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Kidney and Covid 19 Virus Pandemic

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ABSTRACT

COVID-19, a respiratory illness caused by a newly discovered coronavirus, has become a pandemic affecting over 1.9 million people with over 130,000 deaths in 210 countries. Some people become infected with the virus but do not develop symptoms. When they appear, symptoms are non-specific, with fever, cough, shortness of breath, sore throat, fatigue, and headache being the most common. Symptoms are usually mild and benign in a vast majority (>80%) and recede gradually, leading to a full spontaneous recovery.

A small number become seriously ill, develop difficulty in breathing and complications related to other organs. They may require hospitalisation and a smaller subset need ICU care. The mortality is relatively higher in the latter group. This risk goes up in the elderly and those with co-morbidities (such as hypertension, diabetes, cardiac disease, kidney failure). Still, it is essential to emphasise that everybody is at risk for severe disease (including the relatively young and healthy dialysis staff). The strategy of physical distancing, case finding, contact tracing and quarantine/isolation of positive cases and highrisk contacts is critical to controlling the spread of this infection. This strategy is being implemented through nationwide lockdown during the period of intense transmission. Still, physical distancing is likely to remain in force after the end of the current lockdown to prevent disease spread.

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Introduction

A novel coronavirus is a new strain of coronavirus that has not been previously identified in humans. Coronaviruses (CoV) are a large family of viruses transmitting between animals and people that cause 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).

Reports suggest that 2019-nCoV, COVID19, infection can cause mild to severe disease and be fatal in some. Common observed symptoms include fever, cough, shortness of breath, sore throat, and breathing difficulties. In more severe cases, infection can cause pneumonia or severe acute respiratory syndrome, particularly in those with other chronic underlying health conditions, and even death.

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 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 [1-3].

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). 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 [4,5]. As of March 24, 2020, 3,82,000 cases of COVID-19 have been reported worldwide with 192 countries (and a cruise ship) involved with 16,000 deaths. It has set its journey in India too with 500 cases and 10 deaths. According to Indian Council of Medical Research, Phase III (community level transmission) has not yet started but is expected to occur soon.

Kidney involvement in COVID-19 infection

Even though early reports suggested a lower incidence (3%-9%) of AKI in COVID-19 infection, the recent reports suggest a higher incidence (15-20%). A substantial number have hematuria and proteinuria. The postulated mechanisms include sepsis leading to Cytokine Storm Syndrome or direct cellular injury due to virus. AKI is an independent predictor of mortality.In previous reports of SARS and MERS-CoV infections, acute kidney injury (AKI) devel-oped in 5% to 15% cases and carried a high(60%–90%) mortality rate. Early reports suggested a lower incidence (3%–9%) of AKI in those with COVID-19 infection [4,5]. Recent reports, however, have shown higher frequency of renal abnormalities. A study of 59 patients with COVID-19 found that 34% of patients developed massive albuminuria on the first day of admission, and 63% developed proteinuria during their stay in hospital.14 Blood urea nitrogen was elevated in 27% overall and two-thirds of patients who died. Computed to-mography scan of the kidneys

showed reduced density, suggestive of inflammation and edema. Cheng et al.[6]. recently reported that amongst710 consecutive hospitalized patients with COVID-19, 44% had proteinuria and hematuria and 26.7% had hematuria on admission. The prevalence of elevated serum creatinine and blood urea nitrogen was 15.5% and 14.1%, respectively. AKI was an independent risk factor for patients' in-hospital mortality [6,7].

As of March 23, 2020, 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 (30crore) cases in India, out of the 10 crores will face severe COVID infection .Looking at the incidence of 5.1% of AKI in severe cases, there would be 5.1 million AKI patients because of Corona, and presumably, half of them may require renal replacement therapy [8].

