

COVID-19 in Renal Transplantation

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Abstract

During the end of 2019 a group of patients with pneumonia were described in Wuhan city of china with progression to ARDS with variable outcome. Mortality rate was higher in the oldest and in those with comorbid conditions. Kidney transplant recipients as a group of immunocompromised hosts are believed to be a high risk group in case of infection by SARS-CoV-19 virus with unfavorable outcome. On the other hand, cytokine storm with its severe inflammatory response as a major risk factor of mortality may be prevented by ongoing immunosuppressive therapy. Our knowledge about the pathophysiology and treatment options of COVID-19 in kidney transplant recipients are growing on daily bases and at the time being is derived mainly from the few published case reports, reviews and some society guidelines in the published literature.

Keywords: COVID-19; Kidney Transplantation; Children.

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Introduction

As its initial nomenclature the novel coronavirus (2019-nCoV) everything is new in covid-19 and despite hardworking of medical stuffs and clinical researchers there are still so many unknowns. Coronavirus 2 is belonging to β -coronavirus family as the causative agent of SARS and MERS. SARS-CoV-2 has 79% viral sequence homology to SARS-CoV, 2002-2003 and 49% with MERS. The disease could be mild in 80% of cases with spontaneous recovery, 14% more severe and 6% critically ill with 3.5% mortality (1,2,3).

Route of transmission is more or less similar to the previous families of this virus but with a more rapid spread so that within a short period caused the pandemic encountering the whole world (1,2,3). Also in SARS-CoV and MERS there are only a few reports of infection in kidney transplant recipients with variable outcome (4).

The usual presentation is with respiratory involvement but cardiac, gastrointestinal, nervous system and the kidneys are involved during the

course of disease. The majority of deaths are due to ARDS and eventually multi-organ failure. Acute kidney injury and its complications are further risk factors in prognosis. We assume a grave prognosis in immunocompromised hosts in case of infection by SARS-covid 19 virus (5-7).

Regarding the novelty of the disease and lack of enough data nothing is clear-cut and we need to gather data to implement our knowledge for better management of our patients. So far there are a few studies and case reports in patients with ESRD on hemodialysis program and transplantation who developed covid-19. A mortality rate of 17-23% was reported in dialysis or kidney transplanted patients in Spain (8,9).

Clinical and Para-clinical findings

Clinical presentation in transplant recipients is almost similar to normal hosts: fever, fatigue, dry cough, myalgia, generalized body pain, loss of appetite and nausea are common symptoms and a

minority of patients may complain of rhinorrhea and conjunctivitis and nasal congestion. Fever may not be severe due to immunosuppressive therapy. At presentation in the majority of the cases chest radiograph reveal patchy infiltration and ground glass appearance which may progress to white lung in severe cases.

Laboratory findings

Anemia, Leukopenia, severe lymphopenia, elevated LDH, liver enzymes, serum ferritin, CRP and ESR are among the commonest laboratory findings. Very high D dimer and high levels of ferritin and troponin have prognostic significance. Proteinuria 43.9% and hematuria 26.7% are relatively common and AKI 5.1% is a risk factor of death in hospitalized patients (10).

Renal function is impaired to varying degrees in all kidney transplant recipients. Acute kidney injury (AKI) as in non-compromised hosts could be the result of dehydration or secondary to multi-organ dysfunction in critically ill group. AKI may reflect rejection following reduction in immunosuppression or with interferon therapies, or from the inability to monitor calcineurin inhibitor levels in the face of drug interactions with lopinavir/ritonavir therapy. Overall, the progression of disease has varied but appears to be more rapid in immunocompromised hosts with greater rates of ICU admission and death (a fatality rate of ~21.4%). Some recipients may have viral or bacterial superinfection at the time of presentation with COVID-19.

Treatments

To date there are no specific guidelines for treatment of immunocompromised patients including kidney transplant recipients. Reductions in immunosuppression are strongly advocated by many clinicians; this approach risks immune reconstitution and rejection but may improve viral clearance (8,9).

