



Coronavirus Disease 2019 (COVID-19)

Information for caregivers and health care personnel managing children with renal diseases



Drawing by a child in ESRD

Indian Society of Pediatric Nephrology

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The document is based on current information on COVID-19 and will be updated as more facts are available.

The coronavirus outbreak is a rapidly evolving pandemic, placing unprecedented strain on health-care systems. COVID-19 infection presents challenges for management of children with renal disease especially those receiving immunosuppressive medications, including renal transplant recipients, those with CKD or undergoing dialysis. Our preparedness for managing this vulnerable group of children is the need of the hour.

The purpose of this document is to provide guidance to caregivers and health care personnel involved in management of children with renal diseases to ensure their well-being, while protecting staff from infection. Various guidelines and policies released by the Ministry of Health and Family Welfare (MoHFW) and international professional organizations have been used in preparation of this document. We thank the members of the writing committee and advisory board for bringing out this document in very short time. The standard process for guidance development was not followed due to the rapidly evolving situation in the country.

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General Information

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which chiefly affects the respiratory tract. The virus can also affect other organs such as the kidneys, heart, intestines, blood and nervous system. The disease has spread globally since identification of the first case in December 2019. The World Health Organization (WHO) named the illness as coronavirus disease 2019 (COVID-19) and declared it as a public health emergency and later a pandemic.

The disease is contagious with human-to-human transmission *via* droplets from coughing, sneezing or direct contact. Transmission through feces has also been reported. While COVID-19 has an incubation period of 14 (usually 3-7) days, infection may be transmitted even during this period. COVID-19 is a flu-like illness, which in a proportion may progress to pneumonia, acute respiratory distress syndrome (ARDS), and complicated by sepsis, septic shock and multiorgan failure.

Epidemiology

The impact of the disease due to the novel coronavirus, SARS-CoV-2, COVID-19 has been widespread, with 213 countries and territories around the world reporting a total of 16.2 million cases with 100,000 deaths [1]. Children have accounted for 1-5% of diagnosed patients and are less likely to become severely ill or die compared to adults [2]. In a series from China, 13% virologically confirmed patients had asymptomatic infection. Only 5% symptomatic children had dyspnea or hypoxemia, and 0.6% progressed to ARDS or multiorgan dysfunction [3]. While the severity of illness in children is less compared to adults, preschool children and infants have severe clinical features than older children. In India, the total number of cases on 12 April 2020 was 8356 with 273 deaths [4]. Of confirmed cases, 80 were children with one death [5]. Cases of COVID-19 in India are presently related to travel and local transmission from imported cases to their contacts and from hotspots. In adults, the chief risk factors for mortality are older age, presence of hypertension, cardiovascular diseases, diabetes, chronic respiratory diseases, and malignancy [6].

Are patients with kidney disease, including those receiving immunosuppressive agents, those on dialysis & transplant recipients at higher risk for COVID & poor outcomes?

Comorbidities associated with mortality during COVID-19 infection are common in patients with CKD, and those on maintenance dialysis. Patients with advanced CKD are often malnourished and fragile and undergo maintenance dialysis in units where several individuals are treated at the same time, increasing the risk of infection. However, there is no evidence that patients with chronic kidney disease (CKD), especially those on dialysis, transplant recipients or receiving immunosuppressive therapy are at higher risk for COVID-19.

Reports from China suggest a less severe course of the disease in dialysis compared to kidney transplant patients, but also compared to children without kidney disease. At a dialysis center in Renmin Hospital, Wuhan (China), 37 of 230 patients on hemodialysis and 4 of 33 dialysis staff showed COVID-19 infection over 4-weeks [7]. Seven patients died, of which 6 had COVID-19 infection. The deaths were reported as related to cardiovascular etiology, and not directly to the infection. In a report from Brescia 20 transplant recipients with COVID-19, 5 died, 4 were critically ill and 3 completely recovered. Similarly, among 21 hemodialysis patients hospitalized with COVID-19, 5 patients died while 4 completely recovered [8]. In a recent report from a single center in Italy, among 20 kidney transplant patients admitted for COVID-19 pneumonia, 20 % required critical care and 5/20 died [9].

Children with CKD especially stage 4-5, those on dialysis or receiving immunosuppressive medications are considered immunocompromised. However, in Lombardy (Italy) that reported more than 8000 patients with COVID-19, none of the transplanted or dialyzed children were infected [Personal communication: Prof.G. Montini, Pediatric Nephrology Dialysis and Transplant Unit, Milano]. Three of 200 liver transplant recipients in Bergamo were positive for COVID-19, but none developed clinical pneumonia [10].

Clinical Features of COVID-19 Infection

Chief symptoms at onset of the illness are fever, dry cough and difficulty in breathing; other symptoms include expectoration, headache, hemoptysis, diarrhea and lymphopenia (**Fig. 1**).

Diagnosis of COVID-19 Infection

The diagnosis of infection is based on detecting nucleic acid of virus using real-time reverse transcriptase polymerase chain reaction (rRT-PCR) on nasopharyngeal swabs and/or bronchioalveolar lavage.

Following are currently approved criteria for testing patients for COVID-19 [11]:

- All symptomatic children with contact with laboratory confirmed cases or hospitalized children with severe acute respiratory illness (fever, cough, shortness of breath)
- Asymptomatic direct and high-risk contacts of a confirmed case (should be tested once between day 5 and day 14 after contact).
- All symptomatic children with fever, cough, sore throat, runny nose from hotspots/cluster (as per MoHFW) and in large migration gatherings/ evacuees centres within 7 days of illness [after 7 days IgM, IgG based rapid antibody test and if negative, rRT- PCR]

