Indian Society of Nephrology - COVID-19 Working Group Guidelines

Preambles:

Indian Society of Nephrology-COVID 19 working group formulated guidelines/suggestions based on the literature and pieces of information available from across the world during this pandemic. The purpose of the document is to guide and suggest the members involved in the care of COVID patients. SARS-CoV-2 may cause acute kidney injury directly besides respiratory tract involvement. Chronic kidney disease patients, hemodialysis patients, patients with glomerular diseases, and transplantation on immunosuppression need specific suggestions and guidelines on different aspects of prevention and treatment. The guideline on the transplantation aspect was also contributed and endorsed by the Indian Society of Organ Transplantation. The present draft covers all the aspects of kidney diseases with reference to COVID19 and related issues in management.

Disclaimer: Suggestions /recommendations may require a regular update with the changing epidemiology and new information related to COVID19.
Indian Society of Nephrology - Covid-19 Working Group

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**An overview of epidemiology, genomic structure, the molecular mechanism of injury of lung and kidney in coronavirus infection**

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Abstracts:

COVID-19 is a novel beta coronavirus strain that was first discovered in 2019 in Wuhan city of China. Based on virus genome sequencing studies, the bat is suspected as the natural host of virus origin, and COVID 19 might be transmitted from bats via unknown intermediate hosts like reptiles and snakes, etc. to infect humans. COVID 19 is primarily transmitted from person to person contact via droplet infection within the incubation period or after clinical manifestations of fever, cough, sneezing, sputum, dyspnea, and pneumonia. Covid 19 enters the respiratory tract through the ACE2 receptor on alveoli through binding of s-protein of the virus and may cause injuries though the cytopathic effect, as well as cytokines and other mediators, release after developing sepsis. ACE 2 is almost 100-fold higher in kidneys than lung, and the virus can also involve the kidney in the same
manner. Kidney involvement manifests in the form of proteinuria, hematuria, and a rise in serum creatinine and blood urea nitrogen. Kidney involvement is an independent risk factor for mortality. The purpose of the article is to introduce coronaviruses, its genomic structure, mechanism of injury of lung and kidney.

**Keywords:** Coronavirus; severe acute respiratory syndrome; pneumonia; sepsis; mechanisms; acute kidney injury

**Introduction:**

Coronaviruses (CoV), are amongst the newly emerging virus, which affects zoonoses and transmitted between animals and human beings (1). In the past, It caused illness ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV)(2). The SARS was transmitted from civet cats to humans and MERS from dromedary camels to humans. Many other coronaviruses are still circulating in zoonoses that are not found in humans to date.(3,4,5)

COVID-19 is a novel CoV strain that was first discovered in 2019, which was not previously reported in humans(6). This CoV was renamed several times after discovery, first of all, as a newly identified β-coronavirus in Wuhan in the late months of 2019. On 12th January 2020, the World Health
Organization (WHO) renamed it as the 2019-novel coronavirus (2019-nCoV), and on 11th February 2020 again officially rendered it as coronavirus disease 2019 (COVID-19). On the same day, the Coronavirus Study Group of the International Committee on Taxonomy of viruses of WHO proposed the name SARS-CoV-2 for this virus.(7,8,9). At the end of 2019, COVID-19 caused a cluster of pneumonia cases in Wuhan, a Chinese city, on 30th January, the outbreak was declared as Public Health Emergency of International Concern (PHEIC) and now a declared global pandemic by WHO(10). As of date 21st March 2020 WHO reports, there are 266073 confirmed cases, and 11,184 confirmed deaths in 183 countries. The epicenter of pandemic changed from Wuhan city in China to Italy and Spain in Europe.(11,12)

**Structure and viral genome of coronavirus in brief:**

The Covid-19 or SARS-CoV-2 is a β-coronavirus, which is enveloped non-segmented positive-sense RNA virus of subfamily Orthocoronavirinae of the Coronaviridae family (10,13). CoVs are divided into four genera called alpha (α), beta (β), gamma (γ) and delta (δ) CoV. α- and β-CoV can infect mammals, while γ- and δ-CoV tend to affect birds. Members of this large family of viruses can cause respiratory, enteric, hepatic, and neurological diseases in different animal species, including camels, cattle, cats, and bats.(13,14) In the past, six CoVs were discovered as a human-susceptible
virus, among which α-CoVs HCoV-229E and HCoV-NL63, and β-CoVs HCoV-HKU1 and HCoV-OC43 had low pathogenicity, and cause common cold like milder respiratory symptoms. The other two known β-CoVs, SARS-CoV, and MERS-CoV, lead to severe and fatal respiratory tract infections [2,13]. COVID19 one strain of SARS-CoV-2 is 29.9 kb (14), While SARS-CoV and MERS-CoV have positive-sense RNA genomes of 27.9 kb and 30.1 kb, respectively (15). It has been shown that the genome of CoVs contains a variable number (6–11) of open reading frames (ORFs) (16).

Figure-1: Structure of the Coronavirus and the role of different proteins.
Figure-1 depicts the structure of the CoVs. CoVs are round or elliptic and often pleomorphic form, and a diameter of approximately 60–140 nm. The single-stranded RNA genome contains 29891 nucleotides, encoding for 9860 amino acids. Two-thirds of viral RNA, mainly located in the first open reading frame (ORF 1a/b), encodes 16 non-structure proteins (NSPs). The rest part of the virus genome encodes four essential structural proteins, including spike (S) glycoprotein, small envelope (E) protein, matrix (M) protein, and nucleocapsid (N) protein, and also several accessory proteins that interfere with host immune response (17,18).

The sequencing studies of Wu et al. (19) revealed genomic and phylogenetic similarity of COVID 19 with SARS-CoV, particularly in the S-protein gene and RBD. This indicated the capability of direct human transmission like SARS-CoV. The whole-genome sequence studies showed that COVID 19 appears closer to the SARS-like bat CoVs as compared to the known SARS-CoV and MERS-CoV. Chan et al. have proven that the genome of the new HCoV, isolated from a cluster-patient with atypical pneumonia after visiting Wuhan, had 89% nucleotide identity with bat SARS-like-CoVZXC21 and 82% with that of human SARS-CoV (4). For this reason, the new virus was called SARS-CoV-2 (20). The majority of genomically encoded proteins of COVID-19 and SARS-CoVs were similar, except few differences in some amino acid substitutions in NSP2, NSP3, spike protein, receptor binding domains (20,21). Another recent
research suggested (22) that the mutation in NSP2 and NSP3 play a role in infectious capability and differentiation mechanism of COVID-19. A study by Zhang et al. (23) revealed that COVID 19 was mutating in different patients in China. Tang et al. (24) conducted a population genetic analysis of 103 COVID 19 genomes and classified out two prevalent types of COVID, L type approximately 70% and S type approximately 30%. The strains in L type, derived from S type, are evolutionarily more aggressive and contagious. There is a need to keep an eye over this novel CoVs for their virulence and epidemic spread over the globe, at present.

It was also found that the genome sequence of SARS-CoV-2 is 96.2% identical to a bat CoV RaTG13, whereas it shares 79.5% identity to SARS-CoV. Based on virus genome sequencing results and evolutionary analysis, the bat is suspected as the natural host of virus origin, and COVID 19 might be transmitted from bats via unknown intermediate hosts like reptiles and snakes, etc. to infect humans.

**Molecular mechanism of injury by COVID-19(SARS-CoV-2):**

**S-protein** of SARS-CoV-2 binds to host cell receptors, angiotensin-converting enzyme 2 (ACE2), which is a critical step for virus entry (25). ACE2 is a cell receptor for COVID 19 and regulates the transmission across the species and between human beings as well (26,27). S-protein contains two subunits, S1 and S2 (28,32). S1 determines the virus-host interaction and cellular tropism with the vital function domain- receptor-
binding domain (RBD), while S2 mediates virus-cell membrane fusion by two tandem domains, heptad repeats 1 (HR1) [27] and HR2 (30).

S-protein and ACE2 binding efficiency of COVID-19 is 10- to 20-fold higher than that of SARS-CoV (31). For SARS-CoV, the cleavage of trimer S protein is triggered by the cell surface-associated transmembrane protease serine 2 (TMPRSS2) (32) and cathepsin(33), however, the possible molecules facilitated membrane invagination for SARS-CoV-2 endocytosis are still under investigations.

After membrane fusion, the viral genome RNA is released into the cytoplasm, and the uncoated RNA translates two polyproteins, pp1a and pp1ab (34), which encode non-structural proteins, and form replication-transcription complex (RTC) in double-membrane vesicle (35). Continuously RTC replicates and synthesizes a nested set of subgenomic RNAs (36), which encode accessory proteins and structural proteins. Mediating endoplasmic reticulum (ER) and Golgi [37], newly formed genomic RNA, nucleocapsid proteins, and envelope glycoproteins assemble and form viral particle buds. Lastly, the virion-containing vesicles fuse with the plasma membrane to release the virus leading to viremia.

The S2 subunit of Covid-19 containing a fusion peptide, a transmembrane domain, and cytoplasmic domain is highly conserved, which could be a target for antiviral targeting against S-2 (anti-S2) compounds. The spike RBD presents only a 40% amino acid identity with other SARS-CoVs. The
ORF3b has no homology with that of SARS-CoVs and a secreted protein (encoded by ORF8), which is structurally different from those of SARS-CoV, maybe area of interest and research in future (13).

Mechanisms of kidney injuries:

Host susceptibility, particularly elderly and peoples with underlying diseases, hypertension, cardiac diseases, bronchial asthma, diabetes, etc. influence the progression of COVID 19 infection. The mechanism of kidney injury by COVID-19 appears multifactorial and, although precisely, remains unknown(38). The direct viral cytopathic effect on kidney tissue is a postulated mechanism, which is supported by the finding of viral nucleic acid material of CoV in blood and urine in SARS-CoV as well as COVID-19 patients (39,40). The molecular study showed CoV uses angiotensin-converting enzyme 2(ACE2) receptor for cell entry like SARS-CoV. ACE2 and dipeptidyl peptidase-4 (DPP4), both expressed on renal tubular cells, were identified as binding partners for SARS-CoV and MERS-CoV, respectively. It is a fact that ACE2 expression is 100-fold higher in kidney tissues than the lung(41). It makes sense to postulate that ACE2 dependent pathway may be used by CoV to infect kidneys more severely than the lung. However, clinical observation is different from more lung involvement than the kidney.
The direct effector T cell-mediated injury and the immune complex-mediated glomerular injury with viral antigen and specific antibody could be another plausible mechanism. However, the present evidence of information with normal glomerular aspect on microscopy and absence of electron-dense deposit in SARS-CoV patients, do not support this hypothesis(42).

