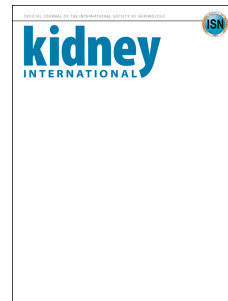


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Managing the COVID-19 Pandemic: International Comparisons in Dialysis Patients

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Nations around the world are working to find the best ways to manage the ongoing COVID-19 pandemic. They are pairing efforts to detect viral infection, prevent transmission and manage infected patients, with knowledge of previous seasonal coronavirus outbreaks and growing experience with COVID-19 to craft best-evidence guidance. Recent data show that as many as 25% of infected patients remain asymptomatic, and viral shedding may begin up to 48 hours before symptoms appear. Worldwide regulatory authorities remain committed to guidance that is clearly evidence-based. As new information appears, updated guidance produces many similarities, and some differences in these guidance documents, in part deriving from regional and population differences. We here review guidance for detecting and mitigating COVID-19 infections in dialysis patients, noting where there is universal agreement and where there are differences.

Preventing epidemic spread of infection requires early recognition of infection, isolation and meticulous tracking of contacts. Reverse Transcriptase Polymerase Chain Reaction (PCR) test kits developed early in this pandemic in Berlin, and deployed by the World Health Organization, assisted many Asian and European countries in limiting infection and “lowering the peak” of infected individuals over time. Limited availability and slow deployment of such test kits in places like parts of the United States and Italy hindered efforts to prevent epidemic spread, with rapidly rising numbers of patients overwhelming parts of the health care system. Once the pandemic was established, efforts switched from prevention to mitigation – with efforts to reduce person-to-person viral transmission and protect the most vulnerable parts of the population. Key features of mitigation include patient and healthcare worker education,

implementation of strategies to prevent further spread such as social distancing, widespread use of facemasks for patients with suspected or confirmed disease to limit transmission, and appropriate personal protective equipment (PPE) for healthcare workers and others who have direct contact with COVID-19 infected patients.

In-center hemodialysis patients are particularly vulnerable to COVID-19 for two reasons. First, while the world's population shelters at home to avoid contact with infected individuals, in-center dialysis patients must come together for hours thrice weekly and travel to and from these treatments, increasing possible exposure. Second, ESKD patients who acquire the infection are at higher risk of complication and death due to older age and common comorbidities that increase mortality risk, including diabetes, heart disease, obesity and hypertension; and in part because ESKD patients may have impaired immune systems. In order to provide information on how to best protect these patients from COVID-19, we examined the guidance provided by the CDC in the US, the European ERA-EDTA, Italy and India (1-5), noting where they provide similar guidance and where there are differences (Table 1 and 2).

1. Education of patients and healthcare workers (HCW): All guidance documents emphasize the basics of hand and respiratory hygiene, coughing etiquette and use of PPE.
2. Screening and recognition of symptoms: All guidance documents advise screening patients for most common symptoms including fever, new cough or dyspnea. There is less uniform screening for sore throat, myalgia, chills, fatigue, conjunctivitis, diarrhea and rhinorrhea. There is also consistency in screening for travel to endemic areas, asking

patients to call ahead if they have symptoms of infection or potential exposure and establishing a triage protocol prior to patient arrival at the facility. All advise masking patients prior to entering the facility and throughout the treatment, and designating a separate waiting area for screening or waiting in a personal vehicle for screening, and treating patients under investigation (PUI), those with moderate or high likelihood of disease before testing confirmation, as potentially positive.

3. PPE: All guidance documents advise use of surgical masks for patients and HCW. While in the US, N95 or higher-level respirators are advised if available, elsewhere N95 masks are advised only for aerosol-generating procedures. Surgical masks are otherwise advised for all HCWs including those cleaning machines. All advise disposable gloves, and most advise face shields or goggles. Some suggest hair covers and shoe covers. In the US, CDC advises PPE competency evaluation for staff, and auditing compliance with PPE and hand hygiene, advice not documented in other guidance documents.
4. Managing symptomatic or COVID-19 positive patients: This is one area where there are differences in guidance around the world, although most guidance is similar. All guidance documents advise cohorting multiple confirmed or PUI cases and assigning designated staff to care for them. The majority suggest that supplies be positioned close to hemodialysis chairs and nursing stations to ensure adherence to hand and respiratory hygiene. Routine cleaning and disinfection procedures are recommended by all guidance documents. For stable PUI or confirmed coronavirus patients, some countries advise hospitalization and admission to an airborne infection isolation room (AIIR). The US CDC specifically states that an AIIR is not needed in the outpatient management of