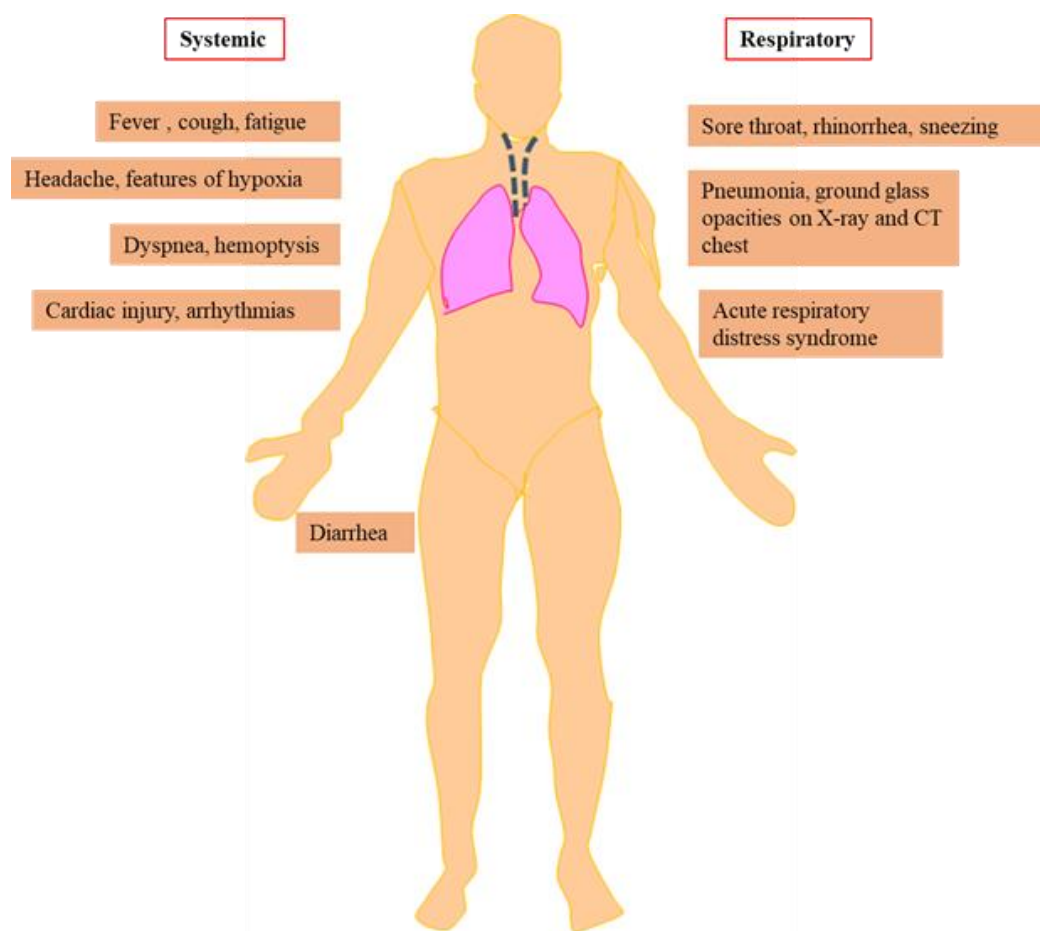


Fig 1: Clinical features of COVID-19 in children

Precautions for Caregivers & Patients

Caregivers refers to parents/guardians taking care of medical and personnel needs of children.

Patients with CKD, those on immunosuppressive medications and transplant recipients, and their caregivers should follow appropriate advice to reduce the risk of getting sick (**Fig. 2**).

Self-isolate and stay at home to minimize contact between people; avoid non-essential travel.

Wash hands frequently with soap and water for 20 seconds. An alcohol-based hand sanitizer with 70% alcohol may be used instead. If hands are dirty or soiled, do not use an alcohol-based sanitizer, but wash hands with soap and water.

While coughing or sneezing, cover nose and mouth with handkerchief or paper tissue. If either is not available, cough into the flexed elbow. Dispose tissue immediately after use and wash hands.

Refrain from touching face, mouth, nose and eyes. To the extent possible, avoid touching commonly touched surfaces in public places, e.g. elevator buttons, door handles, handrails and handshaking with people. Use tissue or your sleeve to cover your hand or finger. Stay at least 1-meter away from those coughing or sneezing.

Regularly monitor body temperature

Avoid crowded places and gatherings, even after the period of lockdown

Use masks (3-layered mask): If a patient develops cough or fever; visiting healthcare facility including dialysis units; contacts of suspect/confirmed cases undergoing home care. A link to the correct procedure of wearing a 3-layered mask and its disposal is provided [12].

Avoid close contact with people who have fever, cough, sore throat or shortness of breath.

During lockdown, ensure at least 4-weeks stock of medications at home.

Contact by phone or email if you are sick or develop fever ($>37.8^{\circ}\text{C}$), cough, shortness of breath with or without runny nose (rhinorrhea), muscle aches and chills.

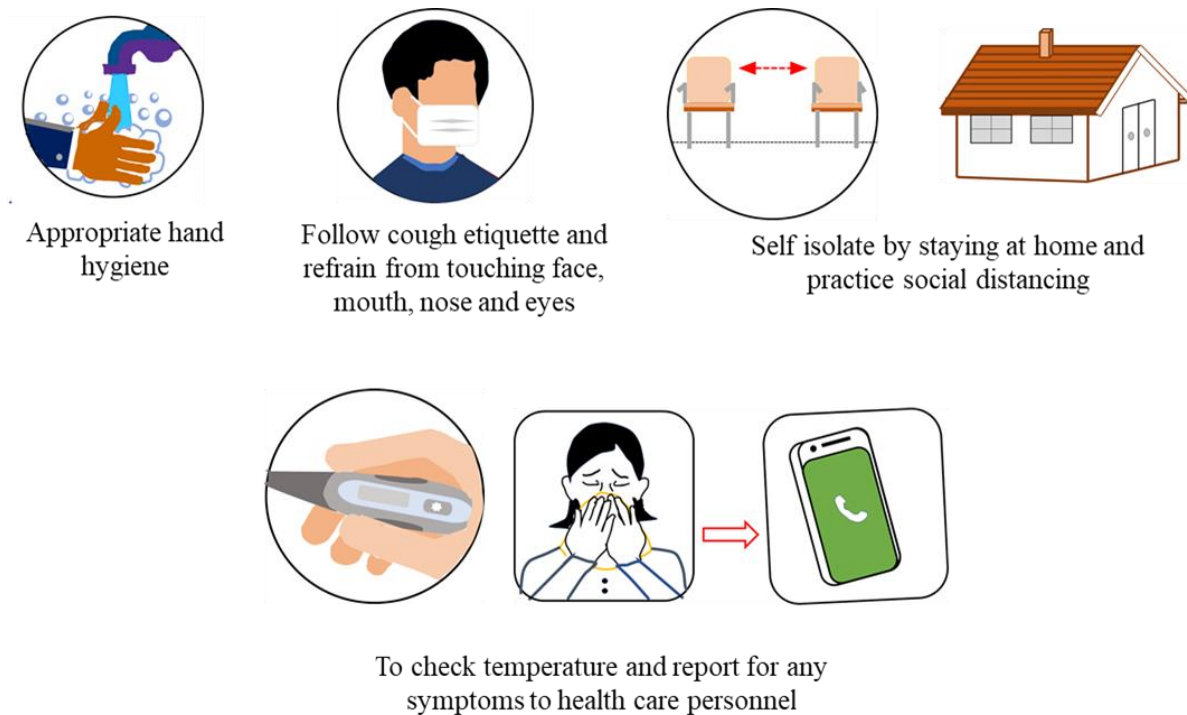


Fig. 2. Steps to reduce risk of infection with novel coronavirus

Information for Health Care Personnel

Health care personnel refers to all who are directly related to provision of health care services.

All staff should receive training in knowledge about COVID-19, and local institutional and national protocols for evaluation and management [13].

Doctors, dialysis nurses and technicians must follow guidelines for infection prevention and control and adhere to national protocols for identifying and reporting of suspected patients of COVID.