The other piece of information could be inducing sepsis and the cytokine storm theory(43). The cytokines and other mediators are released after CoV infection leading to sustained inflammatory response lead to hypotension, hypoxia, shock, and target organ injuries. The clinical pictures of patients with COVID-19 with sepsis support this hypothesis. The manifestations are particularly severe, with a wide range of signs and symptoms of multiorgan involvement. These signs and symptoms include respiratory events such as severe dyspnea and hypoxemia, renal impairment with reduced urine output, tachycardia, altered mental status, and functional alterations of organs expressed as laboratory data of hyperbilirubinemia, acidosis, high lactate, coagulopathy, and thrombocytopenia. However, these findings suggest the probable mechanism of AKI in many terminal cases. Wang et al. showed that 138 patients with COVID-19 disease, who were admitted in ICU, showed a tendency towards increased creatine kinase levels (44). It contributes to AKI indirectly through the effects on renal tissues, because of hypotension,
hypoxia, shock, and rhabdomyolysis. However, such patients develop kidney injuries otherwise also.

**Epidemiology of COVID-19:**

Epidemiological studies in Wuhan at the beginning of the outbreak identified an initial association with a seafood market that sold live animals for food purposes, where most of the early patients had worked or at least visited there. The market was traced as the source, and subsequently, the market was closed for disinfection (45). However, as the outbreak progressed, person-to-person spread became the primary mode of transmission.

The respiratory droplets released during cough, sneezing, talks, and mucus secretion are the dominant medium of transmission. The infection occurs if a person inhales such droplets or touches the contaminated surface with droplets and, subsequently, their own eyes, nose, and mouth (46,47). The droplets do not travel more than 6 feet and do not linger in the air also. However, a report revealed that SARS-CoV-2 might remain viable in aerosols under experimental conditions for at least three hours (46). The possibility of transmission is higher in the early phase as soon as symptoms appear as the viral RNA peaks during that period. However, it
may transmit during the incubation period as well (48). The incubation period is typically within two weeks of exposure, with the majority occurring within 4-5 days of exposure.

According to a joint WHO-China report, the rate of secondary COVID-19 ranged from 1 to 5% among tens of thousands of close contacts of confirmed patients in China (49). In the United States, the symptomatic secondary attack rate was 0.45% among 445 close contacts of 10 established patients (50). Live viruses had also been cultured from stool; however, the fecal-oral transmission did not appear to be a significant factor in the spread of infection(49).

**Sample collection and diagnosis:** The sample collection and storage for the diagnosis in a resource-limited place is also challenging. The WHO recommends collecting specimens from the upper respiratory tract (naso-and oropharyngeal samples); and lower respiratory tract such as sputum, endotracheal aspirate, or bronchoalveolar lavage (BAL). The collection of BAL samples should only be performed in mechanically ventilated patients. The samples require storage at four degrees celsius.

In the laboratory, a reverse polymerase chain reaction (RT-PCR) is used for the amplification of the genetic material extracted from the saliva, mucus, and other samples. It involves the synthesis of a double-stranded DNA molecule from an RNA mold. The search is targeted towards the genetic code of the CoV that is conserved. The probes used are based on
the initial gene sequence released by the Shanghai Public Health Clinical Center & School of Public Health, Fudan University, Shanghai, China on Virological.org, and subsequent confirmatory evaluation by additional labs. If the test result is positive, it is recommended that the test is repeated for verification. In patients with confirmed COVID-19 diagnosis, the laboratory evaluation should be repeated to evaluate for viral clearance before being released from observation.

Clinical features:

There are no specific clinical features that can yet reliably distinguish COVID-19 from other viral respiratory infections. Pneumonia appears to be the most severe frequent manifestation of severe infection, characterized primarily by fever, cough, dyspnea, and bilateral lung infiltrates on chest imaging (51,52,53). In a study describing 138 patients with COVID-19 pneumonia in Wuhan, the most common clinical features at the onset of illness were fever in 99%, fatigue in 70%, dry cough in 59%, anorexia in 40%, myalgias in 35%, dyspnea in 31% and sputum production in 27% (52). Besides lung, kidney involvement also seems to be frequent in symptomatic patients with positive tests. They manifest clinically with proteinuria, hematuria, rise in serum creatinine, and blood urea nitrogen with AKI, an independent risk factor for mortality.
India specific situation: As of March 23, 2020 (54), the Indian Council of Medical Research data showed a total of 18,383 samples from 17,493 individuals had been tested, and 415 individuals were positive for SARS-CoV-2, and seven deaths have been claimed because of COVID-19 infection. In an opinion by the Director of Center for Disease Dynamics, Economics and Policy (CDDEP), applying mathematical models used in the USA or the United Kingdom to India points to a possible 300 million (30 crore) cases in India, out of the 10 crores will face severe COVID infection (55). Looking at the incidence of 5.1% of AKI in severe cases (38), there would be 5.1 million AKI patients because of Corona, and presumably, half of them may require renal replacement therapy. It is estimated that with community spread in India with limited resources and health infrastructure, it could be challenging to combat the situation of patients with multiorgan failure and kidney failure if the disease spreads fast within 2-3 months. However, India can handle the case if the infection spread slowly over a year.

AKI and SARS-CoV-2: clinical manifestations and case fatality

Moreover, COVID-19 appears more contagious than SARS and MERS, spreads by human-to-human transmission via droplets infections or direct contact from person to person. The incubation period ranges from 2 days to 2 weeks (usually 3 to 7 days).
Although SARS-CoV2 or COVID-19 causes diffuse alveolar damage, interstitial pneumonia and acute respiratory failure, the involvement of other organs such as the kidney, heart, digestive tract, blood, and nervous system also need to be explored (15,16). It has been reported that SARS-CoV and MERS-CoV have infected more than 10,000 people in the past two decades, with mortality rates of 10% and 37%, respectively (56,57). In previous reports of SARS and MERS-CoV infections, acute kidney injury (AKI) developed in 5% to 15% cases and carried a high (60%–90%) mortality rate (58). A study reported that although AKI was uncommon in SARS but accounted for the fiercely high mortality of 91.7%, notably 33 out of 36 cases died (42).

Kidney involvement was a strong and independent predictor of mortality as during the SARS and MERS outbreak, that hints out for the special attention for the kidney involvement with COVID-19 infection as well.

The incidence of AKI with COVID infection reported varying from 3%- 9%. (53,59,60,61). A larger prospective study has reported the overall incidence of 5.1% (38). In a study of 59 COVID-19 infected patients with 28 severe cases and three deaths, Li et al. (62) found that 34% of patients had albuminuria on the first day of admission, and 63% developed proteinuria during the hospital stay. Nineteen percent of people showed an elevated level of plasma creatinine. Blood urea nitrogen was elevated in 27% of patients and in two-thirds of patients who died. Each one of those (27/27)
who had computerized tomography (CT) scan showed radiographic abnormalities of the kidneys with reduced density suggesting inflammation and edema. The study also emphasized that renal impairment may be an independent factor of mortality.

In another more extensive prospective study, Cheng Y et al. (38) studied 701 patients (median age 63 years with interquartile range, 50-71 years, and 367 male) admitted in a tertiary teaching hospital with 3 branches in the province following this outbreak of COVID-19 in Wuhan city of China. A total of 113 (16.1%) died in the hospital, and the median time to death was 6 days (IQR 3-12) days. On admission, 43.9% of patients had proteinuria, and 26.7% had haematuria. The prevalence of elevated serum creatinine elevated blood urea nitrogen, and estimated glomerular filtration under 60 ml/min/1.73m\(^2\) were 14.4, 13.1 and 13.1%, respectively. Overall, AKI was reported in 5.1% of patients. Patients with kidney disease had a significantly higher risk of in-hospital death. Cox proportional hazard regression confirmed that elevated baseline blood urea nitrogen (3.97, 2.57-6.14), and elevated baseline serum creatinine (hazard ratio: 2.10, 95%CI: 1.36-3.26) was an independent predictor of mortality. It has also been observed that the hazard ratio also increases with the staging of AKI from 1.9 in stage 1, 3.51 in stage 2, and 4.38 in stage 3 AKI. The hazard ratio of mortality also increased with the degree of proteinuria and haematuria. These factors remain significant factors for in-hospital death.
after adjusting for age, sex, disease severity, comorbidity, and leukocyte count. The incidence of in-hospital mortality in patients with elevated baseline serum creatinine was 33.7% was significantly higher than patients with normal baseline serum creatinine (13.2%). However, the major limitation of the study was that many patients might have concurrent chronic kidney disease.

The JAMA study with 27314 case records showed the overall case-fatality rate was 2.3% in confirmed cases, about 15% elderly patients, in particular those aged ≥ 80 years, 8% in 70 to 79 years of age. About 50% patients who died had comorbidities such as cardiovascular disease, diabetes, chronic respiratory disease, and oncological diseases. The disease was uncommon in very young, and fatality was also very low. (63) The previous study on SARS-CoV, which revealed the fact that the acute kidney injury (AKI) was uncommon in SARS-CoV but accounted for the fiercely high mortality of 91.7%, notably 33 out of 36 cases, died (42). The incidence of in-hospital death in patients with elevated baseline serum creatinine was 33.7%, which was significantly higher than in those with normal baseline serum creatinine (13.2%) (38).

**Treatment strategies for in general for COVID and with AKI:**

At present, the management strategies of COVID-19 with AKI is conservative with good hydration, nutritional support, and paracetamol with
aiming for the self-recovery of the patients in the quarantine. The patient with respiratory distress may require oxygen therapy and intensive care with ventilatory support in case of acute respiratory distress syndrome (ARDS). All confirmed COVID-19 patients need to be isolated. An N95 fit-tested respirator and protective clothing and equipment are essential for patients, and the Caregiver should also use appropriate approved protective masks and clothes.

There is no effective antiviral therapy available. In the most extensive prospective study of AKI with COVID-19, the three most used medicines were antivirals (73.0%), antibiotics (71.0%), and glucocorticoid (36.9%). Antivirals showed mortality benefit, and the glucocorticoids did not, which is possible because clinicians have used steroids mainly in the terminally sick patients. The varieties of antivirals were used, including arbidol hydrochloride, ganciclovir, interferon, lopinavir and ritonavir, oseltamivir, and ribavirin. However, there was no significant difference between patients with AKI and those without AKI (38).