COVID-19 dialysis. While Asian guidance documents advise PUI be admitted to an infectious disease ward, others advise that PUI and confirmed positive patients can be dialyzed in the outpatient unit, if clinically stable. This is to be performed in a designated COVID-19 facility, dialysis shift, an isolation room within a facility that treats non-infected patients, or in a separate room with the door closed. If none of these are available, then the advice is to dialyze these patients at the end of the line or corner position of the facility, with separation from other patients by 6 feet in all directions. For ill patients with progressive dyspnea, organ dysfunction or ARDS, all guidance documents advise hospitalization.

5. Resource utilization: The US CDC discusses supply chain management, preserving and prioritizing PPE, extended use of eye and face protection, recycling of PPE and alternate PPE. They also discuss sick leave policy, cross-training and back-up plans, staff return to work guidelines and after return to work guidance. These recommendations are not provided in publications from other countries although they may exist locally. Telemedicine is widely used worldwide, when technically possible, to minimize face-to-face contact.
6. Home dialysis: There is consistency that home hemo- and peritoneal dialysis patients continue care at home, and HCW use telemedicine or other electronic systems for clinical management, with home visits if necessary. Implementation of these recommendations are likely to be resource and geography dependent.
7. Some guidance documents advise clinicians to consider reducing the frequency of hemodialysis sessions from three to two times weekly in patients who tolerate this

regimen. This would reduce the need to travel by car/ambulance in the event of a shortage of these means of transport, decrease the risk of infection exposure during transport, and reduce the likelihood of dialysis patients spreading infection in the dialysis unit or the hospital. There is consensus to implement reduced individual dialysis in extreme shortage crisis conditions.

Why might regional difference in guidance exist? In countries where early recognition of endemic infection spread was initiated, aggressive steps to identify and isolate COVID-19 patients and identify their contacts permitted a prevention plan that limited their local epidemic. In China, recognition of infection was initially slow in Wuhan, but aggressive preventive measures in other parts of the country were probably successful. While some European countries have been successful in containment and prevention, others were less successful and focused on mitigation strategies. Availability and use of diagnostic tests have been major determinants of prevention, best practice and mitigation. In the US, the limited and slow dispersal of testing capacity has hindered mitigation efforts. Availability and utility of serologic tests may allow accurate identification of patients who have had COVID-19 and developed immunity, including those who are asymptomatic as well as healthcare workers who are no longer at risk, hence allowing them to return to work.

Despite its major unwanted adverse consequences, this major health crisis has perhaps taught us major lessons. Some of these learned so far include:

1. Many people have previously warned that world-wide preparedness for previously unknown epidemic illness is inevitable, and that we must prepare now for this likelihood. This warning has previously received little attention outside Asia. We now know the importance and priority of such readiness.
2. Early recognition of new infectious diseases requires a new discipline, awareness and vigilance. This will require a worldwide effort to record and report symptom clusters, changes in hospitalization, morbidity and mortality rates, and a 21st century epidemiologic registry. Analytic tools can be used to develop new algorithms to assess changes in population health. A new discipline of worldwide surveillance and early recognition will allow countries to contain infection and prevent pandemics.
3. If we have a reactive approach, responding to spreading infection rather than anticipating and containing it, we will fail. A well-designed proactive approach that includes early case identification, careful contact mapping and isolation, and swift implementation of protocols will permit infection containment and substantially reduce population exposure, morbidity and mortality.
4. If implemented appropriately, infection prevention works. This can be observed in countries like Taiwan, New Zealand and Singapore. Information to date also suggests a limited in-facility transmission in dialysis patients, most likely related to an infection prevention culture that has been imbedded in the care of these vulnerable patients.
5. Once a pandemic is established, aggressive mitigation techniques such as social distancing, testing for specific organisms and serologic evidence of infection and immunity are critically important.

6. Equipment and personnel shortages are predictable during a pandemic. National and perhaps world-wide preparedness for this will require new flexible algorithms, coordinating and sharing resources. The 20th century model of independent, sometimes competing healthcare systems using just-in-time ordering to minimize inefficient shelving of supplies, will need 21st century updating to allow international stockpiling of critical equipment with flexible plans to anticipate needs and quickly move them as needed.
7. To prepare for the next pandemic, a multinational research group should be assembled to investigate all aspects of the organism and the host response, including the source reservoir, genetics, host response, vaccination and more. Regional puzzles need investigation – for example why in New York is there a predominance of African Americans affected by COVID-19 and complications leading to death? Frameworks for international trials of vaccines and medications should be prepared and ready to dispatch.