Communicate with patients and their caregivers about the situation, need for self-isolation, and hand and respiratory hygiene. Both unnecessary panic and non-disclosure of seriousness of the situation may cause anxiety and stress. Simple strategies may be employed to support the mental well-being of children and their families and mitigate anxiety and stress [14].

Staff should help minimize hospital visit by patients and their families, using audio or video consultation and follow teleconsultation guidelines [15].

Doctors or nursing staff taking care of dialysis of COVID-19 patients should not take care of non-COVID-19 patients in dialysis unit and avoid meeting friends, colleagues, staff working in non-COVID units. In case unavoidable, doctors or nursing staff should use a facemask while meeting.

Members of the medical-nursing staff must self-monitor their health and report to their superiors, if having symptoms.

Medical, nursing and technical staff should be aware about the utility of personal protection equipment (PPE) while treating patients with suspected or positive COVID. Few staff members in the dialysis unit should be trained in donning and doffing of PPE [16].

Doctors, dialysis nurses and technicians should stagger duties in order to reduce exposure to infection and maintain a reserve force that could be deployed for hospital management of patients with COVID-19 when the need arises [17].

Patients on Immunosuppressive Therapy

Clinical practice and management of COVID-19 patients with kidney disease is evolving. Doctors should therefore stay updated and follow specific developments in the field.

Patients receiving therapy with the following agents should be considered immunosuppressed:

Corticosteroids (prednisolone, methylprednisolone, dexamethasone)

Calcineurin inhibitors (tacrolimus, cyclosporine)

Mycophenolate mofetil, azathioprine

Cyclophosphamide

Rituximab

According to the British Association for Pediatric Nephrology, patients who have received plasma exchange in the preceding 6-weeks are also considered immunosuppressed [18].

Children on immunosuppression are considered high risk, especially those

- i. Receiving intravenous (IV)/oral cyclophosphamide, or rituximab currently **or** within the last 6-months
- ii. Received prednisolone at a dose $\geq 20\text{mg}$ daily for >4 weeks within last 6-months
- iii. Received prednisolone $\geq 5\text{mg}$ daily for >4 weeks with one or more immunosuppressive agents within last 6 months

We suggest the following:

For Caregivers

Patients and their caregivers should follow the guidelines listed in: ‘Precautions for caregivers & patients with renal diseases’, above.

Dose of immunosuppressive medications should not be changed, since the risk of disease flare may be higher and more dangerous than the threat posed by COVID-19.

Advice of your doctor should be sought before changing any medications; self-medication is detrimental to the child’s health

Avoid visiting hospitals for non-emergency purposes. You are advised to contact your healthcare provider over the phone, email or WhatsApp for any concerns.

Avoid public transport to visit hospital.

Stocking up on non-perishable food supplies, and ~4weeks supply of medications is prudent during the lockdown.

For Health care workers

Defer patient visits to the hospital. Replace outpatient consultation visits with video or telephone consultations. The decision to advise physical visits to the hospital should be based on audio/video consults.

Decisions regarding initiating immunosuppressive therapy in newly diagnosed patients with glomerulonephritis should be based on disease severity, renal histology, blood creatinine, severity of proteinuria and co-morbidities, and balancing the risk *versus* benefits of therapy. For children with asymptomatic or low-grade proteinuria and normal renal function, salt restriction, blood pressure control and use of an angiotensin receptor blocker (ARB) may be considered until the pandemic is over [19].

Consider deferring maintenance doses of IV cyclophosphamide or rituximab by few weeks in children in sustained remission and low risk of relapse.

Renal biopsy

Prioritize among patients with indications for renal biopsy. Perform biopsies that are necessary, and have therapeutic implications, *e.g.*, suspected allograft rejection, rapidly progressive glomerulonephritis, small vessel vasculitis, interstitial nephritis.

Nephrotic syndrome

The first episode and relapse of nephrotic syndrome should be treated promptly with standard dose of prednisolone, as under normal circumstances. Delayed initiation of steroid therapy might result in higher risk of complications associated with anasarca and bacterial infections. Therapy with prednisolone may be modified, based on review of urine protein excretion, through teleconsultation, video consults or WhatsApp.

Children on angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARB)

SARS-CoV-2 binds to the SARS-COV receptor, angiotensin converting enzyme (ACE) 2 for entry into target cells, suggesting an increased ability of the virus to enter the lungs in patients on ACE inhibitors or ARBs [20]. While there is debate regarding safety of inhibitors of the renin-angiotensin-aldosterone axis, no studies have evaluated their effects on severity of

illness or mortality in COVID-19. Hence, we recommend continuing ACE inhibitors or ARB in children who are already receiving them [21]. Abrupt discontinuation in patients taking ACE inhibitors or ARB for hypertension may lead to uncontrolled hypertension, and its consequences.

Hydroxychloroquine (HCQ)

Therapy with HCQ should continue in patients who are already receiving the medication (e.g., systemic lupus). Risk of depleting stock of HCQ need to be considered and adequate medication for 2-4 weeks need to be kept at home.

The National Taskforce for COVID-19 recommends prophylaxis with HCQ against coronavirus infection for selected individuals: (i)Healthcare workers involved in care of suspected or confirmed patientswithCOVID-19; (ii)Household contacts of laboratory confirmed cases [22]. We suggest that HCQ not be used for prophylaxis in children <15 years old. In children with CKD stage V and those on dialysis, the dose should be reduced by 50%. Caregivers and the patient should be informed about the rationale of therapy, and adverse effects.

Managing patients on immunosuppression with suspected or confirmed COVID 19

Children on immunosuppression may present with mild symptoms but have high risk of deterioration and require hospitalization for further evaluation and monitoring. Early identification of severe pneumonia and severe acute respiratory illness (SARI) is important as it allows prompt admission to a designated hospital ward or intensive care unit, and initiation of appropriate treatment.

Patient suspected of having COVID-19 infection should be shifted to the isolation facility or designated COVID ward/hospital as soon as possible.

An approach to management of a child on immunosuppression with respiratory symptoms is summarized in **Fig.3**. However, there is no specific guidance on the precise modification in immunosuppression in these patients.