The most recent NEJM study of the randomized controlled trial (64) showed no mortality benefit of treatment with lopinavir-ritonavir (19.2%) as compared to the standard of care arm (25%). The median time of clinical improvement was only one day shorter in the treatment arm. Lopinavir–ritonavir treatment was stopped early in 13.8% because of adverse events. With some success story with remdesivir in COVID-19 treatment, a clinical
trial is currently going on (65), which may divulge results in April of this year. Chloroquine phosphate showed some efficacy against COVID-19–associated pneumonia in a multicentre clinical trial conducted in China(66). The National Taskforce for COVID-19 by ICMR recommended the use of hydroxy-chloroquine for prophylaxis of SARS-CoV-2 infection for selected individuals like asymptomatic healthcare workers involved in the care of suspected or confirmed cases of COVID-19 in a dose of 400 mg twice a day on Day 1, followed by 400 mg once weekly for next seven weeks; and for asymptomatic household contacts of laboratory-confirmed cases in the dose of 400 mg twice a day on Day 1, followed by 400 mg once weekly for next three weeks; that to be taken with meals. The warning with this advisory also mentioned that the health care workers should not have a false sense of security with this chemoprophylaxis, other preventive measures and quarantine process should remain continued. (67,68)

Few retrospective analyses showed benefit with the use of glucocorticoids in SARS-CoV infection(69,70). Metanalysis on the use of glucocorticoids in previous SARS-CoV infection do not support the use of glucocorticoids in COVID infection as well. In a meta-analysis of corticosteroid use in patients with SARS, four studies showed harm with higher psychosis, diabetes, avascular necrosis, and delayed viral clearance(71). WHO does not recommend the use of steroid expecting potential inhibition of viral clearance and prolongation of the duration of viremia(72).
**Experimental therapies:**

There are several future promising therapies are being evaluated and in pipeline. The use of convalescent plasma (clinical trial ChiCTR2000029757), monoclonal antibodies like Tocilizumab, a monoclonal antibody against the IL-6 receptor are under underway (ChiCTR2000029765) awaiting reports, a monoclonal antibody directed against the Ras-binding domain of the S- protein of MERS-CoV are under investigation. However, no such evidence is available against COVID-19 are under underway and awaiting reports.(58)

**Extracorporeal therapy:**

The indirection of dialysis remains standard as for any other AKI patients. CRRT, with high volume hemofiltration that will be capable of removing inflammatory cytokines, appears theoretically promising. CRRT was successfully used in the treatment of SARS, MERS, and sepsis in the past (73,74). A study showed significant improvement in the Sequential Organ Failure Assessment scores at day 7 in patients with sepsis treated with High-volume hemofiltration and removal of IL-6 (75).
In summary, COVID-19 is a novel Beta CoV infection which has genomic homology with Bat CoV and transmitted to human beings through some intermediate host. Person to person transmission in the human being is a major mode of transmission, which lead to pandemic from a small cluster outbreak from Wuhan city of China. The lung is primarily involved; however, the kidney involvement is an independent risk factor for mortality with this novel CoV infection. With the increasing stage and severity of AKI, the hazard ratio of death of patients with COVID also increases. The management strategies applied for AKI in COVID are supportive care with awaiting self-recovery. Many patients with AKI may progress to CKD in future. COVID infected patients need to be quarantined.

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Chapter-2:

**COVID 19 in patients of Chronic Kidney Disease and Hypertension**

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Is there an increased risk of COVID 19 in patients with Chronic Kidney Disease (CKD):

The prevalence of chronic kidney disease (CKD) is very high in all parts of the world, including India. Many CKD patients will also acquire SARS-CoV-2 infection. However, it is not clear whether the CKD patients are at increased risk of getting COVID-19 infections. Elderly patients especially those with associated co-morbidities of diabetes mellitus, hypertension or cardiovascular disease are at higher risk of catching this infection as well as a severe form of infection (1). Many of these patients will also have associated CKD, so apparently CKD patients will also be at higher risk of developing this disease. While on other hand CKD patients have an underlying immunosuppressed state and may not mount an aggressive immune response to this infection, implying that they may asymptomatic or mildly symptomatic disease. In a study from Wuhan city, patients on
hemodialysis (HD) with COVID-19 had less lymphopenia, and lower serum levels of inflammatory cytokines. These patients also had milder clinical disease as compared to other patients with COVID-19 infection (1).

However, patients of CKD should be considered to be at higher risk of developing this infection and thus adequate precautions should be advised to them. They should also be advised to avoid unnecessary hospital visits, and physicians should put more emphasis on providing consults through telemedicine. In India, till date, there were no guidelines or legislation to provide consults by telemedicine. However, the Ministry of Health and Family Welfare has recently released guidelines for physicians to provide consultations through telemedicine (2). In addition, they should also be advised to take measures like social distancing, avoiding crowded places, and proper hand hygiene to prevent the chances of infection.

Many patients of CKD will experience episodes of acute kidney injury after COVID-19 infection, and the renal function will deteriorate after infection leading to acute on chronic kidney disease. Such a decline in kidney function depends on the severity of the infection. SARS-Cov-2 may affect the kidney directly through ACE2 receptors causing direct injury, glomerular injury by affecting effector T cell or immune-complex formation, and as a part of cytokine storm theory after virus-induced sepsis.

**CKD management and COVID:**
CKD patients receive multiple pills for hypertension, metabolic bone disorders, and anemia management. The most important of them are anti-hypertensives, which include calcium channel blockers, centrally acting drugs like clonidine, Beta-blockers, Alpha-blockers, and Angiotensin-converting enzyme inhibitor, and angiotensin receptor blockers. This aspect has been dealt with in detail, subsequently. In addition to this CKD patients are on various other drugs to manage their anemia, metabolic bone disease (MBD), fluid status, etc. There may be a concern whether all these drugs are safe or whether they alter the risk of developing COVID-19.

*Is there any need for changing medications for anemia management?*

Erythropoietin (EPO) is a multi-functional cytokine, which exerts erythropoietic effects but also carries anti-apoptotic and immune-modulatory activities upon binding to two distinct receptors which are expressed on erythroid, parenchymal and immune cells, respectively. The effect of erythropoietin on viral replication, particularly COVID 19, is not well studied. At present, there is no evidence to suggest stopping EPO. Oral iron therapy should be continued, and the use of Intravenous Iron should be discouraged.

Guidelines: We suggest continuing anemia therapy as before the COVID.

*Should patients continue medications for CKD-MBD:*
Medications for CKD-MBD should be continues as before unless there are specific contraindications that appear during the management of COVID 19 infection. As of date, there is no interactions or contraindications to the use of these drugs in CKD-COVID

*What about the link between NSAIDs and COVID-19?*

There are unconfirmed reports of patients who are on NSAIDs having more severe disease compared to acetaminophen/paracetamol. However, we feel that this may be because patients with more severe symptoms are likely to take NSAIDs (versus acetaminophen). This is one more reason why the CKD patients should avoid taking NSAIDs and instead should take paracetamol.

*What is the interaction between COVID 19 and the renin-angiotensin-aldosterone system (RAAS)?*

Angiotensin-converting enzyme 2 (ACE2) functions as a receptor for both Severe acute respiratory syndrome coronavirus 1 and 2 (SARS-CoV-1 and SARS-CoV-2) viruses resulting in this interaction between the RAAS through and COVID (3). COVID 19 viral S protein gains entry into the target cells by getting attached to the surface receptor called angiotensin-converting enzyme-2 (ACE-2) receptor of the cardio-pulmonary cells. As the use of ACE inhibitors/angiotensin receptor blockers (ACEI / ARB) can increase the expression of ACE-2 receptors (Figure 1), these patients may
be at higher risk of infection due to the availability of increased receptors (4, 5).

Figure 1: Interaction between RAAS, SARS-COV2 and ACEi/ARB

With evidence of higher mortality in patients of hypertension, diabetes, cardiovascular disease and old age (6), there was a hypothesis raised, whether the use of ACEi/ARB, which is common in these subsets of patients, can increase the risk and potential threat to COVID 19 infection. This had a major impact on the management of hypertension, and people were concerned regarding the use of RAAS blockers. However, there was immediate rebuttal from various societies, including the European Society of Cardiology, stating that there was no such evidence of ACE-2 activity and COVID 19 associated mortality (Figure 2). It was pointed out that there
are no data on how many of those who died with COVID 19 were on ACEi/ARBs (7).

<table>
<thead>
<tr>
<th>Society</th>
<th>Summary of recommendations</th>
<th>Last Statement Update</th>
</tr>
</thead>
<tbody>
<tr>
<td>European Society of Hypertension</td>
<td>Recommend continuing ACEIs/ARBs due to lack of evidence to support differential use in COVID-19 patients. In those with severe symptoms or sepsis, antihypertensive decisions should be made on a case-by-case basis taking into account current guidelines.</td>
<td>March 12, 2020</td>
</tr>
<tr>
<td>European Society of Cardiology Council on Hypertension</td>
<td>Strongly encourage continuing ACEIs/ARBs due to lack of evidence to support discontinuing</td>
<td>March 13, 2020</td>
</tr>
<tr>
<td>Hypertension Canada</td>
<td>Recommend continuing ACEIs/ARBs due to lack of evidence that patients with hypertension or those treated with ACEIs/ARBs are at higher risk of adverse outcomes from COVID-19 infection</td>
<td>March 13, 2020</td>
</tr>
<tr>
<td>Canadian Cardiovascular Society</td>
<td>Strongly encourage continuing ACEIs/ARBs and Angiotensin Receptor Nephylisin Inhibitors due to a lack of clinical evidence to support withdrawal of these agents</td>
<td>March 15, 2020</td>
</tr>
<tr>
<td>The Renal Association, United Kingdom</td>
<td>Strongly encourage continuing ACEIs/ARBs due to unconvincing evidence that these medications increase risk</td>
<td>March 15, 2020</td>
</tr>
<tr>
<td>International Society of Hypertension</td>
<td>Strongly recommend that the routine use of ACEIs/ARBs to treat hypertension should not be influenced by concerns about COVID-19 in the absence of compelling data that ACEIs/ARBs either improve or worsen susceptibility to COVID-19 infection nor do they affect the outcomes of those infected</td>
<td>March 16, 2020</td>
</tr>
<tr>
<td>American College of Physicians</td>
<td>Encourage continuing ACEIs/ARBs because there is no evidence linking them to COVID-19 disease severity, and discontinuation of antihypertensive therapy without medical indication could in some circumstances result in harm</td>
<td>March 16, 2020</td>
</tr>
<tr>
<td>Spanish Society of Hypertension</td>
<td>Recommend that ACEIs/ARBs should not be empirically stopped in patients who are already taking them; in seriously ill patients, changes should be made on a case-by-case basis</td>
<td>March 16, 2020</td>
</tr>
<tr>
<td>American Heart Association, Heart Failure Society of America, American College of Cardiology</td>
<td>Recommend continuing ACEIs/ARBs for all patients already prescribed them</td>
<td>March 17, 2020</td>
</tr>
<tr>
<td>European Renal Association-European Dialysis and Transplant Association</td>
<td>Recommend continuing ACEIs/ARBs in COVID-19 infection patients due to a lack of evidence to support differential use and the discontinuation of ACEIs/ARBs in COVID-19 patients</td>
<td>March 17, 2020</td>
</tr>
<tr>
<td>American Society of Pediatric Nephrology</td>
<td>Strongly recommend continuing ACEIs/ARBs until new evidence to the contrary becomes available</td>
<td>March 17, 2020</td>
</tr>
<tr>
<td>High Blood Pressure Research Council of Australia</td>
<td>Recommend continuing routine use of ACEIs/ARBs. Patients should not cease blood pressure lowering medications unless advised to do so by their physician</td>
<td>March 18, 2020</td>
</tr>
<tr>
<td>Australian Diabetes Society</td>
<td>Recommend that usual antihypertensive therapy is continued given that speculation about risk of ACE inhibitors and ARBs is purely theoretical</td>
<td>March 29, 2020</td>
</tr>
</tbody>
</table>