Mechanism of kidney injury

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 [6,9]. 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 [6,7]. 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 [8]. In the past, six CoVs were discovered as a human-susceptible virus,The exact mechanism of kidney involvement is unclear: postulated mechanisms include sepsis leading to cytokine storm syndrome or direct cellular injury due to the virus. Angiotensin- converting enzyme and dipeptidyl peptidase-4, both expressed on renal tubular cells, were identified as binding partners for SARS-CoV and MERS-CoV, respectively. Viral RNA has been identified in kidney tissue and urine in both infections. Recently, Zhong's lab in Guangzhou successfully isolated SARS-CoV-2 from the urine sample of an infected patient, suggesting the kidney as the target of this novel coronavirus 19.

Management of Aki Due to Covid19

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).

In the most extensive prospective studyof 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 steroidsmainly 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. The most recent NEJM study of the randomized controlled trial showed no mortality benefit of treatment with lopinavir-ritonavir (19.2%) as compared to the standard of care arm (25%). 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, 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. The National Taskforcefor COVID-19 by ICMR recommended the use of hydroxy-chloroquine for prophylaxisof SARS-CoV-2 infection for selected individuals like asymptomatic healthcare workersinvolved 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. (10,11) Few retrospective analyses showed benefit with the use of glucocorticoids in SARS- CoVinfection [12,13]. 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 [14]. WHO does not recommend the use of steroid expecting potential inhibition of viral clearance and prolongation of the duration of viremia [15].

COVID-19 in patients with kidney disease

Chronic Kidney disease (CKD) is associated with an increased risk of both inpatient and outpatient pneumonia [1]. Moreover, the pneumonia-related mortality rate in CKD patients seems to be 14–16 times higher than in the general population CKD seems to be associated with enhanced risk of severe COVID-19 infection [2]. Patients with CKD should hence be advised to take extra precaution to minimize risk exposure to the virus. Physicians should also be engaged in close monitoring of CKD patients with suspected COVID-19, for timely detecting signs of disease progression. Finally, the presence of CKD shall be regarded as an important factor in future risk stratification models for COVID-19.

The impact of COVID-19 on chronic kidney disease has not been reported.30 COVID-19 infection presents a special threat to patients on dialysis. There are 7184 patients on hemodialysis (HD) in 61 treatment centers in Wuhan City. At a single HD center in Renmin Hospital, Wuhan University, 37 out of 230 patients on HD and 4 of 33 staff members developed COVID-19 infection between January 14 and February 17, 2020.30 A total of 7 patients on HD died, of whom 6 had COVID-19 infection. However, the deaths were deemed to be due to cardiovascular causes and not directly to the COVID-19 infection. Patients on HD with COVID-19 had less lymphopenia, lower serum levels of inflammatory cytokines, and milder clinical disease than other patients with COVID-19 infection.

Summary of guidelines for dialysis

1. A working team consisting of dialysis physicians, nursing staff and technologists should receive training in updated clinical knowledge of epidemic COVID-19, notification of infection at risk,epidemic prevention tools, and guidelines from the government, academic society, and hospital authority. The

list of staff should be recorded and be retained by dialysis hospitals.