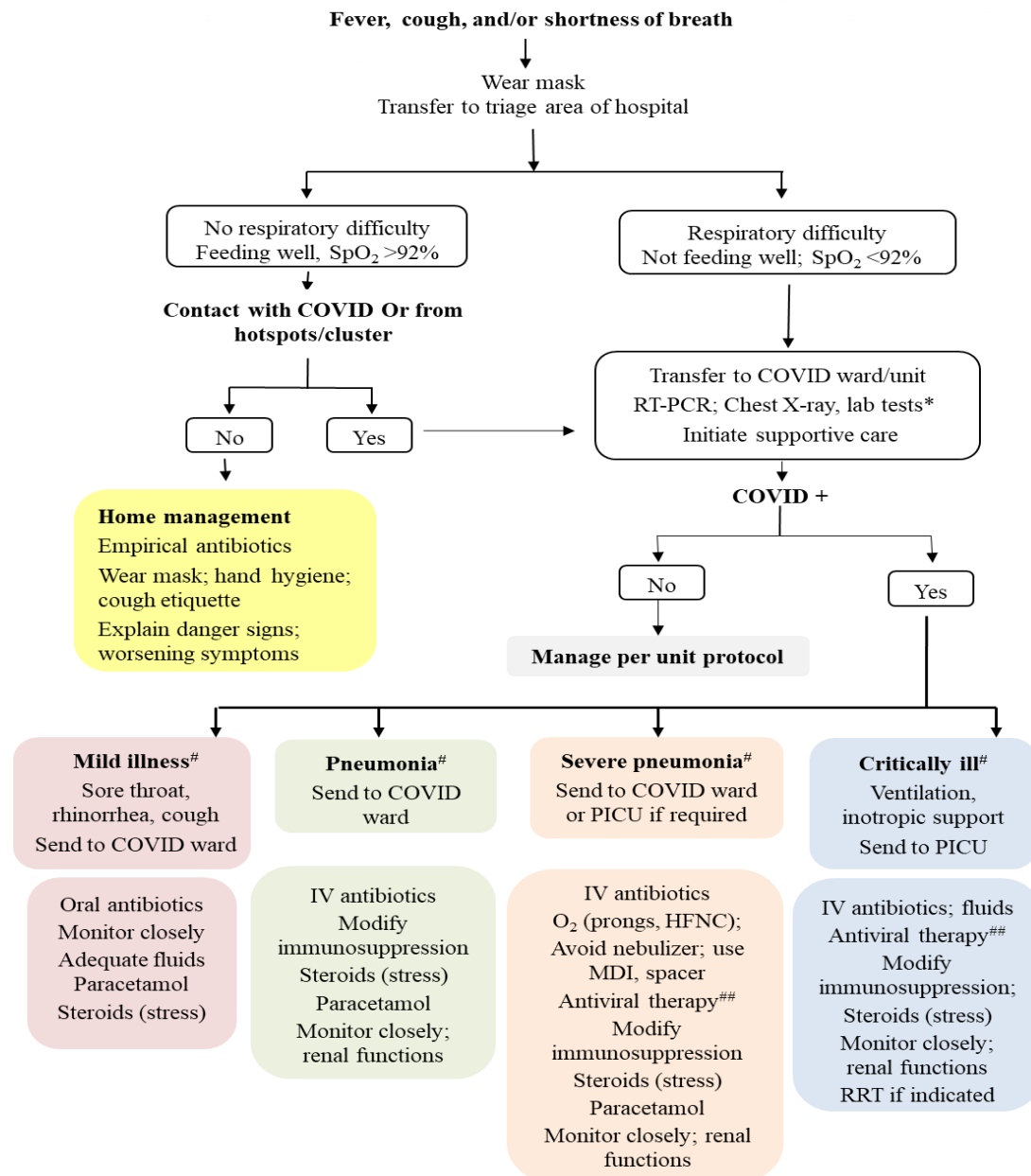


Fig 3: Triaging and management of child on immunosuppression or with chronic kidney disease

HFNC High flow nasal canula , RRT Renal replacement therapy

***Testing:** Nasopharyngeal, posteriorpharyngeal swab; endotracheal aspirate or BAL:RT-PCR for COVID-19 Evaluate with blood counts (CBC); renal and liver function tests; coagulogram, D-dimer, fibrinogen; C-reactive protein; chest radiograph; blood culture

Non-severe pneumonia: Cough or difficulty breathing with fast breathing (<2-months: ≥ 60 ; 2–11 months: ≥ 50 ; 1–5 years: ≥ 40 breaths per minute); and no signs of severe pneumonia. **Severe pneumonia:** Cough or difficulty in breathing, with at least one of the following: (i) central cyanosis or oxygen saturation (SpO₂) <90%; (ii) severe respiratory distress (grunting, very severe chest indrawing); (iii) signs of pneumonia with one danger sign: inability to breastfeed/drink, lethargy/unconsciousness, or convulsions. Signs of pneumonia: chest indrawing, fast breathing (<2-months: ≥ 60 ; 2–11 months: ≥ 50 ; 1–5 years: ≥ 40 breaths per minute).

Critically ill: Features of acute respiratory distress syndrome; shock

LPV/r - Lopinavir/Ritonavir dose is 10 mg/2.5 mg per kg BD for maximum 14 days (maximum 400 mg/100 mg BD). Symp LPV/r 80 mg/20 mg per ml; Tablet LPV/r 100 mg/25 mg; Tablet LPV/r 200 mg/50 mg ; **HCQ - Hydroxychloroquine** 7-8 mg/kg/dose BD for day 1; 7-8 mg/kg once a day from days 2-6; avoid concomitant azithromycin, since can lead to arrhythmias. (Recommendations based on ICMR guidance. Dose for children is extrapolated from that recommended in adults)

Chest X-ray showing bronchiolitis (hyperinflation, no consolidation), or lobar consolidation; lymphocytes $>2500/\text{mm}^3$, neutrophil to lymphocyte ratio $<3:1$: COVID-19 less likely

Chest X-ray with interstitial shadows, ground glass opacities, reticulonodular shadows; lymphocytes $<2500/\text{mm}^3$, neutrophil to lymphocyte ratio $>3:1$: COVID-19 likely

Children with Chronic Kidney Disease

Since children with CKD stage 4-5 are considered vulnerable to infection with coronavirus, it is vital that children and their family follow the ‘Precautions for caregivers & patients with renal diseases’, described above.

We suggest the following:

Patients and their caregivers are advised to maintain contact with health care providers, especially for symptoms of COVID-19, including fever and worsening respiratory symptoms. Paracetamol is safe for fever; treatment with NSAIDs (ibuprofen, naproxen) should be avoided.

Patients should continue to receive antihypertensive medications, targeting systolic and diastolic blood pressures to ~90th percentile for age, sex and height. As mentioned in the previous section, we recommend that therapy with ACE inhibitors or ARB should not be discontinued in patients with CKD, who are receiving such therapy. Abrupt withdrawal of these agents might result in clinical instability and adverse health outcomes.

Children on chronic ambulatory peritoneal dialysis (CAPD) should continue sessions at home, avoid hospital visits, and maintain adequate stock of fluids and consumables. They should be instructed to keep in regular contact with the doctor or dialysis nurse and inform promptly for symptoms of COVID-19. Other causes of fever, including peritonitis, should also be considered.

Hemodialysis Unit and Dialyzing Children with COVID-19

As coronavirus infection spreads in the community, pediatric patients on dialysis are likely to acquire infection. Asymptomatic carriers of coronavirus as well as patients with mild symptoms, who visit the hospital for thrice-weekly maintenance dialysis, thus pose risk of infection spreading among patients and hospital personnel. As pandemic spreads, hospitals will be overwhelmed in terms of infrastructure and manpower.