Figure 2: Professional Societies Recommendations on use of ACEi/ARB (Adapted from NephJC http://www.nephjc.com/news/covidace2)

It was also emphasized that being on these drugs is possible because of more comorbidities like diabetes, hypertension, kidney disease, or cardiovascular disease, which may have increased their mortality. In fact, it
was shown that COVID 19 spike protein led to the down-regulation of ACE-2 and more severe lung injury in mice that could be attenuated by the administration of an ARB (8). It was also explained that high Angiotensin II (in severe cases or in the absence of ACEI/ARB) could open up the ACE-2 receptor by unbinding of ATR-1, thereby making it available for COVID 19 to attach. These findings suggest a protective role of ARB in COVID 19 associated lung injury and give rise to the hypothesis that primary activation of the RAAS in cardiovascular patients, rather than its inhibition, renders them more prone to a deleterious outcome (6).

Anti-hypertensives other than ACEI and Angiotensin 2 receptor blocker:

**Guideline:** We suggest continuing ACEI and ARBs for anti-hypertensive and renoprotective purposes. We suggest continuing other anti-hypertensives as before unless there is some specific contraindication that appears during the infection like hypotension.

The utility of Hydroxychloroquine:

Hydroxychloroquine, which is an immunomodulator, is shown to reduce viral activity *in vitro* in SARS-CoV-2 infected Vero cells (10). In addition, Hydroxychloroquine has been shown to significantly reduce viral load in nasopharyngeal swabs in 20 French patients with COVID-19 (11). So, Hydroxychloroquine has both direct anti-viral effects and anti-inflammatory
effects. Until further evidence in form of clinical trials, it appears theoretically effective in combating severe phase of COVID-19 infection. While its role as a prophylactic therapy is uncertain, it is increasingly being advocated by many nations. Indian Council of Medical Research (ICMR) has also recommended the use of Hydroxychloroquine in selected individuals (12).

Though Hydroxychloroquine is usually safe, there are many side effects of this drug that all the physicians should be aware of. The short-term side effects include nausea, gastrointestinal disturbance, and prolongation of QT interval, while the retinal toxicity is the most dreaded complication over the long term. In addition, there may be significant drug interactions with this drug. It is also advised that the dose of the drug needs to be modified according to the degree of renal impairment to prevent the drug toxicity, although there are no well-defined recommendations according to the glomerular filtration rate.

**Conclusion**

The speculation about the ACEI / ARB use and COVID-19, at present, has no scientific basis or evidence to support its withdrawal. Various guidelines recommended that physicians should not withhold these drugs as they are beneficial and might be rather protective against serious lung complications.
in COVID 19 infections. Hydroxychloroquine may be used judiciously in CKD cases.

References


Chapter-3

Guidelines for Dialysis with Reference to COVID-19 Infection

Valentine lobo, Umesh Khanna, Mohan Rajapurkar, Tripti Khanna, Himanshu Sekhar Mahapatra, Himanshu Verma, Sanjay Kumar Agarwal-
On behalf of Covid-19 Working Group of Indian Society of Nephrology

COVID-19, a disease caused by a novel corona virus (SARS CoV-2), is currently a pandemic, which produces high morbidity in the elderly and in patients with associated comorbidities. Chronic kidney disease stage-5 (CKD-5) patients on dialysis [maintenance hemodialysis (MHD) or continuous ambulatory peritoneal dialysis (CAPD)] are also vulnerable group because of their existing comorbidities, repeated unavoidable exposure to hospital environment and immunosuppressed state due to CKD-5. These patients are therefore not only more prone to acquire infection but also develop severe diseases as compared to general population.
Patients on regular dialysis should adhere to prescribed schedule and not miss their dialysis sessions to avoid any emergency dialysis.

There will be three situations of patients who require dialysis; patients already on maintenance dialysis, patients requiring dialysis due to acute kidney injury (AKI) and patients critically ill requiring continuous renal replacement therapy (CRRT).

General Guidelines for Administration

1. State/UT should identify and earmark at-least one hemodialysis facility with adequate number of dialysis machines, trained staff and other support equipment as preparatory fixed-point dialysis unit in case of rise of Covid-19 epidemic.

2. Health departments may issue directives to the district administrations allowing easy movements of these patients (with one attendant) to dialysis facility. Patients who do not have private vehicles, government run transport system should be organized for facilitating transport of these patients. Patients should use their hospital papers as pass to commute to the dialysis unit.
3. District administration should ensure that service providers for the dialysis consumables, both for MHD and CAPD should be allowed to deliver the material to the hospital or home as the case may be.

General Guidance for Dialysis Unit

1. Adequate medical supplies such as dialysate, dialyzers and tubing, catheters, fistula needles, disinfectant and medicines etc. must be ensured in adequate quantity

2. A sign board should be posted prominently in the local understandable language as well as Hindi and English asking patients to report any fever, coughing or breathing problem in dialysis unit and waiting area. The information including images for education can be obtained on the International Society of Nephrology website https://www.theisn.org/covid-19

3. All hemodialysis units should educate their personnel in hemodialysis units; including nephrologists, nurses, technicians, other staff and all patients undergoing MHD along with their care givers about COVID 19

4. We recommend that All universal precautions must be strictly followed.

5. All staff should strictly follow hand hygiene (seven steps) with soap and water for 20 second before handling any patient and in between two patients. If soap and water are not readily available, use a hand sanitizer
that contains at least 60% alcohol. If hands are visibly soiled or dirty, they should be first washed with soap and water and then an alcoholic hand rub used. Avoid touching your eyes, nose, and mouth with unwashed hands.

6. Medical and support staff treating infected patients should be monitored for COVID infection at the dialysis facility and should take necessary action if found infected.

7. Dialysis units should organize healthcare workers shift duties in a way that work of dialysis unit is not affected.

8. All hemodialysis units should be aware of the testing, triage and notification policy recommended by the local health authorities, regional medical councils and the Union Ministry of health and Family welfare.

9. Some of the dialysis unit staff should be trained for donning and doffing of Personal Protective Equipment (PPE) so that they can be used for treatment of COVID-19 positive patients.

10. All staff should be trained for cough etiquette, hand hygiene and proper use and disposal of mask, gown and eye glasses and the need to protect themselves.

11. All patients with suspected COVID-19 be tested as per the local health authorities’ guidelines.

12. Patients with suspected or positive COVID-19 should be referred to COVID-19 care team as per local guidelines.
GUIDELINES FOR HEMODIALYSIS

I. For Patients

a. Before Arrival to Dialysis Unit

1. All units should instruct their patients to recognize early symptoms of COVID-19 (Recent onset fever, Sore throat, Cough, recent Shortness of breath/dyspnea, without major interdialytic weight gain, rhinorrhea, myalgia/bodyache, fatigue and Diarrhea) and contact dialysis staff before coming to dialysis center. The unit needs to make necessary arrangement for their arrival in the screening area.

2. Patients, who are stable on MHD may be encouraged to come to the unit alone without any attendant

b. Screening Area

1. We recommend that dialysis unit should have a designated screening area, where patients can be screened for COVID-19 before allowing them to enter inside dialysis area.
Where this is not possible, patients may wait away from the dialysis unit until they receive specific instructions from the unit staff.

2. The screening area should have adequate space to implement social distancing between patients and accompanying persons while waiting for dialysis staff. In screening area, every patient should be asked about:
   - Symptoms suspected of COVID-19 as above.
   - History of contact with a diagnosed case of COVID 19
   - History of contact with person who has had recent travel to foreign country or from high COVID-19 prevalence area within our country as notified by the Central and state governments respectively.

3. Patients with symptoms of a respiratory infection should put on a facemask before entering screening area and keep it on until they leave the dialysis unit. Dialysis unit staff should make sure an adequate stock of masks is available in screening area to provide to the patients and accompanying person if necessary.

c. Inside Dialysis Unit
1. Suspected or positive COVID-19 patients should properly wear disposable three-layer surgical mask throughout dialysis duration.

2. Patients should wash hands with soap and water for at least 20 seconds, using proper method of hand washing. If soap and water are not readily available, a hand sanitizer containing at least 60% alcohol can be used.

3. Patients should follow cough etiquettes, like coughing or sneezing using the inside of the elbow or using tissue paper. This may be displayed in pictures which are available from the CDC website [https://www.cdc.gov/coronavirus/2019-ncov/healthcare-facilities/dialysis.html](https://www.cdc.gov/coronavirus/2019-ncov/healthcare-facilities/dialysis.html)

4. Patients should throw used tissues in the trash. The unit should ensure the availability of plastic lined trash cans appropriately labeled for disposing of used tissues. The trash cans should be foot operated ideally to prevent hand contact with infective material.

II. For Dialysis Staff
a. Screening Area

1. The unit staff should make sure an adequate stock of masks is available in screening area to provide to the patients and accompanying person if necessary.

b. During Dialysis

1. We suggest to ensure that a patient and staff in a unit does not become the source of an outbreak.

2. Each dialysis chair/bed should have disposable tissues and waste disposal bins to ensure adherence to hand and respiratory hygiene, and cough etiquette and appropriate alcohol-based hand sanitizer within reach of patients and staff.

