The prevalence of chronic kidney disease (CKD) is very high in all parts of the world, including India. Although there is no literature available, being in an immunocompromised state, these patients are likely to be at high risk of COVID-19. It is likely that many CKD patients will also acquire SARS-CoV-2 infection. The data as coming from various countries is showing that elderly patients especially those with associated co-morbidities of diabetes mellitus, hypertension, or cardiovascular disease are not only at a higher risk for this infection but the severity of infection is also more.[1] Diabetes and hypertension being the commonest cause of CKD, many of these patients will also have associated CKD. 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 have different pattern of presentation of the 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 less symptomatic disease as compared to other patients with COVID-19 infection.[1] Therefore, besides avoiding unnecessary hospital visits, physicians should put more emphasis on providing consultations using information technology/telemedicine. In India, till recently, there were no guidelines or legislation to provide consultations by telemedicine. However, the Ministry of Health and Family Welfare has recently released guidelines for physicians to provide consultations through telemedicine.[2]

It is anticipated that few patients of CKD will experience episodes of acute kidney injury (AKI) following COVID-19 infection, and the renal function will further deteriorate. Such a decline in kidney function will however depend upon the severity of the infection. SARS-CoV-2 may affect the kidney directly through angiotensin-converting enzyme 2 (ACE2) receptors causing direct injury, glomerular injury by affecting effector T cell or immune-complex formation, and as a part of cytokine storm after virus-induced sepsis.

**CKD Management and COVID**

Most CKD patients are on multiple drugs to manage anemia, metabolic bone disease (MBD), fluid status, diabetes, and hypertension. Anti- hypertensives include diuretics, calcium channel blockers, centrally acting drugs, beta-blockers, alpha-blockers, angiotensin- converting enzyme inhibitor, and angiotensin receptor blockers. There may be a concern about the safety of all these drugs.

**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 known. At present, there is no evidence to suggest stopping or changing EPO doses. Oral iron therapy should be continued, and the use of intravenous iron should be discouraged during COVID-19.

**Management of CKD-MBD**

Medications for CKD-MBD should be continued as before unless there are specific contraindications that appear during the management of COVID-19 infection. As of date, there are no interactions or contraindications to the use of these drugs during COVID-19. Some patients with CKD-MBD may require pain killers.

There are unconfirmed reports of patients who are on non-steroidal anti-inflammatory drugs (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.

**COVID-19 and 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) resulting in possible interaction between the renin–angiotensin–aldosterone system (RAAS) and COVID-19.[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 risk of more severe infection due to the availability of increased receptors.\(^4\,^5\)

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

Patients are likely on these drugs because of associated co-morbidities like diabetes, hypertension, 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

| Society                                      | Summary of recommendations                                                                                               | Last Statement Update      |
|---------------------------------------------|------------------------------------------------------------------------------------------------------------------------|---------------------------|
| European Society of Hypertension            | 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. | March 12, 2020            |
| European Society of Cardiology Council on Hypertension | Strongly encourage continuing ACEIs/ARBs due to lack of evidence to support discontinuing                                    | March 13, 2020            |
| Hypertension Canada                         | 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. | March 13, 2020            |
| Canadian Cardiovascular Society             | Strongly encourage continuing ACEIs/ARBs and Angiotensin Receptor Neprilysin Inhibitors due to a lack of clinical evidence to support withdrawal of these agents. | March 15, 2020            |
| The Renal Association, United Kingdom       | Strongly encourage continuing ACEIs/ARBs due to unconvincing evidence that these medications increase risk.              | March 15, 2020            |
| International Society of Hypertension      | 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 or do they affect the outcomes of those infected. | March 16, 2020            |
| American College of Physicians             | 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. | March 16, 2020            |
| Spanish Society of Hypertension            | 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. | March 16, 2020            |
| American Heart Association, Heart Failure Society of America, American College of Cardiology | Recommend continuing ACEIs/ARBs for all patients already prescribed them. | March 17, 2020            |
| European Renal Association - European Dialysis and Transplant Association | 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. | March 17, 2020            |
| American Society of Pediatric Nephrology   | Strongly recommend continuing ACEIs/ARBs until new evidence to the contrary becomes available. | March 17, 2020            |
| High Blood Pressure Research Council of Australia | Recommend continuing routine use of ACEIs/ARBs. Patients should not cease blood pressure lowering medications unless advised to do so by their physician. | March 18, 2020            |
| Australian Diabetes Society                | Recommend that usual antihypertensive therapy is continued given that speculation about risk of ACE inhibitors and ARBs is purely theoretical. | March 29, 2020            |

Figure 2: Professional Societies Recommendations on use of ACEi/ARB (Adapted from NephJC http://www.nephjc.com/news/covidace2)
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 patients, rather than its inhibition, renders them more prone to a deleterious outcome.\cite{6,9} Therefore, we suggest continuing ACEI and ARBs for anti-hypertensive and renoprotective purposes. Other anti-hypertensive drugs should also be continued 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.\cite{10} In addition, hydroxychloroquine has been shown to significantly reduce viral load in nasopharyngeal swabs in 20 French patients with COVID-19.\cite{11} So, hydroxychloroquine has both direct anti-viral effects and anti-inflammatory effects. Until further evidence in the 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.\cite{12}

Though hydroxychloroquine is usually safe, there are 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, whereas the retinal toxicity is the most dreaded complication over long term use. In addition, there may be significant drug interactions with this drug. There are no well-defined recommendations for dose modification according to the glomerular filtration rate. Therefore, hydroxychloroquine may be used judiciously in CKD cases.

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Conflicts of interest

There are no conflicts of interest.

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