Inpatient and outpatient pediatric dialysis facilities must be prepared for patients with coronavirus disease. The goals of management are to protect patients as well as health care workers. The Ministry of Health and Family Welfare (MoHFW) has prepared comprehensive guidelines for hemodialysis of COVID-19 patients in India [23]. The guidelines below are adapted from the guidance from the Ministry of health and family welfare and specific for children.

Pediatric nephrologists, technicians and nursing staff of HD unit should be trained and equipped to:

- Prevent spread of coronavirus infection in dialysis unit
- Identify patients with possible COVID-19; follow institutional protocols for isolation and transfer for further management; and communicate with appropriate authorities
- Provide dialysis to patients with confirmed or suspected COVID-19
- Advise healthcare staff exposed to a patient with confirmed COVID-19

Children require hemodialysis in two scenarios:

- i.* Maintenance hemodialysis for end stage renal disease
- ii.* Dialysis for acute kidney injury (AKI), which is either related or unrelated to COVID-19

Children on Maintenance Hemodialysis

Principles

- Patients on dialysis are not advised to postpone their dialysis schedule
- Phone number(s) and contact information of dialysis unit should be provided to patients
- Pediatric units should be aware of the testing, triage and notification policy, as recommended by their respective institutions and Ministry of Health and Family Welfare.

- Travel and contact history of dialysis personnel, and patients and their attendees should be periodically updated.
- Units should educate and counsel personnel (doctors, nurses, technicians, staff) and patients about COVID-19. Patients and dialysis personnel must be provided with instructions (local language, English) about hand hygiene, respiratory hygiene and cough etiquette.
- Posters with information about hand hygiene, covering nose and mouth when coughing or sneezing, use of facemasks, disposal of tissues and contaminated items in waste bins should be displayed in the dialysis area and outside the unit.
- All hemodialysis staff should be trained for proper use and disposal of mask, gown and eyeglasses, and the need for personal protection.
- Duties of healthcare workers should be organized as per institutional policy, with an overall aim to maintain a pool of staff on reserve. It is preferable not to change dialysis shifts, to avoid cross contamination and infections.
- Universal precautions should be strictly followed.
- All surfaces of the dialysis unit should be sanitized twice a day with appropriate disinfectants (see below).
- Each dialysis bed and nursing station(s) should be equipped with alcohol-based sanitizers. Each bed should have disposable tissues and waste disposal bins to ensure adherence to hand and respiratory hygiene, and cough etiquette.
- To prevent spread of the infection, rounds by group of staff, group studies, and case discussions should be minimized.
- Optimal supplies of material such as dialysate, dialyzers and tubing, catheters, fistula needles, disinfectant and medicines etc. should be ensured.

Recommendations for Prevention and Early Identification [Fig. 4]

On arrival to the dialysis unit

Patients with clinical features of respiratory infection (e.g., fever, cough) should be identified *before* they enter the dialysis area.

- (a) Instruct parents and other caregivers to *call the unit* to report fever or respiratory symptoms, so that they can be directed appropriately to either the dialysis unit or COVID-19 triage in the hospital.

- (b) At each visit for dialysis, a staff member must perform a structured interview for the patient and parents, asking for: history of fever, cough, respiratory difficulty; exposure to confirmed patient with COVID; and travel history. This should be recorded.

Children should be advised to use a three-layer surgical facemask while in the waiting area, during dialysis and until they reach home.

Seats in the waiting area should be separated by at least 1 meter. To avoid overcrowding, children should be accompanied by only one attendant.

In dialysis unit and during dialysis

- Dialysis beds should be spaced at a minimum distance of 2 meters.
- Patients should be told to wash their hands and fistula arm before starting dialysis; puncture areas should be disinfected.
- All patients should preferably wear a surgical facemask through the procedure.
- Most pediatric units do not require a parent to be present during dialysis. In case necessary, the attendant/parent should wear a surgical mask.

Patients should discard used paper napkins in foot-operated plastic lined trash cans.

Advice for Parents, Family Members

- Parents and siblings should follow standard guidelines to prevent person-to-person and within family transmission of infection, which include measurement of body temperature, personal hygiene, hand washing, and reporting if sick.
- Dialysis patients, who have a parent or family member on 14-days quarantine, should continue to receive haemodialysis during this period.
- Once the family members or caregiver of dialysis patients are confirmed as COVID positive, caregivers should ensure that child is immediately isolated from the confirmed patient and instructed to *call the unit before arriving for dialysis sessions*, and to report fever or respiratory symptoms, so that they can be directed to the COVID-19 triage area in the hospital. In case the child had a direct contact with confirmed COVID-19 and remains asymptomatic, they should be tested on day 5 and 14. The dialysis staff should ensure that child uses a three-layer surgical facemask while in the waiting area, during dialysis and until they reach home in addition to following hand hygiene and cough etiquette.

Dialyzing Patient with Suspected or Confirmed COVID-19

Most pediatric hemodialysis units in developing countries are relatively small, comprising 3-6 beds. In order to prevent transmission of infection within the Unit, it is advised that patients with suspected or confirmed COVID-19 be dialyzed in a separate room, with separate access and with the door closed.

If a separate room is not available, the suspected patient may be dialyzed in a corner or end-of-row station, maintaining at least 2 meters separation in all directions. The patient, as well as other patients and dialysis personnel, should wear triple-layer surgical masks throughout the procedure.

Units which do not have enough space and/or dedicated work force for dialyzing suspected or confirmed COVID-19 children should coordinate and facilitate transfer of these children to the government designated hemodialysis facility or to adult or pediatric units with the required facility until the testing is negative. This possibility should be clearly communicated to the caregivers in advance which will help them prepare accordingly.

Additional guidelines are as follows:

- Minimize time in waiting area for the patient and parent(s)
- Dialysis personnel should not touch the patient or use stethoscope unless necessary
- Separate equipment is used, including stethoscopes, thermometers, saturation probes, and blood pressure cuffs, with cleaning and disinfection between shifts. Stethoscope tubing and diaphragms are cleaned with an alcohol-based disinfectant. Sphygmomanometer cuff are made of rexine and should be cleaned by alcohol-based disinfectant or 1% sodium hypochlorite solution.
- All surface and equipment (including dialysis machine) located within 1 meter of the patients should be disinfected (see below). All disposable supplies should be discarded.
- Dialysis personnel taking care of a patient with suspected COVID-19 should not look after other patients during the same shift.
- Staff treating infected patients should self-report symptoms of fever, cough and/or breathlessness.
- Institutional and national guidelines should be followed for managing patients with suspected or confirmed COVID [13].
- For dialysis of critically ill patients on maintenance hemodialysis who are admitted to intensive care units, please see section on dialysis of COVID positive patients with AKI.