3. Dialysis personnel, attendants and caregivers should also wear a three-layer surgical facemask while they are inside dialysis unit.

4. Ideally all patients with suspected or positive COVID-19 be dialyzed in isolation. The isolation ideally be in a separate room with a closed door, but may not be possible in all units. The next most suitable option is the use of a separate shift, preferably the last of the day for
dialyzing all such patients. This offers the advantage of avoiding long waiting periods or the need for extensive additional disinfection in between shifts. The next suitable option is to physically separate areas for proven positive and suspected cases. Where this is also not possible, we suggest that the positive or suspected patient may be dialyzed at a row end within the unit ensuring a separation from all other patients by at least 2 meters.

5. Staff caring for suspected or proved cases should not look after other patients during the same shift.

6. Dialysis staff should use of all personal protective equipment (PPE) for proven or strongly suspected patients of COVID-19. We suggest that isolation gowns should be worn over or instead of the cover gown (i.e., laboratory coat, gown, or apron with incorporate sleeves) that is normally worn by hemodialysis personnel. If there are shortages of gowns, they should be prioritized for initiating and terminating dialysis treatment, manipulating access needles or catheters, helping the patient into and out of the station, and cleaning and disinfection of patient care equipment and the dialysis station. We suggest that sleeved plastic aprons be used in addition to and not in place of the PPE recommended above.
7. We suggest separating equipment like stethoscopes, thermometers, Oxygen saturation probes and blood pressure cuffs between patients with appropriate cleaning and disinfection in between shifts.

8. Stethoscope diaphragms and tubing may be cleaned with an alcohol-based disinfectant including hand rubs in between patients. As most NIBP sphygmomanometer cuffs are now made of rexine they may also be cleaned by alcohol or preferably hypochlorite-based solutions however the individual manufacturers manuals may be referred to.

9. Staff using PPE should be careful for following issues:
   - While using PPE, they will not be able to use wash room so prepare accordingly
   - After wearing eye shield, moisture appears after some time and visibility may become an issue. Therefore, machine preparation can be done in non-infected area before shifting to near the patient
   - If dialysis is to be done bed-side in the hospital, portable RO should be properly disinfected with hypochlorite solution between use of two patients

DISINFECTION AND DISPOSAL PRACTICES IN DIALYSIS UNIT
- We recommend that bed linen be changed between shifts and used linen and gowns be placed in a dedicated container for waste or linen before leaving the dialysis station. Disposable gowns should be discarded after use. Cloth gowns should be soaked in a 1% hypochlorite solution for 20 minutes before sluicing and then be transported for laundering after each use.

- We recommend that inside unit, clean and disinfect frequently touched surfaces at least thrice daily and after every shift. This includes Bedside tables and lockers, dialysis machines, doorknobs, light switches, countertops, handles, desks, phones, keyboards, toilets, faucets, and sinks.

- We recommend that solutions for disinfection be composed either of hypochlorite, alcohol, formaldehyde or glutaraldehyde for disinfection of surfaces in accordance with the manufacturer’s instructions. A more complete list of all disinfectants approved by the CDC is available on the CDC website [https://www.cdc.gov/coronavirus/2019-ncov/infection-control/control-Recommendations.html](https://www.cdc.gov/coronavirus/2019-ncov/infection-control/control-Recommendations.html). Almost all common disinfectant solutions are effective in killing the virus on surfaces, the key is effective and frequent cleaning.
**Bleach solution**

- Mix 1 liter of Medichlor with 9 liters of water. This solution can be used for up to 24 hours after which it should be discarded and a fresh solution prepared.
- As an alternative, 10 Grams of household bleaching powder can be dissolved in a liter of water and used for a period of 24 hours.

**Alcohol based solutions**

- Ensure solution has at least 60% alcohol. Appropriate commercially available solutions include Aerodosin a mixture of isopropanol, glutaraldehyde and ethanol or lysoformin a mixture of formaldehyde and glutaraldehyde

- Wear unsterile but clean disposable gloves when cleaning and disinfecting surfaces. Gloves should be discarded after each cleaning. If reusable gloves are used, those gloves should be dedicated for cleaning and disinfection of surfaces for COVID-19 and should not be used for other purposes. Clean hands by above method immediately after gloves are removed.
For soft (porous) surfaces such as carpeted floor, rugs, and drapes, remove visible contamination if present and clean with appropriate cleaners indicated for use on these surfaces. After cleaning launder items as appropriate in accordance with the manufacturer’s instructions. If possible, launder items using the warmest appropriate water setting for the items and dry items completely,

- Wear disposable gloves when handling dirty laundry from an ill person and then discard after each use. Do not shake dirty laundry. This will minimize the possibility of dispersing virus through the air.

- Clean and disinfect clothes buckets or drums according to guidance above for surfaces. If possible, consider placing a bag liner that is either disposable (can be thrown away) or can be laundered.

**DIALYSIS PATIENT WITH ACUTE KIDNEY INJURY**

A small proportion of patients (~5%) of COVID develops AKI. The disease is usually mild but a small number may require RRT. In addition, even smaller proportion of patients with secondary bacterial infection will have
septic shock, drug nephrotoxicity or worsening of existing CKD severe enough to require RRT

- **We suggest** that all modalities of RRT may be used for patients with AKI depending on their clinical status.
- Patient admitted in other ward of the hospital with AKI should be preferably given bed-side dialysis rather than shifting patient in main dialysis unit.
- In such situation portable reverse osmosis water in a tank will serve the purpose for the dialysis.
- If more dialysis are expected in selected area, dialysis machine may be left in the same area for future dialysis.

CONTINUOUS RENAL REPLACEMENT THERAPY (CRRT)

- CRRT machines are free standing and can function anywhere in the hospital using sterile bagged replacement fluid and dialysate, but operating costs are high.

OTHER EXTRACORPOREAL THERAPY FOR COVID-19
- Use of cytokine removal therapies with Cytosorb, Oxiris and other similar devices is unproven and is not recommended except in the context of a clinical trial.
- Cytokine storm associated with elevated levels of IL-6, IL-18 and IFN gamma are associated with more severe disease and higher mortality. Extracorporeal therapies using high volume hemofiltration or adsorption to decrease cytokine levels may theoretically be expected to confer benefit and 1 study of HVHF at 6L/hr showed cytokine reduction and improvement in SOFA scores in septic patients.

**PERITONEAL DIALYSIS**

1. Patients already on CAPD
   - Patients who are already receiving peritoneal dialysis (PD) treatment have the relative advantage over patients who are receiving hospital or satellite-based haemodialysis treatment as they will not be exposed to hospital environment. This will reduce their exposure to infection. However, they should arrange their delivery of supply well in time to avoid missing dialysis exchanges.
   - Used dialysis bags and tubing should be properly disposed using 1% hypochlorite solution first and disposed in a sealed bag. Used dialysis fluid should be drained in the flush
2. New patient planned for CAPD

- It will be difficult to maintain a service that can commence new patients on PD, mainly through a lack of healthcare worker to insert PD catheter and to provide the intensive training required. Therefore, initiation of new patient should be avoided.

3. Acute PD

- Use of acute peritoneal dialysis can be lifesaving and should be used as and when required and, in the setting, where hemodialysis facility is not available. Health care worker should use all precaution while initiating acute PD and discard used consumable properly.

PERSONAL PROTECTIVE EQUIPMENTS (PPE)

Personal protective equipment must be used while dialyzing COVID-19 positive patients. These include:

- Shoe covers
- Gown
- Surgical cap or hood
- Goggles or eye shields
- Mask: Ideally all masks should be N95 respirators with filters. However, as the life of such masks is approximately 6-8 hours and
they can be uncomfortable over a long term and are also in short supply they should be prioritized for aerosol generating procedures, namely intubation, open suction and bronchoscopy. Surgical triple layer masks and cloth masks can be used as alternatives for all other procedures.

- Surgical gloves.

The correct method of donning and doffing personal protective equipment’s (PPE) can be viewed on YouTube at https://www.youtube.com/watch?v=kKz_vNGsNhc. However, it is always better to give hand-on training of donning and doffing to staff who is going to handle suspected or positive patients.

Chapter-4:

Transplant specific guidelines during covid-19 outbreak


Organ transplant recipients are at risk for more severe COVID-19 if they get SARS CoV-2 viral infection. Furthermore, there is a potential risk of
infection transmission from the donor to recipient through organ transplantation. Also, there are issues in recipient and donor selection for transplant. In view of these issues and organ transplants at the time of COVID-19 pandemic should be undertaken with caution and should be done only at the center where facilities of management of COVID-19 patients are available.

1. The pre, peri, and post-transplant areas, including the operation theaters need to be specifically earmarked for this purpose.

2. Staff involved in the care of transplant patients may not be involved in the care of other patients.

3. There has to be adequate availability of PPE for the care of these patients

4. The center should not be one earmarked for the treatment of COVID-19 patients and needs to have protocols for patient movement around the hospital to prevent the nosocomial acquisition of COVID

1. **DeceasedDonors Transplants**

Following individuals with any of the following criteria, who are potential deceased donor should NOT be accepted as deceased donors:

   a. **Epidemiological criteria** –
      - International travel in the last 14 days before the onset of current
event leading to brain stem death
- Contact in last 14 days before the onset of current event leading to brain stem death with a confirmed case of COVID-19 or a healthcare worker with direct patient contact

b. Clinical criteria –
- Where the cause of death was due to unexplained respiratory failure
- where there was a history of Fever or Acute respiratory infection (e.g., shortness of breath, cough, sore throat) with or without fever.
- Severe bilateral community-acquired pneumonia in the absence of any other cause

c. Laboratory criteria -
- Confirmed Covid-19 positive case or test found positive while donor workup is being done

Routine testing of deceased donors
Routine COVID-19 (SARS-CoV-2) viral testing should be undertaken in all potential deceased donors within 72 hours prior to donation, both for assessment of donor fitness as well as for improving safety of staff
involved in transplantation. Even though the potential deceased donor is fit to donate organs, every hospital and organ transplant system must balance between care of other COVID-19 positive patients in their healthcare setting against the organ transplant vis-a-vis availability of resources for safely conducting the organ transplant.

