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Transplantation in the COVID-19 Era

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Introduction

Much concern has been raised about the implications of infection with the novel coronavirus, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), which causes coronavirus disease 2019 (Covid-19), in transplant recipients. Epidemiologic data from China [1] and the US [2] demonstrate that patients with chronic diseases and those who are immunocompromised comprise a significant proportion of those who are infected and come to medical attention. With newer emerging data, the risk of severe disease in transplant recipients is being increasingly recognized, such that many transplant centers have put a temporary hold on performing new transplants. While the optimal management approach in transplant patients with Covid-19 remains to be determined, there are some data that suggest better outcomes can be achieved if such patients are managed on a dedicated nephrology/ transplant unit [3].

Case reports of Covid-19 in transplant recipients from across the world demonstrate that transplant patients may present with atypical features [4,5]. Differences include the absence of respiratory symptoms as a key presenting feature, a more common presence of gastrointestinal symptoms such as diarrhea and vomiting, and unilateral, as opposed to the classic bilateral, infiltrates on radiographic imaging of the chest when respiratory symptoms do develop. Like in non-transplant patients, the disease can be rapidly progressive and therefore early diagnosis may be important, so that management can be started promptly.

The recent data on Covid-19 in this vulnerable population come from New York [6]. The authors describe the course of 36 renal transplant patients at their center, over a 2-week period, 28 of whom were admitted to the hospital. The most common presenting features were fever (although this was only present in 58%) and cough (53%), with diarrhea being a common symptom (22%). Eleven patients (39%) needed mechanical ventilation and 6 (21%) received renal replacement therapy. As of the time of the report, 10 patients (28%), including 7 of the 11 patients who were intubated (64%), had died. As expected, patients had elevated inflammatory markers, lymphopenia and many had low CD3, CD4 and CD8 counts.

To reduce viral replication, immunosuppressive management in transplant recipients has included reduction/withdrawal of their ant metabolite and in some instances their calcineurin inhibitor. Experimental therapies including hydroxychloroquine [4-6], the CCR5 inhibitor leronlimab [6], the interleukin-6

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receptor antagonist tocilizumab [6], interferon [4], and lopinavir/ritonavir [4,5] have been attempted. Since the latter is an inhibitor of cytochrome P450 (CYP) 3A enzyme, dose reduction and drug level monitoring of calcineurin inhibitor therapy, if that is being continued, is warranted. The rationale for many of these medications is based on the hypothesis that Covid-19 has a bi-phasic pathophysiology; in the first phase of the disease (from onset of the symptoms up to 7-10 days) direct viral cytopathic effects predominate and there for the focus should be on instituting antiviral therapy. In the second phase of the disease, it is the dysfunctional immune response against the virus that leads to tissue injury and inflammation including hemophagocytic syndrome, and therefore during this phase, immunosuppressive strategies (with glucocorticoids or anti cytokine agents) may be useful [3].

However, in-spite of such management, early mortality remains very high and outcomes remain poor [6], clearly pointing to the need for additional studies to help reduce morbidity and mortality in transplant patients.

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