Personal Protective Equipment (PPE) for Dialysis Personnel

- All hemodialysis staff should be trained for proper use and disposal of mask, gown and eyeglasses, and the need for personal protection.
- Some dialysis staff should be trained for donning and doffing of PPE, should a need arise for treatment of COVID-19 positive patients.
- Staff caring for patients with respiratory symptoms or undiagnosed respiratory infections should follow standard contact and droplet precautions with use of gowns, gloves, N95 mask, goggles or a disposable face shield that covers the front and sides of the face.
- Dialysis staff involved in direct care of a patient with confirmed COVID-19 should use appropriate PPE, as recommended by MoHFW guidelines [16].
- Staff members should avoid dining together. Goggles, masks and caps are removed prior to meals, and hands washed with soap and water. Talking during meals is avoided to reduce droplet spread.

Disinfection and Disposal Practices in Dialysis Units

Bed linen should be changed between shifts and used linen and gowns should be placed in dedicated containers for linen or gowns. Disposable gowns should be discarded after use. Cloth gowns should be soaked in a 1% hypochlorite solution for 20 minutes before sluicing, and then transported for laundering [23].

Disposable gloves should be used when handling laundry from an infected patient; gloves are discarded after each use. Dirty laundry should not be shaken to minimize the possibility of dispersing virus through air.

Surfaces and equipment in the dialysis unit should be cleaned and disinfected at least twice daily; and after each patient shift. This includes bedside tables and lockers, dialysis machines, patient monitors, syringe pumps, sphygmomanometers, doorknobs, light switches, counter tops, handles, desks, phones, keyboards, toilets, faucets and sinks.

For soft (porous) surfaces such as carpeted floor, rugs, and drapes, visible contamination is removed, followed by appropriate cleaners indicated for these surfaces. After cleaning, items should be laundered in accordance with the manufacturer instructions and dried completely.

Effective solutions for disinfection include those based on hypochlorite and alcohol. Bleach could be used to disinfect surfaces that do not soak up water (e.g.: floor). Disposable gloves should be used cleaning and disinfecting surfaces. Gloves are discarded after each cleaning. If reusable gloves are used, these gloves should be sent for cleaning and disinfection.

- *Bleach solution:* Mix 1 liter of Medichlor with 9-L water. The solution can be used for upto 24-hr following which it should be discarded. Alternatively, 10 g household bleaching powder can be dissolved in 1-L water and utilized over 24-hr.
- *Alcohol based solution:* The solution should contain at least 60% alcohol.

Dialysis in children with COVID-19 and Acute Kidney Injury (AKI)

The incidence of AKI in patients with COVID-19 ranges from 6-15%; data from children is not available [24]. In addition, patients with end stage kidney disease on maintenance dialysis may require care in an intensive care unit. A proportion of patients with bacterial infection will have septic shock, drug nephrotoxicity or worsening of existing chronic kidney disease, severe enough to require renal replacement therapy (RRT).

The goal is to deliver RRT in a safe and timely manner, while minimizing exposure to the staff. The children may need to be dialyzed in shared spaces with adults if dedicated space in wards or PICU is unavailable due to resource and infrastructure constraints. Centres should anticipate surge in COVID-19 related AKI and need for dialysis may outpace the abilities to provide dialysis especially if such a facility only exists in designated hospitals for COVID patients.

We suggest the following:

- If possible, patients should be co-located or cohorted in dedicated ICUs per individual institution's policies.
- Indications for initiating RRT and choice of modality including acute peritoneal dialysis, continuous renal replacement therapy (CRRT) and sustained low efficiency dialysis with or without hemodiafiltration (SLED or SLEDf) is based on availability of resources and expertise, patient status and cost as in any other patients with AKI. PD may not be possible in critically ill who require prone ventilation.
- Access: Central venous catheter for HD or PD catheter should be placed by an experienced nephrologist or intensivist with complete PPE as recommended for procedures. For ESRD patients who have already have AVF, CRRT and SLED using AVF could be considered when careful monitoring of the patient for needle dislodgement and exsanguination is possible [25]
- Prescription of RRT: The prescription of RRT should be as per unit protocol. In centers having facility for CRRT, the treatment time for CVVHDF may be reduced to 10 -12 hours in order to make the machine available for a greater number of patients. In case of anticipated shortage

of replacement fluids for CRRT, the dose could be reduced to 10-15 ml/kg/hr instead of 25 ml/kg/hr, especially after the first few hours once metabolic control has been achieved. Alternatively, 0.9 % Normal saline could be used as replacement fluid.

- Anticoagulation: Centers dialyzing patients with COVID have reported circuit clotting in CRRT and SLED if anticoagulants are not used. Hence anticoagulation should be considered as per individual unit's protocol. In case of unavailability of pumps for heparin, low molecular weight heparin could be used [Enoxaparin single dose -0.5 -1 mg/kg or Daltaparin 40 IU/kg ;<15 kg 1,500 IU: 15-30 kg 2500 IU] [26].
- In order to minimize/avoid daily patient contact, nephrologists should collaborate with the ICU team and rely on their assessment for relevant physical examination, interpretation of laboratory investigations and ultrasound findings, such as volume status
- Nephrologists and dialysis staff should follow the MoHFW recommended PPE and safety guidelines during their interactions with the patient.
- If ICU nurses are trained and competent to handle HD or CRRT machines, hemodialysis nurses/technician do not need to have direct contact with patients, thereby limiting healthcare staff exposure.
- Consider setting up the CRRT or HD machine and priming outside the patient area and then take the machine into the room and connect the patient in the room in order to minimize exposure and limit use of PPE.
- After treatment, dialysis equipment should be cleaned as described in previous section. The equipment should be disinfected before removed from the room. If portable reverse osmosis (RO) unit is being used it should be properly disinfected with hypochlorite (1% sodium hypochlorite) solution between use of two patients.
- Transport to a central dialysis unit for dialysis of *non-critically ill suspected or confirmed COVID patients* with AKI or ESRD not admitted in ICU is generally NOT recommended. These patients should be preferably given bed-side dialysis using portable RO unit in the dedicated COVID 19 ward if indicated. If more dialysis is expected in selected area, dialysis machine may be left in the same area for future dialysis with due precautions and disinfection. Health care providers caring for these children should use PPE and N95 masks.
- Acute peritoneal dialysis should be considered when hemodialysis machines are continuously in use. If available, automatedycler should be used to minimize patient contact. While

performing acute PD the drain fluid should be carefully handled by the staff and disposed as per protocol for disposal of medical waste.

- All disposable RRT machine consumables like tubings, dialyzers, replacement solutions bags should be discarded as per local hospital infection control & policy
- Experimental drugs used in treatment of COVID [lopinavir/ritonavir, chloroquine/hydroxychloroquine, tocilizumab] do not require dose adjustment with RRT.