2. **Living related Transplants**

The living donor transplant programme may be temporarily suspended in line with the MoHFW’s advisory for Hospitals and Medical Institutions dated 3rd March 2020, accessible at [https://www.mohfw.gov.in/pdf/AdvisoryforHospitalsandMedicalInstitutions.pdf](https://www.mohfw.gov.in/pdf/AdvisoryforHospitalsandMedicalInstitutions.pdf).

However, if a transplant is being done in view of the emergency medical need of the recipient, following individuals, who are living donor should NOT be accepted as donors:

- **Epidemiological criteria** –
  - International travel in the last 14 days
  - Contact in last 14 days with a confirmed case of COVID-19 or a healthcare worker with direct patient contact
b. **Clinical criteria** –

- History of Fever or Acute respiratory infection (e.g., shortness of breath, cough, sore throat) with or without fever.

c. **Laboratory criteria** -

- Confirmed Covid-19 positive or test found positive while donor workup is being done

RT-PCR test of potential donors should be undertaken as suggested for deceased donors

**Emergency lifesaving Transplantation**

In case a transplant is to be done due to the emergency need of the recipient, it should be performed with an appropriate assessment of COVID-19 infection in the recipient. Further, appropriate counseling of both the donor and recipient, as well as their families, should be done, and a high-risk informed consent was taken before proceeding with the transplant.

3. **Transplantation Recipients**

Similar to the general population, transplant recipients should also strictly follow the travel advisories issued by the various ministries of the
Government of India from time to time. They should take extra precautions as they have a risk of developing severe COVID-19 disease if they acquire SARS CoV-2 viral infection.

4. **Transplant Recipients returning from abroad**

All transplant recipients who have been exposed to a confirmed or suspected COVID-19 patient within the last 14 days or who have returned from nations with COVID-19 outbreaks should undergo quarantine and isolation for 14 days and should be tested for SARS CoV-2 infection.

If any transplant recipient has fever, cough or breathing difficulty, they should immediately call their respective transplant centres. All transplant centres must have guidelines in place specifying which patients need testing and inpatient management and which patients can stay at home with close follow up with various means like mobile and email etc.

If they are advised to visit the hospital, they should wear a mask while coming to hospital premises. In case of a medical emergency like difficulty in breathing, they should report to the nearest emergency department.

5. **Treatment and modification of immunosuppression**
There are two issues of management of organ transplant patients with COVID-19

a. Management of COVID-19 in transplant patient

There is scarcity of data and consensus on effective treatments of COVID-19 as such and more so in transplant patients. Few centres have tried antivirals, hydroxychloroquine and macrolides in COVID-19 patients with variable results. However, as of now, there is no treatment approved by the Central Drugs Standard Control Organization (CDSCO) or Foods and Drug Administration (FDA) for COVID-19.

b. Handling of immunosuppressive medicines with COVID-19

There is no consensus regarding modification in the immunosuppressive regimen of transplant recipients with COVID-19. The dose adjustment has to balance the infection control and the organ rejection. However, there is overall agreement of stopping antimetabolite drugs and decrease calcineurin inhibitors by 50%. Steroid should be continued on same doses. (Massachusetts General Hospital COVID-19 Treatment Guidance).
6. Post-transplant follows up measures

Transplant patients are at risk for severe COVID 19 if they acquire infection due to their immunosuppressed state. They may not manifest symptoms like general population. Fever may be absent as reported from study from China. Transplant units are advised to consider ways to limit hospital attendance for patients, such as:

1. Rescheduling non urgent out-patient appointments
2. Virtual or telemedicine or telephonic appointments
3. Home delivery of immunosuppression if feasible

Patients with stable graft function and adequate drug supply can avoid routine follow up visits to transplant hospitals.

7. Tissue Transplantation

At present, there is no evidence to suggest the transplant of Coronaviruses by blood transfusion.

Tissue and Eye Donation Criteria:

The deferral will be based upon infection status in the last 28 days before donation:
- A positive test for COVID-19
- Symptoms consistent with COVID-19 infection (e.g., unexplained fever, cough, shortness of breath) in a patient with suspected COVID-19 infection
- Donor defined as a Person under Investigation (PUI)
- Fever with severe acute lower respiratory illness (e.g., pneumonia, ARDS)

Additionally, the deferral will be based upon exposure in the last 28 days before donation:
- Close contact with a person who has confirmed COVID-19
- Close contact with a Person under Investigation (PUI) for COVID-19
- International travel

8. Personnel Precautions working in the program:
The health and safety of all the healthcare workers in the transplant program is of paramount importance. Transplanting hospitals are advised not to expose any of their staff if there is even the slightest risk of virus transmission from both epidemiological and clinical criteria.

It is likely that this pandemic may require the current resources to be utilized elsewhere, hence there is even more reason to practice caution.
when deciding on proceeding with donation and transplantation. It is with this in mind that all elective live living kidney and liver transplant should be postponed.

**General principles for handling SARS CoV-2 infection in transplant center**

1. Personnel should follow all hospital-based protocols for the isolation and management of COVID-19 patients.
2. Any questions or concerns about the infectious status of a potential donor should be referred to your Medical Director / Organ sharing body for further guidance.
3. If a donor is being ruled-out due to hospital considerations, local or national health authorities, be sure to record the information. This information must be documented clearly and accurately. Documentation should include transmittable disease status, COVID-19 testing status/high-risk suspicion and/or individual organ suitability.
4. Screening questions should reflect updated COVID-19 national guidelines

Please refer to below links for more information:

- Coronavirus (SARS-CoV-2) causing COVID-19: Information for donation and transplant professionals Version 1 dated 18-3-2020
– BY Donate Life & The Transplant Society of Australia & New Zealand

- [https://www.mohfw.gov.in/pdf/AdvisoryforHospitalsandMedicalInstitutions.pdf](https://www.mohfw.gov.in/pdf/AdvisoryforHospitalsandMedicalInstitutions.pdf)
- Guidelines for Liver Transplantation and COVID-19 Infection, as received from the President, Liver Transplant Society of India (LTSI) via official correspondence on 23-03-2020.

**Disclaimer:**

The current outbreak is unpredictable. If widespread community-transmission occurs, healthcare infrastructure and capacity issues may have further impact on donation and transplantation. These recommendations may require regular updates to account for the changing epidemiology and new information regarding treatment and testing. All
transplant units must be aware of national and local guidance for managing patients with COVID-19.

No suit or legal proceedings shall lie against any person for anything done or intended to be done in good faith under this suggestions/advisory unless proved otherwise.

26th March, 2020

Chapter-5

Glomerular diseases on immunosuppression

Sanjeev Gulati, Narayan Prasad, Manisha Sahay on behalf of COVID-19 Working Group of Indian Society of Nephrology

Patients with Nephrotic Syndrome and Glomerulonephritis like Systemic Lupus Erythematosus (SLE), ANCA associated Glomerulonephritis and patients with other glomerular diseases who are on moderate to high
doses of immunosuppression are at an increased risk of COVID because of their immunosuppressed state. However, there are no studies to quantify the increase in risk in relation to the amount of immunosuppressant medications or their duration of use. We acknowledge that presently there is no data on this aspect, and what is being suggested is based on logic and extrapolation of evidence from other infections.

A simple way to evaluate these patients is to classify them into newly diagnosed patients and those on follow up on immunosuppressant medications.

1. For newly diagnosed patients:
   a. **We suggest** that newly diagnosed patients with Idiopathic nephrotic syndrome due to MCD, FSGS IgA Nephropathy, and Membranous Nephropathy as well as patients with SLE, ANCA associated GN with normal renal functions should be managed conservatively with diuretics, salt restriction and use of ACEI or ARBS. Unless there is a progressive deterioration of renal functions, steroids and immunosuppressive agents should be withheld. At the same time, these patients should receive the Pneumococcal vaccine to reduce the chances of secondary Pneumococcal pneumonia.
b. We suggest using immunosuppression if there is a rapid worsening of kidney functions after COVID testing and explaining the risk-benefit ratio to the patient.

2. For a Follow-up Patients on Immunosuppression:  These patients may be in the induction phase or in the maintenance phase

- **Induction phase:**

As per the present evidence, patients should plan to complete standard induction medication unless directed otherwise by their renal team. There is currently no policy that asymptomatic patients should be swabbed for COVID-19 before each dose of intravenous induction therapy. As testing becomes more widely available, this policy may change, but current studies suggest, patients with early disease may have negative nasal swabs in 30% of cases. All patients should be triaged on arrival before any infusion to exclude symptoms of active COVID-19 infection and to check for raised temperature. Those who are considered to have a possible infection can then be seen in a separate area away from other at-risk patients and appropriate treatment plans made. If nephrology departments are unable to deliver intravenous induction medication due to staff shortages or patients being unable to attend hospital, **we suggest** the following options:
- In vasculitis: If it is possible for the patient to continue hospital visits (and recognizing the risks during COVID-19) and given the risks of uncontrolled disease, we suggest to continue the ongoing use of IV cyclophosphamide-based induction regimens as compared to oral ones. However, rituximab affords fewer hospital visits and less monitoring.

- If the patient is unable to travel because of lockdown and transportation issues or intravenous infusions are not available, we suggest switching over to oral induction. The treating team should closely monitor this. As it is has been shown that oral cyclophosphamide is an alternative to IV cyclophosphamide (but is associated with higher infective complications).

- We suggest using Oral MMF (mycophenolate mofetil) in patients with low risk of relapse with GFR >15mls/min and without rapidly deteriorating renal function. It also requires concomitant steroid dosing, although high dose steroids should be avoided if possible in COVID-19.

- In SLE, oral MMF can be used as a well-established alternative to iv cyclophosphamide in induction therapy.

- If possible, to administer rituximab, it may be worth considering the Rituxilup protocol, which is steroid-sparing. In general, to reduce
infection risk, we suggest minimizing steroids promptly in line with protocols in the PEXIVAS trial and the Aura-LV Trial.

We recommend a risk stratification approach to help manage these patients. Some patients, particularly those on steroids, intravenous cyclophosphamide, and biologics, will be significantly immunosuppressed and should, therefore, be considered ‘high risk’. This is particularly true in the induction phase of their treatment. Others on steroid monotherapy may be at intermediate risk.

- Maintenance Phase

If doing well, all patients should continue to take their maintenance medication unless directed otherwise by their treating team. Patients should stay on their maintenance immunosuppression and steroids, provided they are infection-free.