2. Information on travel, occupation, contacts, and clusters history(TOCC) of each medical staff, dialysis patient, their family members, residents of the same institution, and colleagues at work should be collected and updated regularly.
3. Latest care recommendations and epidemic information should be updated and delivered to all medical care personnel as needed.Training can be done peer to peer or online.
4. Group activities, including group rounds, group studies, and case discussions should be minimized.
5. It is recommended that staff members have meals at different time to avoid dining together. Goggles, masks, and hats should be removed before meals, and hands washed with flowing water. Talking during meals should be minimized to reduce the spread of droplets.
6. Staff should self-monitor their symptoms and should inform the team leader in case they or their family members develop symptom(s) suggestive of COVID-19 infection.
7. Entrance control, identification and shunting of people at risk of infection, body temperature measurement, hand washing, wearing proper (surgical or N95) masks throughout the process, machine disinfection, environmental cleanliness, good air conditioning and ventilation conditions, should be instituted.
8. Patients and accompanying persons should be given hands-free hand sanitizer while entering the dialysis room. Patients should wear medical masks and avoid meals during dialysis. They can bring convenience food such as candy to prevent hypoglycemia.
9. Patients with suspected or confirmed COVID-19 infection should be admitted to negative pressure isolation ward of specified hospitals. If the capacity of the isolation facility is overloaded, the "Fixed Dialysis Care Model" as below is recommended for dialysis patients under the 14-day period of quarantine for possible contact with COVID-19.
10. Place of dialysis treatment: patients should continue hemodialysis at the original hemodialysis center and not change to another center.
11. Dialysis shift and personnel: Do not change dialysis shifts and caregiver staff to avoid cross contamination and infection. Minimize the relevant contacts.
12. Patients who need vascular access surgery should be screened for novel coronavirus before the surgery. Operations on patients with confirmed or suspected novel coronavirus infection should be carried out in a designated room with necessary protection for medical staff.
13. Transportation: Public transport should not be used. Patients should arrange personal transportation and take fixed transportation routes. Transport personnel and escorts should wear surgical grade or N95 masks throughout.
14. All patients who have fever should be screened for novel coronavirus infection, and should be given dialysis in the last shift of the day until infection is excluded.
15. Pass route for entering hospital and dialysis unit: The pick-up and drop-off should not be shared with other dialysis patients. Entering and exiting with other patients at the same time shouldbe avoided. The route, mode and time of transport of dialysis personnel should be fixed.
16. Precautions in dialysis unit: Patients should not be in close proximity; treatment and waiting areas should have good air conditioning and ventilation to remove droplet particles from theair.
17. Designated care personnel: All personnel involved in direct patient care should undertake full protection, including long-sleeved waterproof isolation clothing, hair caps, goggles, gloves and medical masks (surgical mask grade or above). Hand hygiene should be strictlY implemented.
18. Dialysis machine: Equipment that may come into contact with patients or potentially contaminated material should be disinfected according to standard protocols.
19. If a new confirmed or highly suspected case of novel coronavirus infection in dialysis centers is identified, disinfection should be carried out immediately. Areas in close contact with these patients should not be used for other patients until cleared.
20. The medical waste from confirmed or suspected patients with novel coronavirus infection should be considered as infectious medical wastes and disposed accordingly.

Operational strategies for family member and caregivers

1. All the family members living with dialysis patients must follow all the precautions and regulations given to patients to prevent person-to-person and within family transmission of the COVID-19, which include body temperature measurement, good personal hygiene, handwashing, and prompt reporting of potentially sick people.
2. Dialysis patients, who have a family member or caregiver subject to "basic quarantine", can have dialysis as usual in accordance during the 14-day period.
3. Once the family members or caregiver of dialysis patients have been converted to a confirmed case, the patient's identity should be upgraded and treated in accordance with the above-mentioned conditions [16].

Treatment of Covid Positive Dialysis Patients (24)

1. At the moment, the therapeutic strategies to deal with the infection are only supportive and prevention aimed at reducing transmission in the community.
2. Asymptomatic patients to come for dialysis in private vehicles following all the above said precautions. Rest of the time, they can be quarantined at their homes in well ventilated preferably separated rooms.
3. Symptomatic Covid-19 patients should be hospitalized in isolation room and should be monitored adequately by the medical team.
4. As of now, no specific anti virals have shown to be of proven benefit in treating Covid-19. Multiple RCTs are ongoing, hopefully they will bring us some information soon.
5. Based on the available evidence, the nephrologist can decide on the treatment protocol. A focus is placed on drugs like Lopinavir/Ritonavir and Hydroxychloroquine since these agents are currently available. Available evidence suggest that it is better to start the drugs early in the course of the illness before it becomes more severe.
6. Dose is 400/100 mg per orally 12th hourly for Lopinavir/Ritonavir (dose modification is not required and is not cleared by hemodialysis) and for HCQS, it is 400 mg 12th hourly x 1 day followed by 200 mg 12th hourly x 4 days.
7. To give Oseltamivir 150 mg twice daily x 5 days (to avoid patient worsening due to influenza).
8. Anti-bacterial antibiotics can be initiated to treat secondary bacterial pneumonia according to the hospital antibiotic policy.
9. For critically ill patients requiring ventilatory support, involve intensivist and pulmonologist in the treatment [17-25].

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