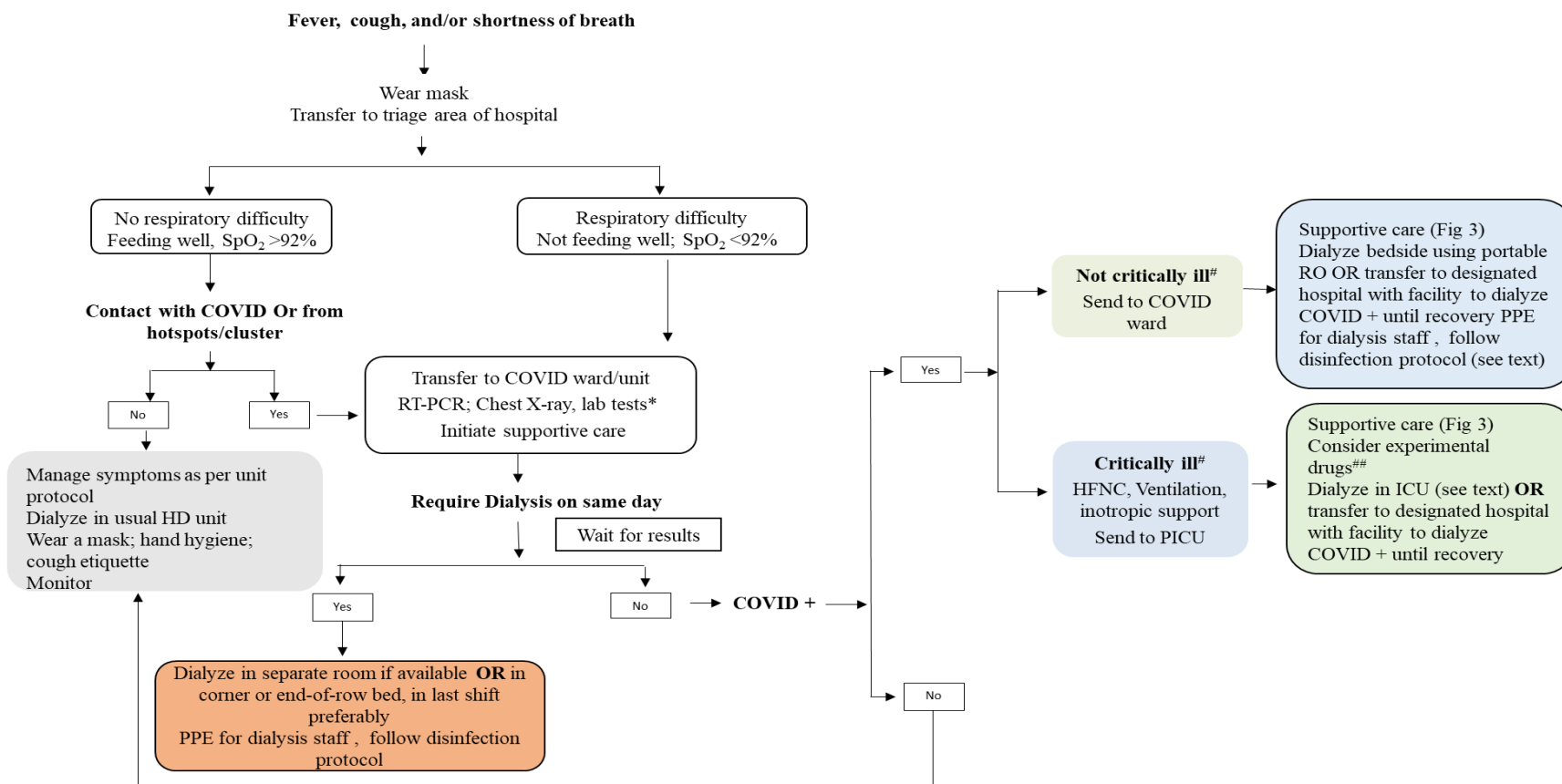


Fig 4: Managing child on chronic hemodialysis with COVID-19

RO Reverse osmosis, PPE Personal protection equipment, HFNC High flow nasal canula

***Testing:** Nasopharyngeal, posterior pharyngeal swab; endotracheal aspirate or BAL: RT-PCR for COVID-19 Evaluate with blood counts (CBC); renal and liver function tests; coagulogram, D-dimer, fibrinogen; C-reactive protein; chest radiograph; blood culture

Not critically ill : Non-severe pneumonia: Cough or difficulty breathing *with* fast breathing (<2-months: ≥ 60 ; 2–11 months: ≥ 50 ; 1–5 years: ≥ 40 breaths per minute); *and* no signs of severe pneumonia ; **Critically ill:** Severe pneumonia: Cough or difficulty in breathing, *with* at least one of the following: (i) central cyanosis or oxygen saturation (SpO_2) $< 90\%$; (ii) severe respiratory distress (grunting, very severe chest indrawing); (iii) signs of pneumonia with one danger sign: inability to breastfeed/drink, lethargy/unconsciousness, or convulsions. Signs of pneumonia: chest indrawing, fast breathing (<2-months: ≥ 60 ; 2–11 months: ≥ 50 ; 1–5 years: ≥ 40 breaths per minute) OR features of acute respiratory distress syndrome; shock

LPV/r - Lopinavir/Ritonavir dose is 10 mg/2.5 mg per kg BD for maximum 14 days (maximum 400 mg/100 mg BD). Symp LPV/r 80 mg/20 mg per ml; Tablet LPV/r 100 mg/25 mg; Tablet LPV/r 200 mg/50 mg ; HCCQ - Hydroxychloroquine 7-8 mg/kg/dose BD for day 1; 7-8 mg/kg once a day from days 2-6; avoid concomitant azithromycin, since can lead to arrhythmias. (Recommendations based on ICMR guidance. Dose for children is extrapolated from that recommended in adults)

Transplant Recipients and Caregivers

Recipients of kidney transplant are immunocompromised, and vulnerable for coronavirus infection. However, information on COVID-19 in transplant patients is limited. Among the 53 adult COVID + renal transplant recipients reported in UWSOT database, 60% required hospitalisation. Of these, a third were treated in the ICU. All the 3 patients who died had other chronic illnesses [27]. Data on pediatric allograft recipients is not available. Therefore, the suggestions in this guideline are based on the limited data from the literature and should be used in conjunction with local or national guidance for management of COVID-19 patients.

We suggest the following:

Recipients and caregivers

- In order to minimize the risk of COVID-19 in transplant recipients, follow the ‘Precautions for caregivers & patients with renal diseases.’ They should limit movement outside the home, follow hand hygiene practices and defer scheduled follow up visits to hospitals.
- A triple layer mask use is recommended when leaving home, to reduce the risk of viral transmission and prevent touching of nose and mouth. Use of N95 mask is not required.
- Teleconsultation facilities should be utilized for follow up.
- Ensure adequate stock of medications at home; aim for 3-4 weeks’ supply. Let your doctor know if you are running out of medications.
- Transplant recipients *must call* before visiting the hospital if they are sick with a fever or other symptoms that are persisting for more than 24 hours.

