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COVID-19 and organ transplant recipients, risk factors and considerations: A mini-review

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Abstract

The emergence of coronavirus 2 is distinctive and created an unprecedented obstacle in the entire history of organ transplantation. Transplant patients are more susceptible to COVID-19 infection due to various medical comorbidities and immunosuppressive therapy. The mortality rate was also reported as up to 30% in transplant patients. The fundamental implications of COVID-19 are different depending on the organ transplanted and the receiver's comorbidities. In addition to this, non-pharmacological interventions and vaccines help prevent COVID-19 in transplant patients. In this mini-review, we focused on summarizing current literature associated with transplant patients with COVID-19 infection, clinical outcomes, risk factors, and precautions to be taken during the pandemic.

Keywords: Covid-19; Transplant patient; Risk Factor; Considerations

1. Introduction

SARS-CoV-2 was first ascertained in 2019 and later specified as causing coronavirus disease. Since then, the coronavirus pandemic has impacted healthcare facilities, the global market, and lifestyles. Organ transplantation has also been drastically impacted during the COVID-19 pandemic, leading to a considerable reduction in transplantation and an escalation in mortality rate due to infection in SOT patients [1]. In this mini-review, we summarize the overview of transplant patients with COVID-19 infection, clinical outcomes, risk factors, and precautions to be taken during the pandemic.

The coronavirus family is well-known to cause illness in animals and human beings. Some species of human coronaviruses (229E, OC43, and NL63) affect only the upper airways and lead to mild symptoms such as fever, headache, and shortness of breath. Nevertheless, SARS-CoV-1 or coronavirus-1, MERS-CoV, and SARS-CoV-2 can increase their number in the lower airways and lead to pneumonia [2,3,4]. The S protein, also called spike protein, made up of significant components including S1 and S2, is usually present on the viral surface, giving SARS-CoV a “crown-shaped” appearance. SARS-CoV-2 produces infection by infecting angiotensin-converting enzyme two and surface receptors such as TMPRSS2. The innate immune system discharges immunoregulatory cytokines that prevent viral replication, trigger the acquired immunity, and gather other innate cells to the infection site [4,5]. A viral infection can be blocked by neutralizing the antibodies. Dendritic cells trigger T cells to produce adaptive immunity, which removes the infection-causing cells before the spread of the virus. Both T lymphocyte cells and B lymphocyte cells against SARS-CoV-2 can be found in the patient's blood approximately one week after COVID-19 symptoms onset [6,7,8]. CD8+ T cells play a crucial role in killing the virus-infected cells directly, while CD4+ T cells help to hire other cells and are also important

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to prepare CD8+ T cells and B cells. Natural killer (NK) cells perform their role but kill infected cells through the process of degranulation, programmed cell death, and Antibody-dependent cellular toxicity. Eventually, the complement cascade also helps recruit immune cells, triggering and demolishing pathogens. These fundamental responses generated by the immune system play a major role in eradicating pathogens or virus with minimum damage to the lungs and leads to recovery [5].

In some patients, the symptoms of coronavirus two gradually worsen in less than a week, indicating that serious COVID-19 infection could occur due to immune dysregulation. An abnormal and unique inflammatory activity can be seen in transcriptional profiling of COVID-19 individuals [5]. Type-I interferons are essential to possess antiviral immunity. Impaired type-I interferons response and increased production of IL-6 and TNF-alpha can be seen in patients suffering from COVID-19 [9]. More elevated circulation of IL-6, IL-1Ra, CCL2, CCL8 and other cytokines can be seen in patients with SARS-CoV-2+ compared to the patients with other respiratory complications [10]. Increased levels of cytokines may be considered a fundamental factor associated with specific pathology noticed in coronavirus two patients [11]. Elevated cytokine levels and uncontrolled inflammation may cause multiorgan damage-inducing renal, liver, or cardiac failure. IL-6 is considered one of the most cytokines in COVID-19 pathogenesis, and elevated levels of IL-6 are affiliated with mortality [12,13,14]. Some studies have suggested using cannabidiol to reduce the inflammation caused by these cytokines [15].

Several studies have indicated that genetic factors may also cause severe clinical symptoms in coronavirus two patients, especially in younger individuals unaccompanied with other medical issues [1,16]. Therefore, RT-PCR, serologic assays, and viral antigen testing can be helpful for SARS-CoV-2 diagnosis. The FDA also approved several vaccines, such as Pfizer BioNTech and AstraZeneca, to fight against coronavirus two infection [1,17,18].

2. Clinical outcomes and risk factors

Half of the transplant patients with COVID-19 have pyrexia at presentation, several patients have tussis and dyspnea, while some may have upper airway complications and gastrointestinal symptoms [19,20,21,22]. A study showed that 5% of coronavirus two patients showed gastrointestinal manifestations without any respiratory manifestations [19]. Even 80% of coronavirus two patients with mild respiratory manifestations showed pneumonia [12,19]. Transplant patients with COVID-19 usually show the same manifestations reported in the general population [19].

