

COVID-19 and the Kidney: Another Target to Attack

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Evidence is mounting that kidneys are a target for COVID-19, and if that proves to be the case, special tactics will be required to improve patient outcomes, experts explained at the virtual European Renal Association–European Dialysis and Transplant Association (ERA-EDTA) 57th Congress.

"Patients with kidney disease are particularly vulnerable to COVID-19, as well as to complications that can arise from it," said Elion Hoxha, MD, from University Medical Center Hamburg-Eppendorf in Germany, during a press conference.

This vulnerability is likely multifactorial.

It could reflect the fact that patients with [chronic kidney disease](#) (CKD), especially those who require dialysis, and patients who have undergone [kidney transplantation](#) typically have comorbidities that caused their kidneys to fail in the first place, Hoxha said.

Plus, kidney disease and the immunosuppressive therapies used to treat it can often impair the immune system, he explained.

And just the practical logistics of patients having to visit a dialysis center three times a week, where they come into at least indirect contact with others, ups their chance of infection.

Dialysis Patients Are Hard Hit

The fact that dialysis patients are at high risk for COVID-19 was confirmed in an analysis of data from a German registry. By the end of May, about 2% of the dialysis patients had tested positive for the virus.

As it turned out, these patients had a poor prognosis, with a mortality rate of around 20%, Hoxha reported. The same high mortality rate for dialysis and kidney transplant patients is being reported in Italy, Spain, and other European countries.

In Spain, for example, 5.0% of the dialysis population treated at the Vall d'Hebron University Hospital in Barcelona has tested positive for COVID-19, compared with approximately 0.5% of the general population.

This suggests that the incidence of COVID-19 is indeed higher for dialysis patients than it is in the general population, María José Soler Romeo, MD, a nephrologist at the hospital and chair of the ERA–EDTA paper selection committee, reported at the opening of the ERA-EDTA conference.

The COVID mortality rate among dialysis patients at this one center was 24%, which is similar to the rates seen in an analysis of the Spanish COVID-19 Dialysis/Transplantation Registry: 27% for hemodialysis patients and 23% for kidney transplant patients.

In Italy, more than 20% of patients who died from COVID-19 had CKD, and nearly 2% of these were dialysis patients.

As of June 1, data on 1073 patients with COVID-19 and kidney failure from 26 countries had been entered in [ERACODA](#), the ERA–EDTA COVID-19 database established in March. At 28-day follow-up, 21% of kidney transplant patients had died, as had 25% of dialysis patients.

ERACODA also showed that the COVID-19 mortality rate was 45% for transplant patients and 53% for dialysis patients admitted to the intensive care unit, reported Luuk Hilbrands, MD, PhD, from the Radboud University Medical Center in Nijmegen, the Netherlands, during the press conference.

COVID-19 and Kidney Function

There is some evidence that COVID-19 interferes with kidney function itself, as [previously reported](#) by *Medscape Medical News*. There is also a clear signal, although not yet proven, that kidney function is not normal in patients COVID-19 who are admitted to the hospital.

In an [early report](#) from China, 44% of COVID patients admitted to a tertiary teaching hospital had [proteinuria](#) and 26.7% had hematuria. Also high was the prevalence of elevated serum [creatinine](#), at 14%, of elevated blood [urea](#) nitrogen, at 13%, and of

estimated glomerular filtration rate (eGFR) below 60 mL/min per 1.73 m², at 13%.

It is not clear whether these urine abnormalities are a sign that patients will develop more severe COVID infection or whether they are at risk for specific complications, but if they are, "these patients would have to be checked more intensively and treated for complications to try to prevent worse outcomes," Hoxha told *Medscape Medical News*.

The risk for [acute kidney injury](#) (AKI), even in COVID patients who have normal kidney function at hospital admission, is also very high.

The progress of 5449 patients admitted to one of 13 hospitals in and around New York City between March 1 and April 5 was [assessed](#) by a team from the Northwell COVID-19 Research Consortium.

There were no transplant or dialysis patients in the study cohort, yet even without compromised kidney function, more than 36% of the patients developed AKI, 14% of whom required dialytic support. In addition, almost 90% of the patients who required [mechanical ventilation](#) developed AKI, and almost one-quarter of these needed dialysis.

"The fact that patients require mechanical ventilation is an indication that they are sicker than those who do not, but we don't know if they develop AKI more often because they are sicker," Hoxha said.

"What we can say is that AKI occurs very frequently among patients with COVID-19, that it occurs early, most in temporal association with respiratory failure, and that it is associated with a poor prognosis," he added.

In a [French study](#) of 71 patients with severe lung injury related to COVID-19, 11% had already developed AKI by the time they were admitted to the intensive care unit (ICU).

At a median follow-up of 17 days, 80% of those patients had developed AKI, with roughly equal numbers of stage 1, stage 2, and stage 3 disease. Of the patients with AKI, 18% required dialysis and 10% died.

"Kidney involvement in critically ill COVID-19 patients was very common, with AKI lasting longer than 3 days in most cases, and almost one in five of those having to be dialyzed," investigator Sébastien Rubin, MD, from Bordeaux University Hospital in France, said in a statement.

This French study "underscores the importance of follow-up nephrological care of patients after discharge from hospital, [as] it is well known that AKI patients have a higher risk of developing CKD and ESRD later on," said Alberto Ortiz, MD, PhD, from the School of Medicine at Universidad Autonoma de Madrid, who is editor in chief of the *Clinical Kidney Journal*, in the same statement.

High AKI Risk

Why are patients with COVID-19 at such high risk for AKI?

One possibility is that the virus directly attacks the kidney. An [autopsy series](#) of 27 patients who died from COVID-19 showed that the more coexisting conditions, the greater the likelihood that SARS-CoV-2 would be found in the kidneys, even in patients without CKD.

And an examination of viral load in the kidneys showed that SARS-CoV-2 preferentially targets glomerular cells.

"On the basis of these findings, renal tropism is a potential explanation of commonly reported new clinical signs of kidney injury in patients with COVID-19, even in patients with SARS-CoV-2 infection who are not critically ill," the investigators conclude.

Hoxha said he agrees, cautiously, noting that "we don't yet know whether viruses in the kidney are directly damaging the kidney, though this is a possibility."

"However, the fact that the virus affects the glomerular cells in particular, which are responsible for the filtration of the urine, is consistent with findings showing that patients with COVID-19 have abnormalities in their urine early in the course of the disease," he said.

In fact, this seems to have been confirmed in a [study](#) showing that proximal tubule injury can cause Fanconi syndrome, the hallmark of which is increased excretion of substances in the urine.

In the analysis of 42 patients hospitalized with COVID-19, 75% of developed incomplete Fanconi syndrome at a mean follow-up of 19.7 days. The most frequent features were proteinuria (in 88% of patients), phosphate loss in urine (55%), increased uric acid excretion (43%), and glucosuria (30%).

Fanconi syndrome also preceded severe AKI in 88% of patients, the investigators report. Seven of the 42 patients died, six of whom were in the ICU with AKI.

Proximal tubular cells express the ACE2 cell surface receptor that SARS-CoV-2 uses to invade host cells and, thus, serve as a specific target for SARS-CoV-2, the investigators explain.

The presenters disclosed no relevant financial relationships.

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