Diagnosis

In patients in University of Washington database, the chief symptom was cough (90%); fever was observed only in 50%. One-third also had diarrhea and 50% had lymphopenia. Hence, a high index of suspicion is necessary to diagnose COVID-19 in transplant recipients. Transplant recipient presenting with cough or shortness of breath with or without fever, history of contact with a patient of COVID-19, or with features of severe acute respiratory illness should be screened for coronavirus infection by RT-PCR of nasopharyngeal swabs.

Treatment [Fig 5]

Other causes for fever, including bacterial or viral infections should be ruled out by appropriate investigations. Treatment with antibiotics is instituted for bacterial infections.

Immunosuppressive therapy in mild COVID-19 disease should not be modified, to reduce the risk of allograft rejection and graft loss.

Antiproliferative agents (mycophenolate, azathioprine) may be discontinued in non-critically ill children with pneumonia or severe pneumonia.

Consider reducing the dose of calcineurin inhibitors (CNI) to target lower CNI levels in these children.

Consider reducing dose of CNI to lowest dose possible or discontinue in children who are critically ill requiring ventilation and inotropic support [28, 29].

The dose of prednisolone may be increased to 0.5-1 mg/kg in children where antiproliferative agents are discontinued. A higher dose of steroids might be considered in patients not receiving CNI.

Immunosuppressive therapy should restart if patient is afebrile for 3-days and increased to pre-illness dose 14-days after two nasopharyngeal swabs are negative for the virus.

Specific therapy

The supportive management of renal transplant recipients with COVID-19 should be as shown in **Fig 3**.

At present, there is no proven antiviral treatment for COVID-19. Drugs that are being examined include lopinavir/ritonavir, remdesivir, favipiravir, hydroxychloroquine, tocilizumab, interferon beta and intravenous immunoglobulins.

Interaction of the above medications with CNI and sirolimus need to be considered, and appropriate monitoring performed. Lopinavir/ritonavir, darunavir/ritonavir, chloroquine and hydroxychloroquine can potentially increase the levels, while tocilizumab decreases CNI and sirolimus levels.

Performing Renal Transplantation during the COVID-19 Pandemic

Transplantation is an elective procedure, performed in a relatively stable patient who is otherwise receiving maintenance dialysis either through chronic peritoneal dialysis or hemodialysis. During transplant surgery and thereafter, transplant patients may require respiratory support and stay in the intensive care, facilities that are scarce in this pandemic. Similar support may be required for living-related donors. Use of limited facilities, for donors and recipients, might therefore deny such services for critically ill patients with COVID-19. Finally, transplantation results in a state of immunosuppression, which would be detrimental during this outbreak.

Thus, the risks of performing transplantation outweigh the benefits, both from a patient and a healthcare system perspective. It is recommended that living donor transplants be postponed until the pandemic has abated. Each transplant center should take institutional decisions on their approach to deceased donor transplantation.

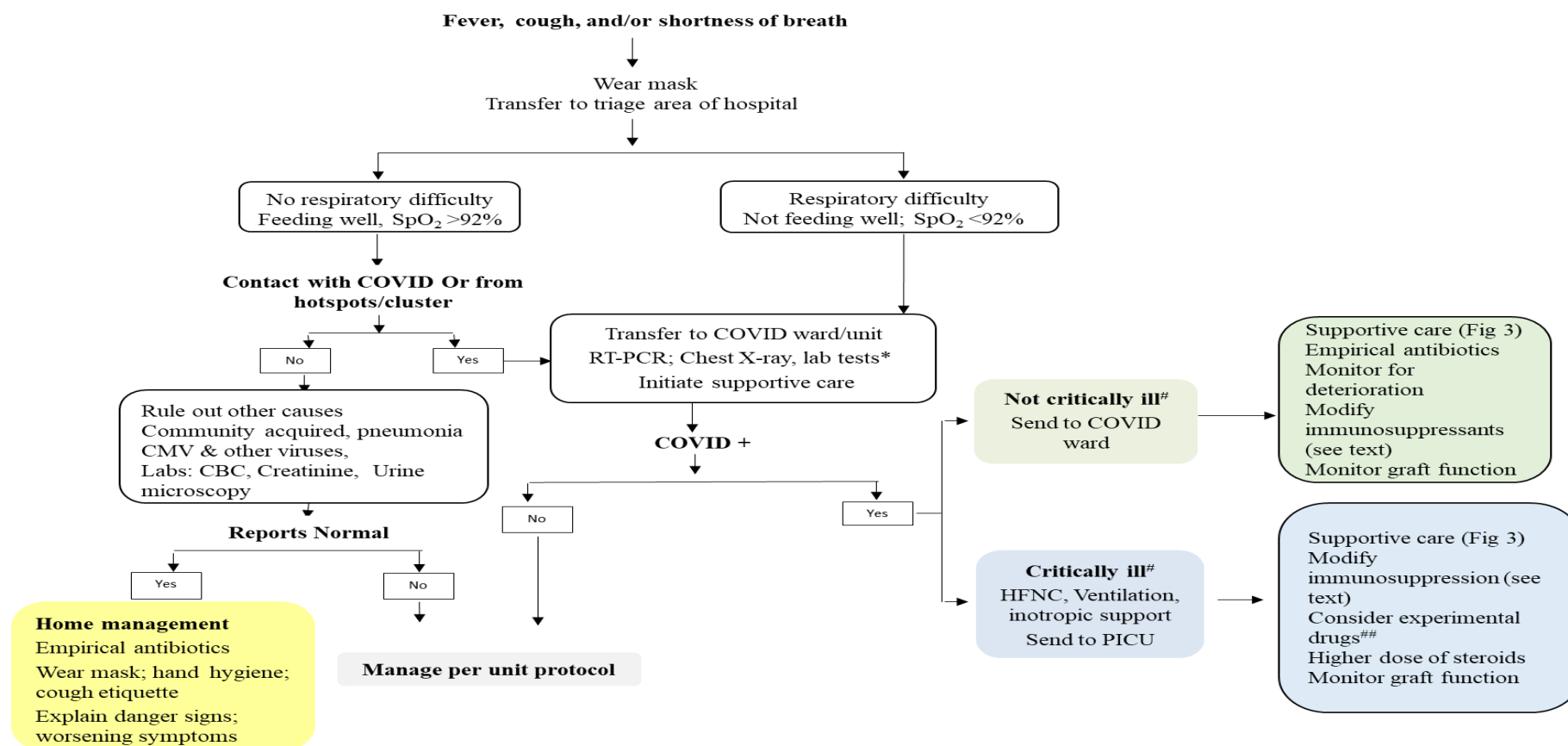


Fig 5: Algorithm for management of renal transplant patient with suspected or confirmed COVID-19

HFNC High flow nasal canula ; ***Testing:** Nasopharyngeal, posterior pharyngeal swab; endotracheal aspirate or BAL: RT-PCR for COVID-19 Evaluate with blood counts (CBC); renal and liver function tests; coagulogram, D-dimer, fibrinogen; C-reactive protein; chest radiograph; blood culture

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