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Review: Management of patients with kidney transplantation during the global pandemic COVID-19: Situation in Uzbekistan.

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Abstract: The current epidemic situation of COVID-19 in the whole world is at full blast now, and although the acquisition knowledge is increasing rapidly, there are many unknowns for the community in general and particularly for the transplant patients. Just like times of war, the challenges of the coronavirus crisis change our views in almost any aspect.

Transplant patients and those with end-stage organ failure are in a particular vulnerable position. Elective surgeries including live donor transplant procedures have paused in many countries. Exchanging of knowledge is a critical component of the present crisis. Responses, experiences, and outcomes have been different around the world as different countries and regions experience different impacts and different rates of infection and death. Sharing how others have coped in practice will assist in planning and managing this most stressful and challenging situation for patients and health workers alike.

However, it is imperative to anticipate the potential impact on the transplant population to avoid serious consequences. The recommendations may change as we learn more about the infection. This report is designed to assist in understanding the approaches taken in other countries and different phases of the epidemic.

Keywords: Covid-19, immunosuppression, kidney transplantation, outcomes, SARS-CoV-2, solid organ transplantation, waiting list.

The COVID-19 pandemic has hit the entire world in an almost unprecedented way. The crisis has spread rapidly, disease burden and casualties continue to rise, and the impact of the crisis is spreading through developing countries. Social distancing, travel restrictions, and intensified testing have improved the rate of the rise in new cases in some regions; however, it remains unclear when normality will return. Mechanisms of the disease remain largely unclear; treatment, if available, is mostly supportive.

Deceased donor transplants, where the procedure is established, continue in some countries, albeit with modified donor and recipient criteria, in an attempt to reduce the risk of COVID transmission or an infection after transplantation. Those who are immunocompromised are probably at increased risk of severe disease, though the role of immunosuppression is debated and uncertain.

As a transplant community, many are currently engaged in optimizing our immediate responses. With our actions largely based on epidemiological assessments, there is a critical lack of data on the consequences of COVID on transplant patients or those with end-stage organ disease.

There are new opportunities coming to the forefront in these otherwise gloomy days: virtual meetings, clinical visits, increased use of electronic communication, and improved remote monitoring may very well be one of the beneficial legacies of this crisis and our responses.

Editors and contributors to *Transplantation* have shared their thoughts on how they are dealing with the current crisis. While we understand that the information of today may be quite different tomorrow in this fast-moving pandemic, this report will open our forum of an international exchange on COVID for the transplant community. [1].

Most of the major medical centers in Uzbekistan already have cases of kidney transplant patients affected by COVID-19 that have not been published. Therefore, it is essential the collaboration between countries in the preparation of national registries to learn with detail the epidemiological characteristics of this infection in patients with solid organ transplants, including kidney transplantation.

The country is seeing a steadily increasing number of patients each day, so because of this testing capacity is increasing but remains insufficient. Uzbekistan continues life-saving transplantation with informed consent about the risks for kidney recipients, but it has been recommended to postpone status 1 liver transplants. We recommend test screening of those with significant exposure to COVID-19, travel history to high-risk countries, or with fever and respiratory symptoms. But NAT testing is not mandatory for donors, though preferable. It is recommended that living donors for kidney and liver transplant stay at home or isolated in hospital for 14 days before the donation to avoid unnecessary exposure. Where testing is available, it is recommended 14 days and 1 day before transplantation in both donors and recipients. Chest CT scans are also recommended before transplantation in donors and recipients.

Specialists recommend education of all transplant patients about general procedures to avoid infection, extended periods between outpatient visits for as long as possible, and prescription of additional drugs to prepare for possible national lockdown. We have recommended preparation of institutional policies on acceptance of transplanted patients with COVID-19 and extensive use of the telephone for follow-up of patients.

[\[1\]](#)

Does the disease present differently in transplant recipients?

Given the fact that 50–80% of infected patients may be asymptomatic or mildly symptomatic makes comparisons of clinical manifestations between transplant recipients and non-recipients perplexing. [\[4-6\]](#).

There is a relatively low rate of confirmed symptomatic cases among the transplant population, raising the possibility of higher prevalence of asymptomatic disease in this patient population: a speculation that remains hard to prove. [\[7-10\]](#).

Based on the figures from various reports and registry data, the frequency of the clinical manifestations in transplant recipients compared to the general population may generally be rounded up as follows[\[11,12-21\]](#). Amongst symptomatic patients, breathlessness occurs at roughly the same frequency (60–80% of transplant patients and non-transplant patients). Cough and fatigue/myalgia may be more common in

transplant recipients: roughly 40% and 20%, respectively, compared to around 4–30% and 10%, respectively, in non-transplant patients. Febrile illness is a major concern that is also difficult to define due to heterogeneous reporting.

Roughly 50% of non-hospitalized confirmed cases are febrile and, with a few exceptions, fever occurs in 90–98% of hospitalized nontransplant patients with moderate to severe disease in contrast to only 50–70% of hospitalized transplant patients. [11,12-21].

General considerations in kidney transplant patients.