Immunosuppressive therapy needs to be reviewed on a case by case basis balancing the risk of inadequately treated disease, or acute relapse, against the risk of the effect of COVID-19 infection in the individual patient. Patients on long term glucocorticoids (steroids, prednisolone) SHOULD NOT stop these abruptly. Patients receiving hydroxychloroquine SHOULD CONTINUE this as it may afford some protection against COVID-19.
In patients who have had prolonged disease remission and the risk of severe COVID-19 infection is felt to be high, the nephrologist may consider modifying maintenance immunosuppression regimens on a case by case basis. In the case of long acting rituximab maintenance regimens, delaying intervals between rituximab infusions could be considered for patients where the risk of disease progression or flare is deemed low as in membranous nephropathy and the risk of adverse outcomes with COVID-19 infection is high. Lower doses of rituximab may be considered given evidence from the Mainritsan study suggesting equivalent efficacy. Children with idiopathic nephrotic syndrome who are on alternate day prednisone and develop symptoms of upper respiratory tract infection (URTI) should not be switched to daily prednisone until symptoms of URTI subside.

Where standard immunosuppression protocols are modified on a balance of risk, we recommend to optimize surveillance for relapse with increased clinical assessment, autoantibody screening and lymphocyte subset analysis where possible.

**Policy on isolation for patients with glomerular diseases**

**We suggest** that these patients should be risk-stratified into the following three groups:

**Group A (High Risk):**
These patients are at the highest risk because of concurrent use of immunosuppressive agents. They should all be advised to self-isolate for at least 12 weeks.

These include the following groups of patients who:

(1) Are currently on intravenous immunosuppressive cyclophosphamide, rituximab or other biologics within the last six months

(2) Are currently on oral Cyclophosphamide or MMF

(3) Have received a Steroids in a dose of $\geq$ prednisone 20mg/day or 35mg/m2/day for $>4$ weeks in the last 6 months

(4) Have received 2 immunosuppressants: $>5$ mg/day, or $>0.25$mg/kg/day, prednisolone (or equivalent) for $>4$ weeks plus at least one other immunosuppressive medication within the last 6 months

(5) Have current nephrotic range proteinuria or who have a history of frequently relapsing nephrotic syndrome.

(6) Have an overall high cumulative burden of immunosuppression (IS) over a number of years even if their current IS is in stable maintenance phase e.g. patients who have received repeated courses of cyclophosphamide/biologics/or repeated high dose corticosteroids
(7) Are currently on stable (possibly modest) maintenance IS but whose additional comorbidities make them susceptible to a severe course in COVID-19 – (a) age > 70 years (b). Those with any non-autoimmune underlying co-morbidity of `COAD, CVD, hypertension, or diabetes mellitus

(8) Have CKD stage 3 or above

(9) Have previously manifested adverse infectious complications of immunosuppression

(10) Those who have received plasmaphresis in last 6 weeks

Group B (intermediate risk):

We suggest that these patients need not to self-isolate but may be moved into Group A at a later stage as more data emerges. These include the following patients:

(1) Those with well-controlled disease activity and no co-morbidity are on a single oral immunosuppressive drug. This group would
consist of most children with idiopathic nephrotic syndrome who are frequent relapser or steroid-dependent

(2) Those who, despite completing biologic induction treatment like rituximab more than 6 months previously and remain B cell deplete.

(3) Patients who are in remission on low dose prednisone. We recommend not to stop medications as this can lead to the relapse of the disease or nephrotic syndrome.

**Group C**

We suggest that these patients may not require self-isolation in the first instance but should follow all hygiene measures listed below. These include:

(1) Children with idiopathic nephrotic syndrome who are on Levamisole or low dose alternate-day prednisone.

(2) Children with idiopathic Nephrotic syndrome who are infrequent relapsers.

(3) Patients < 60 years who are generally well and whose disease (SLE, AAV, MCD, FSGS, Membranous Nephropathy, or IgA Nephropathy) have been stable for > 6 months and off immunosuppression.

(4) SLE patients who are on hydroxychloroquine alone.

The following are some FAQs on this topic.
What are the special precautions to be taken by the patient and his family?

We suggest that patient and his immediate family members take the following precautions to prevent or delay the spread of the coronavirus and limit his personal risk of exposure to it.

- **Wash your hands frequently.**
  - Regularly and thoroughly wash your hands with soap and water for at least 20 seconds, especially after using the washroom, blowing your nose, coughing, or sneezing, or having been in a public place.
  - If soap and water are not available, use a hand sanitizer that contains at least 60% alcohol.
  - Why? The virus can be transferred in bodily fluids, including saliva and stool. Washing your hands with soap and water or using alcohol-based hand sanitizer kills viruses that may be on your hands.

- **Avoid touching your eyes, nose, and mouth.**
  - Why? Hands touch many surfaces and can pick up viruses. Once contaminated, hands can transfer the virus to your eyes, nose, or mouth. From there, the virus can enter your body and can make
you sick. If possible, all right-handed persons should use the left hand for such activities.

**Keep space between yourself and others.**

- Maintain at least 3 feet of distance between yourself and anyone who is coughing or sneezing.
- Why? When someone coughs or sneezes, they spray small liquid droplets from their nose or mouth, which may contain the virus. If you are too close, you can breathe in the droplets, including the COVID-19 virus if the person coughing has the disease.

**Practice good respiratory hygiene.**

- Make sure you, and the people around you, follow good respiratory hygiene. This means covering your mouth and nose with your bent elbow or tissue when you cough or sneeze. Then dispose of the used tissue immediately.
- Why? Droplets spread the virus. By following good respiratory hygiene, you protect the people around you from viruses such as cold, flu, and COVID-19.

**Clean and disinfect your home.**

- Practice routine cleaning of frequently touched surfaces (for example: tables, doorknobs, light switches, handles, desks, toilets, faucets, sinks & cell phones) using a regular household cleaning spray or wipe.
Why? Current evidence suggests that novel coronavirus may remain viable for hours to days on surfaces made from a variety of materials. Cleaning and disinfection is a best practice measure for the prevention of COVID-19 and other viral respiratory illnesses in households and community settings.

**Avoid crowds as much as possible, cruise travel, and any non-essential air travel.**

- Your risk of exposure to respiratory viruses like COVID-19 may increase in crowded, closed-in settings with little air circulation if there are people in the crowd who are sick.

During a COVID-19 outbreak in your community, **stay home as much as possible** to further reduce your risk of being exposed.

Please ensure you remain well hydrated as per your fluid targets

**Do not stop your medication.** Some drugs you have may even have beneficial effects on a virus infection.

**Have an extra supply of medication** so that there is no discontinuation because of shortage

**Should You continue your routine follow up?**

Yes, because of the need to optimize immunosuppression you should continue to be in touch with your treating team. However, we suggest that **Avoid hospital visits and**, instead, use Teleconsults with your
nephrologist for triaging. If going to the hospital, you should minimize sitting in waiting rooms and time spent in hospitals as much as possible.

**Are there any drugs to be avoided?**

Yes, there are some preliminary data that patients who are on NSAIDs may have a poorer outcome in case they develop COVID infection. Hence in case of flu-like symptoms, they are advised to take paracetamol.

We suggest patients should continue ACEI or ARBS. Although there has been a concern regarding the use of ACEI and ARBS, it is believed that there is insufficient data at present to suggest withholding these agents. The benefit of antiproteinuric effect and blood pressure control outweighs the theoretical risks that may appear. Various societies, including the European Society of Cardiology, have come out with position statements stating that there was no such evidence of ACE-2 activity and COVID 19 associated mortality

**What are the Special issues for Children?**

COVID-19 may cause pneumonia and heart problems so call immediately if your child develops respiratory symptoms beyond a mild cough.

Symptoms of COVID-19 infections are similar to those of a lower respiratory infection.

Red flag signs
Use the following guidelines to determine whether or not your child needs medical care:

- Respiratory symptoms beyond a mild cough: difficulty breathing, rapid or deep breathing, or a severe cough
- Shortness of breath from continued coughing
- Refusing liquids with decreased urine frequency
- Crying without the ability to be consoled
- Fever that is not responsive to fever-reducing medications
- Behavior that is not normal for your child

Bringing your child to an ER or hospital “to get tested” or for minor symptoms is currently not recommended since many sites are not offering testing, and there is a risk of exposure to COVID-19 and other serious infections.

These recommendations are and will remain dynamic and change as new data emerge. For the most up-to-date information, refer to your local government’s website, and guidelines from the ICMR for high-risk populations and children.

What about those who become COVID positive?

- Reduction of IS ie reducing steroids to 50% and stopping antimetabolites if patient is infected
Ritonavir/Lopinavir used for treatment in some studies interfere with metabolism of CNI and mTOR and increase their levels and may cause toxicity. Hence should be avoided.

References:


Chapter-6:

**Anti-corona vaccines and drugs - current scenario**

Edwin Fernando, Sishir Gang, and Arpita Roy Chaudhary on behalf of COVID-19 Working Group of Indian Society of Nephrology

In late December 2019, an outbreak of an emerging disease (COVID-19) due to a novel coronavirus (named SARS-CoV-2 latter) started in Wuhan, China, and rapidly spread in China and outside. The WHO declared the epidemic of COVID-19 as a pandemic on March 12th 2020. The overall case-fatality rate is about 2.3% but reaches 8.0% in patients aged 70 to 79 years and 14.8% in those aged >80 years.

No therapeutics have yet been proven effective for the treatment of severe illness caused by SARS-CoV-2. Infected patients should receive supportive care to help alleviate symptoms. Vital organ function should be supported in severe cases.

**VACCINES**


No vaccine is currently available for SARS-CoV-2.

Avoidance is the principal method of deterrence.

A phase 1 clinical trial is now planned for an experimental vaccine against SARS-CoV-2, mRNA-1273 by Moderna.

Numerous collaborative efforts to discover and evaluate effectiveness of antivirals (eg, remdesivir), immunotherapies (eg, hydroxychloroquine, sarilumab), monoclonal antibodies, and vaccines have rapidly emerged.

**ANTIVIRAL THERAPY**

**Lopinavir/Ritonavir**

The guidelines of the Chinese National Health Commission recommend aerosolized inhalation of interferon and lopinavir/ritonavir. (1)

The specific therapeutic value and safety of lopinavir/ritonavir in patients with COVID-19 are under investigation.

