclerotic vascular disease, heart failure, and others that are themselves likely to confer increased risk for COVID-19 and COVID-19–related death. An early indication that kidney disease is a risk factor for COVID-19–related death emerged from the UK's National Health Service OpenSAFELY registry, an electronic health record database encompassing about 40% of patients in England.[2] The adjusted hazard ratio (AHR) for COVID-19–related death associated with maintenance dialysis (considered as a comorbidity) was approximately 3.7, with a kidney transplant was 3.5, and with CKD glomerular filtration rate categories 4 and 5 (G4-G5) was 2.5—much higher, after adjustment, than was the case for other factors such as diabetes and chronic cardiac disease (both AHRs ≤2).[2,3] Remarkably, even chronic lung disease was associated with an AHR <2. Further, data from the European Renal Association's COVID-19 Databases (ERA-CODA) suggests that *among* patients receiving maintenance dialysis with COVID-19, there was no association of diabetes, coronary artery disease—and, most surprisingly, chronic lung disease—with COVID-19–related death.[3] These findings appear to provide evidence that much, and perhaps most, of the risk of COVID-19–related death in people with kidney disease may be captured by the presence of kidney disease itself, and somewhat less by any accompanying comorbidities.

In terms of the association between COVID-19 and death in people with kidney disease, evidence from several sources generally corroborates the authors' findings of a high risk of mortality. A study from the UK Renal Registry reported that the 14-day mortality among in-center hemodialysis patients in the United Kingdom was approximately 20%.[4] Data from the ERA-EDTA registry showed that the 28-day mortality was approximately 20%—about 18-fold higher than the percentage of patients receiving dialysis who died without a COVID-19 diagnosis.[5] A study conducted in US patients receiving maintenance dialysis reported 90-day mortality at approximately 25%, or about 7-fold higher than in such patients who were not diagnosed with COVID-19.[6]

The percentage of people with kidney disease who die in the weeks and months following COVID-19, while high, are even more striking when placed in the context of other acute illnesses. In US patients receiving maintenance dialysis who are *hospitalized* with a cardiovascular event, for example, about 4.0% die during the index hospitalization and a further 4.5% of live discharges die in the ensuing 30 days.[7] Even more relevantly, in US patients receiving dialysis who are hospitalized for an infection of any type, 9% die during the index hospitalization and a further 7% die within 30 days of a live discharge.[8] Note that the COVID-19 patients in the studies described above were not necessarily hospitalized; death rates in patients sick enough to have been hospitalized with COVID-19 may well have been higher still.

While comparisons with other disease are helpful for contextualization, COVID-19 constitutes a unique case because the associated risks can, of course, be mitigated by vaccination in a way that the risks for other clinical events cannot. Data generated by the nephrology and public health communities can therefore be used to bring about policy changes, most importantly via efforts to increase access to vaccination for people with kidney disease and to support efforts to educate skeptical patients about the importance of vaccination. In the state of Minnesota, initial published data on poor outcomes in COVID-19 patients receiving maintenance dialysis was presented to the state's Department of Health in a successful effort to add patients receiving maintenance dialysis to the select list of patient groups who were to be prioritized for vaccination (K. Johansen, personal communication).

The implications of the social and legal policies adopted as a result of the pandemic must be carefully considered when interpreting epidemiologic data. Chung et al note that the COVID-19 incidence rate in patients with CKD is substantially higher than the overall global incidence rate. They suggest that this may be a result of ascertainment bias because "people with CKD are more likely to receive close healthcare monitoring than the general population." This is highly plausible, but other mechanisms may also be operative. It is also likely that people with risk factors such a kidney disease engaged in some degree of "shielding behavior"[9] and either did not seek as much health care as they otherwise would have or relied on telehealth ambulatory contacts rather than in-person encounters, as was occurring in the general population.[10] As a possible indication of this phenomenon, the overall census of US dialysis patients fell dramatically after the onset of the pandemic.[11] Indeed, the number of patients initiating treatment for kidney failure during the first quarter of 2021 fell to levels not seen since 2011, which is likely because nephrologists were avoiding initiating patients on dialysis as the pandemic raged.[12] Avoidance of care owing to fear of infection, difficulty with or concerns about using transportation (especially public transportation or services in which rides were shared with other patients), and the acute economic hardship that often strikes people with a heavy burden of chronic disease may contribute to an undercount of the number of both infections and deaths related to COVID-19.

The findings presented by Chung et al should be viewed with caution. They are frank about the relatively low certainty of evidence for their findings, and they report relatively wide 95% prediction intervals for their estimates. However, their work should be considered foundational because it leverages all known studies on this topic in their attempt to quantify the incidence of COVID-19 and COVID-19–related death in people with kidney disease. Together with other work, their findings demonstrate the dangers posed by the pandemic to people with kidney disease, thereby contributing to the chorus of voices urging public health authorities worldwide to prioritize people with kidney disease for surveillance, education, vaccination, and other public health measures.

Article Information

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