In kidney transplant recipients, due to their status of immunosuppression, the clinical manifestations, treatment, and prognosis of COVID-19 pneumonia may differ from the general population, hence the importance of early diagnosis by SARS-CoV-2 screening, in those cases where the infection is suspected. In general population, lymphopenia has been observed in up to 63% of patients, [2] but many kidney transplant recipients have drug-induced lymphopenia, therefore, this finding does not help the diagnosis. Therefore, special attention should be paid to this type of immunosuppressed patients, evaluating the early detection of this infection by appropriate diagnostic test and the admission to the hospital in case of infection.

The first case of COVID-19 pneumonia in a kidney transplant recipient has been published recently. [3] The clinical features (symptoms, laboratory tests and chest CT scan) were similar to non-transplanted patients with COVID-19.

Specific recommendations for kidney transplant patients suspected of SARS-CoV-2 infection.

According to the latest document from the Ministry of Health of Republic Uzbekistan: *Temporary guidelines for prevention, diagnosis, treatment and rehabilitation in coronavirus infection (COVID-19) of September 2020*, all patients, including kidney transplant recipient patients with suspected SARS-CoV-2 infection have indication of diagnostic test and assessment of admission if the result is positive, and the initiation of a specific treatment. All kidney transplant patients with symptoms compatible with COVID-19 are recommended to contact their transplant specialist or primary care physician (preferably by telephone), indicating clearly their

chronic diseases and the type of treatment they take regularly. Depending on the symptoms presented, it is recommended:

- Mild symptoms (without dyspnea/tachypnea) and temperature $<38^{\circ}\text{C}$ in a kidney receptor with adequate functional reserves: the patient will be asked to contact by phone with phone number that has been given health authorities at the primary care level to have the diagnostic test performed and remain at home monitoring symptoms and alarm signs with telephone monitoring by the transplant team every 24–48 h.
- Moderate/severe symptoms, temperature $>38^{\circ}\text{C}$ or fragile receptor: the patient will be instructed to go to the Hospital Emergency Department to be clinically evaluated.

Table 1. Workflow adjustment program for kidney transplantation under the COVID-19 epidemic.

Transplant processes	Adjustment methods
<ul style="list-style-type: none"> • Donor and recipient screening 	<ol style="list-style-type: none"> 1. Within 14 days, the donor or the recipient had no history of staying in the epidemic area and no history of contact with COVID-19 patients. None of the people in close contact with them had a history of sojourn in the epidemic area 2. There are no fever, progressive dyspnea, dry cough, diarrhea, and other related symptoms within 14 days before the onset of the primary disease 3. Chest CT and laboratory examination showed no pneumonia 4. Nasopharyngeal swabs, sputum, lower respiratory tract secretions, blood, feces, and other specimens tested negative for new coronavirus nucleic acid 5. All were limited to one escort, who had no epidemiological history and normal body temperature 6. The hospital ethics committee examines the authenticity of the worker's willingness to donate and the legality of the source of the donor

<ul style="list-style-type: none"> • Donor maintenance 	<ol style="list-style-type: none"> 1. Single-room medical unit, fixed personnel to participate in the maintenance 2. Screening the coordinator and donor and transplant staff 3. The apparatus and equipment needed for organ acquisition shall be packed with protection; after the operation is completed, store the protective layer of the outer packaging of the instruments should in a centralized manner and dispose of it medical waste as medical waste contaminated by viruses; after the acquisition personnel return, sterilize the exterior of the organ preservation device, refrigerator, and other instruments
<ul style="list-style-type: none"> • Operation and postoperative management 	<ol style="list-style-type: none"> 1. Strengthen the health investigation and management of medical staff 2. Independent operating room and postoperative laminar flow ward 3. In case of suspected infection of COVID-19 during the perioperative period, the transplant recipient shall be isolated in a single room immediately and report to the relevant department of the hospital for consultation. When the patient is confirmed to be infected with COVID-19, the patient is transferred to the special ward of the hospital immediately and the medical staff who contacted the patient are isolated for 14 days 4. Strict implementation of disinfection and isolation system 5. Implement the system of professional responsible persons to improve the quality of care [22].

Thereby, the following conclusions arise based on the above data:

- Hospital facilities and workforce are being diverted from transplantation to COVID-19.

- There is uncertainty about the risks of transmission from use of COVID-19–positive donors.
- There is prioritization of intensive care capacity for COVID- 19 patients and thus restricted availability for care of both donors and postoperative nonrenal transplant recipients.
- There is substantial concern about creation of high-risk immunosuppressed patients from stable medium-risk dialysis patients with reduced staff available to look after them postoperatively.
- Most programs have moved to telephone consultation for outpatient follow-up, and the busiest services are using telephones for inpatient management as much as possible.
- There is no agreement on how to manage immunosuppression in the context of COVID-19.[\[1\]](#)

In conclusion, we can say with confidence that the optimization of diagnostics, treatment and the development of preventive measures aimed at combating infection before and after kidney transplantation can give a significant clinical and economic effect. It is necessary to search for new strategies for the treatment and prevention of COVID-19 infection. There are some common themes arising in different nations including the Republic Uzbekistan, depending on the phase of the epidemic and the underlying health services capacity. At the moment, there are no fully developed guidelines and protocols for patients with this pathology. The Covid-19 epidemic has not spared our country either, which has led to an urgent need to develop recommendations for special measures, taking into account the features of chronic renal failure in the Uzbek population.

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