In a randomized, controlled, open-label trial of hospitalized adults (n=199) with confirmed SARS-CoV-2 infection, recruited patients had an oxygen saturation of 94% or less on ambient air or PaO2 of less than 300 mm Hg and were receiving a range of ventilatory support modes (eg, no support, mechanical ventilation, extracorporeal membrane oxygenation [ECMO]). These patients were randomized to receive ritonavir/lopinavir 400 mg/100 mg PO BID for 14 days added to standard care (n=99) or standard care alone (n=100). Results showed that time to clinical improvement did not differ between the two groups (median, 16 days). The mortality rate at 28
days was numerically lower for lopinavir/ritonavir compared with standard care (19.2% vs 25%) but did not reach statistical significance. In hospitalized adult patients with severe Covid-19, no benefit was observed with lopinavir-ritonavir treatment beyond standard care. Future trials in patients with severe illness may help to confirm or exclude the possibility of a treatment benefit.(2)

An editorial accompanies this study that is informative in regard to the extraordinary circumstances of conducting such a study in the midst of the outbreak.(3)

**Remdesivir**

The broad-spectrum antiviral agent remdesivir (GS-5734; Gilead Sciences, Inc) is a nucleotide analog prodrug. Several phase 3 clinical trials are underway for testing remdesivir for use in COVID-19 in the United States, South Korea, and China.

An in vitro study showed that the antiviral activity of remdesivir plus interferon beta (IFNβ) was superior to that of lopinavir/ritonavir (LPV/RTV; Kaletra, Aluvia; AbbVie Corporation). Prophylactic and therapeutic remdesivir improved pulmonary function and reduced lung viral loads and severe lung pathology in mice, whereas LPV/RTV-IFNβ slightly reduced viral loads without affecting other disease parameters. Therapeutic LPV/RTV-IFNβ improved pulmonary function but did not reduce virus replication or severe lung pathology (4)
Successful treatment with remdesivir has been reported in a patient with COVID-19; a clinical trial on the efficacy of remdesivir in patients with COVID-19 is currently underway in China (NCT0425266; NCT04257656) and is expected to be completed in April 2020.

**Chloroquine**

Chloroquine phosphate has been shown to have some efficacy against COVID-19–associated pneumonia in multicenter clinical trials conducted in China.(5) According to a consensus statement from a multicenter collaboration group in China, chloroquine phosphate 500-mg twice daily in tablet form for ten days may be considered in patients with COVID-19 pneumonia(6) Wang et al. reported that chloroquine effectively inhibits SARS-CoV-2 in vitro.(7)

On 20th March 2020, the ministry of health and family welfare has suggested the use of chloroquine in the following circumstances

1. Asymptomatic health care workers involved in the care of suspected or proven cases of COVID-19

2. Asymptomatic household contacts of laboratory-confirmed cases

The recommendations are not evidence-based. Further, this should not instill a sense of false security. They must continue to follow the preventive norms and behavior, as suggested by local health authorities.

**Glucocorticoids**
In a retrospective study of patients with SARS-CoV and sepsis, steroids, at a mean daily dose of 105.3 ± 86.1 mg in 147 of 249 noncritical patients (59.0%), reduced mortality rate and shortened duration of hospitalization, whereas 121 of 152 critical patients (79.6%) received corticosteroids at a mean daily dose of 133.5 ± 102.3 mg, and 25 died. (8)

A subsequent retrospective, observational study of 309 patients with MERS showed that those who received high-dose steroids were more likely to require mechanical ventilation, vasopressors, and RRT. (9)

In a meta-analysis of corticosteroid use in patients with SARS, 4 studies provided conclusive evidence of harm (psychosis, diabetes, avascular necrosis, and delayed viral clearance). (10)

Therefore, the use of steroids is controversial and not recommended by the World Health Organization because of potential inhibition of viral clearance and prolongation of the duration of viremia. (11)

**Convalescent plasma.**

Preliminary clinical studies in China have shown that early application of convalescent plasma in patients with COVID-19 could accelerate clinical recovery. (12)
Currently, two trials, an open-label, nonrandomized clinical trial (NCT04264858) and a multicenter, randomized, and parallel controlled trial (ChiCTR2000029757) on the efficacy of convalescent plasma in patients with COVID-19, is underway in China.

**Monoclonal antibody.**

A monoclonal antibody against COVID-19 has not yet been developed. A monoclonal antibody directed against the RBD domain of the S protein of MERS-CoV has been found to have neutralizing activities in plaque assays in vitro. (13)

Tocilizumab, a monoclonal antibody against the IL-6 receptor, has achieved encouraging preliminary clinical results. The safety and efficacy of tocilizumab in COVID-19 infection are undergoing evaluation by a multicenter randomized controlled trial (ChiCTR2000029765).

**Hydroxychloroquine and azithromycin**

In an open-label non-randomized French clinical trial confirmed COVID-19 patients were included in a single-arm protocol from early March to March 16th, to receive 600mg of hydroxychloroquine daily and their viral load in nasopharyngeal swabs was tested daily in a hospital setting. Depending on
their clinical presentation, azithromycin was added to the treatment. Untreated patients from another center and cases refusing the protocol were included as negative controls. Presence and absence of virus at Day6-post inclusion was considered the end point. Six patients were asymptomatic, 22 had upper respiratory tract infection symptoms and eight had lower respiratory tract infection symptoms. Twenty cases were treated in this study and showed a significant reduction of the viral carriage at D6-post inclusion compared to controls, and much lower average carrying duration than reported of untreated patients in the literature. Azithromycin added to hydroxychloroquine was significantly more efficient for virus elimination. Despite its small sample size our survey shows that hydroxychloroquine treatment is significantly associated with viral load reduction/disappearance in COVID-19 patients and its effect is reinforced by azithromycin.(14)

The Covid-19 outbreak is a stark reminder of the ongoing challenge of emerging and re-emerging infectious pathogens and the need for constant surveillance, prompt diagnosis, and robust research to understand the basic biology of new organisms and our susceptibilities to them, as well as to develop effective countermeasures.
No drugs or biologics have been proven to be effective for the prevention or treatment of COVID-19. Numerous antiviral agents, immunotherapies, and vaccines are being investigated and developed as potential therapies.

References:


2. B CaoA Trial of Lopinavir-Ritonavir in Adults Hospitalized with Severe Covid-19 NEJM 2020 March 18


6. Multicenter collaboration group of Department of Science and


Chapter-7:

Infection Prevention and Control Guidelines for COVID

Sandip Mahajan, HS Kohli, Manish Rathi, and KL Gupta on behalf of COVID-19 Working Group of Indian Society of Nephrology

The best way to prevent corona virus disease 2019 (COVID-19) is to avoid exposure to the virus. There is currently no effective vaccine to prevent
COVID. With the information available now, the main route of spread is person-to-person, either from a symptomatic affected person or from an asymptomatic carrier, via respiratory droplets or contact. The limited health infrastructure available and the impending risk of a potentially explosive outbreak necessitates urgent measures to control this pandemic. Social distancing and the following recommendations are found to be most useful to control the epidemic. The following recommendations apply for all general public in addition to patients with chronic kidney disease.

**General Advice**

- Avoid agglomerations and closed crowded spaces.
- Maintain a distance of at least 1 – 2 meters, especially from persons with respiratory symptoms.
- Stay home if sick or with any respiratory symptoms or even if asymptomatic, if there is contact with a suspected COVID patient.
- Avoid non-essential travel.

**Hand hygiene**

- Wash hands with soap and water for at least 20 seconds especially after blowing your nose, coughing, sneezing or being in any public place.
- If the hand is not soiled and/or soap is not available, use a hand sanitizer with at least 60% alcohol.
• “My 5 moments for hand hygiene” are a simple, effective guide on how to perform hand hygiene.

• If soap or alcohol-based hand rub is not available, chlorinated water (0.05%) can be used – Repeated use may lead to dermatitis and should be watched out for.

• Refrain from touching your eyes, nose and mouth with unwashed hands.

• Dry your hands with a clean, dry cloth, single-use towel or hand drier as available.

Respiratory etiquette

• Cover the nose and mouth with a tissue when you cough or sneeze or use the inside of your flexed elbow. The tissue has to be disposed in the trash immediately.

• Immediately wash your hands with soap and water or use a hand sanitizer as advised earlier.

Face mask

• Use a facemask only when you have respiratory symptoms, you care for those with respiratory symptoms or when entering a healthcare provider's place.

• Facemasks are required for caregivers and healthcare providers

• Do not use facemasks if there is no indication.

• A triple-layered surgical mask is sufficient for personal protection.
Masks management

- Mask must cover mouth and nose minimizing all gaps between the mask and face
- Do not touch the mask when in use.
- Remove masks by removing the lace from behind. If in contact with the front of the mask / damp mask – perform hand hygiene and replace the mask
- Do not re-use single-use masks
- If face masks are not available, homemade masks like scarfs can be used as a last resort, and it should cover the entire front and sides of the face and should extend to the chin or below.

General Cleaning

- Like other coronaviruses, COVID-19 can survive on surfaces for 2 hours to 9 days, depending on a number of environmental factors.
- Clean frequently used objects/surfaces daily – phones, tablets, handles, keyboards, and switches, etc.
- Common disinfectants such as 70% ethanol or sodium hypochlorite (0.5%) and diluted household bleach (1 part bleach to 9 parts water) used for one minute should be effective.
- List of household detergents effective against COVID-19 is available in https://www.epa.gov/pesticide-registration/list-n-disinfectants-use-against-sars-cov-2.
- Cleaning with soap and water can be done if surfaces are dirty.
- Clothes of COVID-19 suspected patients should be machine washed separately with warm water at 60 – 90 °C and following any contact with such clothes, proper hand hygiene should be performed.

**Water supply**

- Though COVID-19 has not been yet detected in drinking water, like other coronaviruses chlorination and disinfection with ultraviolet light as done in conventional, centralized water treatment methods should be effective.
- If a centralized supply is not available, household water treatment methods, including boiling, using nanomembrane filters, chlorine, or UV irradiation, may be used.

**Chemoprophylaxis**

The National task force for COVID-19 by ICMR has recommended the use of hydroxy-chloroquine for prophylaxis in high-risk population viz. asymptomatic health-care workers involved in the care of suspected/confirmed cases of COVID-19 and asymptomatic household contacts of confirmed cases. The doses recommended are 400 mg twice a day on day one followed by 400 mg once a week for seven weeks for health care workers and 400 mg twice a day on day 1, followed by 400 mg once a week for three weeks for asymptomatic household contacts of confirmed cases.
References


The pandemic of COVID-19 occurred due to the novel SARS-CoV-2. At present, therapy and outcome data are sparse. The current draft has been made for the awareness for the medical fraternity and personnel involved in the management of kidney diseases in reference to COVID. No suit or legal proceedings shall lie against any person for anything done or intended to be done in good faith under these suggestions/advisory unless proved otherwise.