As the COVID-19 pandemic spread around the world, lessons learned from its challenges have shaped the guidance offered in each region. It is striking that this guidance, as it matured around the globe, has largely come together in uniformity. If we are to learn from this experience and be better prepared for the next epidemic challenge, it will be wise to think globally, act locally and create an international structure to anticipate and guide best practice.

Table 1: A comprehensive list of approaches to prevention and control of COVID-19 infection in dialysis facilities.

- **EDUCATION**

Education of patients and related individuals

- 1) Hand and respiratory hygiene and coughing etiquette
- 2) Use of masks
- 3) Basic signs and symptoms associated with the disease
- 4) Place signs to direct symptomatic or exposed patients to a designated screening location in an appropriate space

Education of healthcare workers

- 1) Training for appropriate use of PPE
- 2) Re-emphasis of universal precautions for infection control in the facility

- **SCREENING**

- 1) Instruct all patients to call ahead
- 2) Temperature check for all patients upon arrival and departure
- 1) Implement triage protocol for suspected COVID-19 patients
- 2) Transfer sicker patients to emergency departments
- 3) Perform screening rtPCR test in all dialysis patients
- 4) Prioritize testing of dialysis personnel

- **MANAGEMENT OF PATIENTS WITH SYMPTOMS OR ILLNESS**

Administrative preparedness

- 1) Create back-up lists if staff become sick
- 2) Create COVID-19 teams
- 3) Implement workflow to protect non-working HCWs from potential exposure to (Healthy back-up)
- 4) Cross-train staff when applicable

Transportation

- 1) Personal transportation: Use, fixed route, no public, driver mask
- 2) EMT/Ambulance: CDC guidance (

Facility workflow

- 1) Define separate area and shift for patients with symptoms (COVID-19 positive section)
- 2) Separate all COVID-19 positive patients 6 feet in all directions from each other
- 3) PPE utilization
 - a. Provide all patients surgical mask
 - b. Use of eye and face protection for management of suspected or positive patients
- 4) Separate medical equipment for patients with suspected or positive disease
- 5) Maintain routine cleaning and disinfection procedures

OTHER RECOMMENDATIONS

Clearance of recovered patients

- 1) Negative rtPCR test
- 2) Resolution of symptoms

Return to work for recovered HCW

- 1) Best-evidence guidance using timing after symptom cessation, negative PCR testing and serologic testing

Routine care for dialysis patients

- 1) Minimize face to face physician rounding
- 2) Distance HCWs during team rounds
- 3) Consider telehealth for care planning
- 4) Prioritize access surgeries and procedures
- 5) Consider decreased frequency during peak periods

Table 2: Comparison of COVID-19 guidance provided at different geographic regions in the world. The data are excerpted from available publications and is not intended to be inclusive of all available local documents. * **US guidelines are based on CDC and published recommendations to date; X indicates availability of a recommendation that is similar across different regions; ^ Limited guidance from CDC; N/A: Not available; NSG: No specific guidance; RS: Region specific with different recommendations**

	US*	Europe	ASIA/OTHER
EDUCATION			
PATIENTS			
Basic hygiene and disease education	X	X	X
HEALTH CARE WORKERS			
PPE training and evaluation	X	N/A	N/A
SCREENING			
Symptom check upon arrival	X	X	X
Temperature check upon arrival and departure	X	X	X
Screening diagnostic test in all dialysis patients	NSG	NSG	NSG
MANAGEMENT			
ADMINISTRATIVE			
COVID-19 Teams	X	X	X
Back-up Lists	X	N/A	N/A
FACILITY WORKFLOW			
Dedicated space and shift	X	X	X
Surgical Facemask to ALL patients	X	X	X
Routine cleaning and disinfection procedures	X	X	X
SUPPLY CHAIN			
Recycling of PPE	X	X	N/A
OTHER RECOMMENDATIONS			
TRANSPORTATION	X^	NSG	NSG
RETURN TO WORK FOR HCWs	X^	NSG	NSG
CLINICAL MANAGEMENT of PUI or INFECTED PATIENTS	RS	RS	RS

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