During the initial stages of the coronavirus two pandemic, transplant patients showed escalated mortality and morbidity rates. In the US, many transplant patients with coronavirus 2 demanded hospital admission. Among them, 40% needed intensive therapy, approximately 30% needed assisted ventilation, and 25% needed vasopressor support [19,21]. A mortality rate of up to 32% was seen in hospitalized transplant patients with coronavirus two infection [23]. However, a study found a remarkably lower mortality rate among patients with liver transplants than other matched cohorts [20].

Older age, pulmonary complications, heart failure, cancers, and escalated COVID-19 manifestations such as leukopenia and pneumonia are risk factors associated with an increased mortality rate among transplant patients with coronavirus two infection [19,24]. A study conducted on 54 lung transplant patients showed that lung grafting was linked to a higher mortality rate than non-pulmonary transplant patients. Nevertheless, the study had some limitations [25]. Another investigation on 30 lung transplant patients found an increased mortality rate among lung transplant patients. However, no relationship was found between transplanted organ type and mortality in a study conducted for age and co-occurring complications [19]. Moreover, no specific drug or immunosuppression therapy was linked with a higher mortality rate among transplant patients with coronavirus two infections. Although, one clinical investigation showed that immunosuppression therapy containing mycophenolate is associated with mortality and mechanical ventilation [23].

3. Acute kidney (renal) injury (AKI)

The incidence rate of AKI in hospitalized individuals with coronavirus two was up to 50%, while fewer cases were proclaimed in China compared to other countries [26,27]. In addition, risk factors such as mechanical ventilation, old age, need for high FiO2, sex, race, and chronic conditions are associated with AKI in COVID-19 [23,26,28].

Transplant patients with coronavirus two infection are susceptible to AKI due to kidney disorders, chronic diabetes, high BP, and calcineurin inhibitor (CNI). A study conducted on 482 SOTR with coronavirus 2 showed that several hospitalized patients evolved AKI, whole some required renal replacement treatment. Furthermore, it was observed that diarrhea was present in half of the SOTR patients with coronavirus 2, which decreases the efflux pump expression

from cells present on the surface of intestinal epithelium resulting in CNI toxicity. In addition, the use of ritonavir or protease inhibitors regimen for COVID-19 treatment may increase CNI levels, leading to nephrotoxicity [23].

4. Allograft dysfunction

In COVID-19, allograft dysfunction must be discriminated from graft rejection because cardiac, renal, and pulmonary injuries are well-known after-effects of SARS-CoV-2 infection in populations without SOT. In addition, various infections such as cytomegalovirus (CMV) increase the reactivity of alloantigen, thereby placing the issue that either transplant patients with COVID-19 are susceptible to allograft rejection or not. Currently, more studies are required related to allograft rejection in coronavirus two diseases, but sufficient data is available related to biopsy-proven organ rejection [23]. A study was carried out on 482 transplant patients with COVID-19 for 28 days; the results showed acute cellular rejection (ACR) and antibody-mediated rejection in some patients. However, their allograft rejection in patients with COVID-19 is rare [19].

5. Concurrent Infections or co-infections

Individuals suffering from COVID-19 may have other pathogenic illnesses during infection. For example, respiratory tract injury and ciliary dysfunction may cause secondary infections in individuals with various pulmonary illnesses. Large-scale studies suggested that secondary infections may occur in hospitalized COVID-19 patients. In comparison, small-scale studies suggested that the rate of patients surviving the Introductory staves of disease is higher [23,29]. In addition, some studies concluded that bacterial pathogens such as Aspergillus pneumonia and Cryptococcus are more likely to cause secondary infections [19].

6. Precautions while accepting organs during the COVID-19 pandemic

Non-therapeutic interventions, including face coverings, mouthrinses, and social distancing, are necessary for immunocompromised individuals. Studies suggested that despite the presence of lymphopenia in transplant patients during infection, most patients achieve an active immune response compared to non-SOT individuals. Neutralization of antibody levels is considered one of the most effective surrogates of protection against infections and mortality. All available vaccines have a good safety profile in transplant patients. Nevertheless, contrary to equivalently responsive mRNA-based vaccines, only a few transplant receivers may develop anti–SARS-CoV-2 antibodies even after two-shot series. The third shot of mRNA-based coronavirus two vaccines is found may increase the number of antibodies. Several studies suggested that transplant patients show a better immune response to mRNA-based vaccines than to adenovirus-type vector vaccines. Although antibody responses are significantly lower in transplant patients with COVID-19 in contrast to the general population, some studies showed that vaccination could help in the reduction of up to 80% of COVID-19 incidences in transplant patients [30-32].

7. Conclusion

The knowledge related to SARS-CoV-2 virology has grown during the pandemic. Outcomes and risk factors associated with transplant patients with COVID-19 are almost similar to those observed in the non-transplant COVID-19 patients. Precautions such as non-pharmacological interventions and vaccines significantly reduce the mortality rate among transplant patients with COVID-19. More efforts are required to increase the efficacy of vaccines in transplant receivers.

Compliance with ethical standards

Disclosure of conflict of interest

There is no conflict of interest between the authors.

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