The most commonly used medications are hydroxychloroquine (75%), lopinavir / ritonavir (47%), steroids (15%), interferon (11%), tocilizumab (3%) and Remdesivir and recently favipiravir which showed better therapeutic responses on COVID-19 in terms of disease progression and viral clearance (11,12). Convalescent Plasma and Hyperimmune

Immunoglobulin has been used in critically ill patients with acceptable results (13).

Soler noted that although lopinavir/ritonavir showed no greater efficacy than standard care in COVID-19 in a recent randomized clinical trial, she suspects the drug combination may have a better effect if started earlier in the disease course. Steroid is not suggested at the first phase of disease but may be of some benefit in second phase with or without tocilizumab for treatment of cytokine storm.

In 2003 during SARS-CoV infection WHO recommendation was to avoid use of steroids for its effect on prolongation of viremia but if this could be applied to SARS-COV2 is not known. Discontinuation of Calcineurin and mTOR inhibitors and replacing them with protease inhibitors Lopinavir/Ritonavir has been suggested. Since they can't be taken simultaneously because of severe drug interactions. Regarding the off-label use of Lopinavir/Ritonavir in COVID-19 infection and lack of confirmatory evidence for its therapeutic efficacy risk of rejection should be weighed with therapeutic efficacy. The first published case of kidney transplantation with COVID-19 treated successfully with reduction of immunosuppressive medication and low dose methyl prednisolone (14,15).

The recommendation of British Transplantation Society for transplant recipients suspicious to COVID-19 or mild cases is to discontinue antimetabolite (mycophenolate, Azathioprine), reduce the dose of calcineurin inhibitors (CNI) and continue the steroid with the same dose. For patients who are very ill and admitted in ICU and in need of ventilatory support, discontinue antimetabolite, reduce or discontinue CNI and increase the dose of steroid. Early thromboprophylaxis is mandatory and antiviral therapy has to be started according to local protocols. Patients need to be closely monitored for deterioration. Circulatory volume needs to be maintained but hypervolemia should be avoided. Restarts the immunosuppression 14 days after onset of symptoms and when the patient is afebrile without antipyretics for 3 days (16).

Transplant Activity in COVID 19 ERA

The latest guidelines of The European Economic Area (EEA) and European union (EU), British society of transplantation and Association of organ procurement organization are more or less similar

This is a challenging issue for both living related and deceased donor transplantation. Since this is a new issue in organ allocation program from the point of view COVID-19 transmission from the infected donors to the recipients or transplantation of a recipient during an active infection. Since at the time of transplantation with maximum intensity of immunosuppression healthcare takers will encounter serious and life threatening situation. It is recommended that we gather enough information about our donors and recipients and their contacts in the preceding 14-28 days and also from they travel to the countries with COVID-19 pandemics (Travel geographic areas designated by CDC as Warning Level 3 or Alert Level 2 regardless of symptoms). For potential living donors in case of COVID-19 infection at least 14 days after recovery with repeated negative nasopharyngeal PCR they could be permitted for donation. Also in case of close contact with a COVID-19 patient they have to be in quarantine for 2 weeks and then with negative PCR they could be selected. Brain deaths from COVID-19 and suspicious cases must be omitted from selection as donors. With keeping in mind all of the above conditions and negative nasopharyngeal PCR of donors and recipients at the time of transplantation enough discussion should be done with the recipients and their care givers and then obtain an informed consent and then go through the process of transplantation (16-18).

Conclusion

In conclusion kidney transplant recipients are a very high risk group in case of COVID-19 infection. Antimetabolites must be discontinued as soon as diagnosis is made and CNI dose to be reduced and if the disease was progressive and they were in need of ventilatory support steroid dose have to be increased. For transplant activity at COVID-19 era transplant teams should update themselves on daily bases and specially transplant coordinators have to work hard for obtaining a precise history from potential donors and recipients and they should be familiar with symptoms and signs of COVID-19.

Conflict of Interest

The author declares no conflicts of interest.

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Authors Contributions

Ali Derakhshan drafted, reviewed and finalized the manuscript.

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