

Position Statement of Transplant Activity in the Middle East in Era of COVID-19 Pandemic

Ahmed Zidan, MD, PhD,¹ Saleh Alabbad, MD,¹ Tariq Ali, MD,¹ Imran Nizami, MD,¹ Mehmet Haberal, MD, PhD,² Yaman Tokat, MD, PhD,³ Refaat Kamel, MD, PhD,⁴ Hany Said, MD, PhD,^{4,5} Amr Abdelaal, MD, PhD,⁴ Magdy Elsharkawy, MD, PhD,⁴ Amr El Fouly, MD, PhD,^{6,7} Hatem Sayed, MD, PhD,^{4,5} Mustafa Al-Mousawi, MD,⁸ Mohammed AlGhonaim, MD,⁹ and Dieter Broering, MD, PhD¹

AROUND THE WORLD REPORT ON TRANSPLANTATION IN THE MIDDLE EAST DURING THE COVID-19 PANDEMIC

The outbreak of severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) has led to global changes in the management of transplantation. It has been assumed, correctly as it has turned out, that use of immunosuppression increases vulnerability and that transmission of SARS-CoV-2 could occur from organ donors.¹ This report highlights and summarizes the position of organ transplantation in the Middle East during this period.

KINGDOM OF SAUDI ARABIA

The Saudi Center for Organ Transplant (SCOT) released a position statement on organ transplant and developed policies and recommendations for deceased and living donation during the coronavirus disease pandemic. All

deceased donors are to be screened for COVID-19 with PCR from bronchoalveolar lavage or tracheal aspirate. All positive donors are to be declined for donation of all organs; COVID negative donors are to be considered on a case to case basis assessing high-, intermediate-, or low-risk exposure and confirmed following a discussion between SCOT and the Transplant Center.

King Faisal Specialist Hospital & Research Center/Riyadh implemented COVID-19 emergency procedures by early March. All the elective surgeries were put on hold, >300 floor and 110 intensive care unit (ICU) beds were reserved for COVID-19 patients. Non-ICU physicians and nurses were prepared to manage intensive care patients, if needed.

King Faisal Specialist Hospital & Research Center performed 186 liver transplants in 2019, of which 159 were from living donors; >150 patients are on the waiting list. SCOT guidelines for deceased donor liver transplant offers have been implemented, and all recipients of deceased donor organs were tested for COVID-19 at admission. Patients with a living donor were divided into urgent and nonurgent cases. MELD >25, hepatocellular carcinoma beyond Milan criteria but within University of California San Francisco (UCSF) criteria, acute fulminant liver failure, and those with recurrent decompensations were defined as urgent. These patients completed their transplant work up and were scheduled for transplant. Those with stable disease were considered nonurgent and were postponed until further notice.

To decrease the potential of developing COVID-19 infections among both donor and recipients, patients were admitted 1 week before transplant and categorized into high and low risk based on the risk of COVID exposure (history of travel outside the country; living in a high COVID incidence areas; direct or indirect exposure to COVID-19 positive individuals and clinical symptoms including cough, fever, and fatigue. Donor and recipients in high-risk groups were tested for COVID-19 on the day of admission. In case of COVID positivity, the transplant was cancelled. In case of a first COVID-19 testing, a second test is done before surgery. Low-risk patients require 1 negative PCR test at admission.

Between February 1 and April 15, 33 liver transplants including 25 from living donors have been performed without COVID-related complications. Our outpatient

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¹ King Faisal Specialist Hospital & Research Centre, Riyadh, Saudi Arabia.

² Baskent University, Ankara, Turkey.

³ Transplantation Center Florence Nightingale Hospital, Istanbul, Turkey.

⁴ Ain Shams University, Cairo, Egypt.

⁵ Cairo Fatemic Hospital, Cairo, Egypt.

⁶ Helwan University, Cairo, Egypt.

⁷ Air Force Specialized Hospital, Cairo, Egypt.

⁸ Hamid Al-Essa Organ Transplant Center, Kuwait City, Kuwait.

⁹ Saudi Center for Organ Transplantation, Riyadh, Saudi Arabia.

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Correspondence: Dieter Broering, MD, PhD, FEBS, FACS, Department of Surgery, King Faisal Specialist Hospital & Research Centre (Gen. Org), MBC 96, PO Box 3354, Riyadh 11211, Saudi Arabia. (dbroering@kfshrc.edu.sa).

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clinics, providing care for almost 5000 transplant patients from across the country are the main challenge. To maintain social distancing, we have implemented telemedicine and phone clinics; blood tests are offered either in our hospital or in the nearest local laboratory of our hospital network. Results are discussed over the phone and medications shipped to the patient's home. A small proportion of patients, particularly those who were recently transplanted continued to be seen in clinic. We have only 1 patient postliver transplant in 2016 was diagnosed to be positive PCR presented with fever and cough, no changes on immunosuppression was done as he was not on anti metabolites or steroid and low dose of calcineurin inhibitor (CNI) (he did not require oxygen supply).

We performed 239 kidney transplants in 2019 (206 from living donors); only 40 kidney transplants were performed from February 1 to April 2020; 7 of those were from deceased donors; there was no COVID-related complication. Three kidney recipients presented with fever, cough, and fatigue and tested positive for COVID; a chest CT chest showed pneumonic patches consistent with the diagnosis of COVID-19 infection. They were treated with azithromycin, hydroxychloroquine, and ceftriaxone and maintained on low levels of tacrolimus and steroids. One of them continued to shed virus for >5 weeks, but all are well clinically and have not required ICU admission. With an additional positive COVID test in a healthcare worker, we placed our living donor kidney program on temporary hold until first week of May when it is resumed back again as number of diagnosed cases in the country was plateauing.

In 2019, we had performed 38 lung transplants with 91% 1-year patient survival. Notably, between February and April 2020, we have performed only 1 uncomplicated lung transplant. Our lung transplant program does deceased donor procedures only; criteria for recipients have not been changed during COVID and SCOT criteria are observed. There is 60% decrease in the number of offers comparing this time period in 2020 with the same period in 2019.

TURKEY

Our center in Ankara performed 38 liver transplant and 127 kidney transplants in 2019. In contrast, from February 1 to April 1, 2020, we have only performed 4 liver and 10 kidney transplants. All private and foundation hospitals were designated as COVID-19 pandemic hospitals as of March 20, 2020. All elective surgeries have been postponed in both public and private hospitals in Turkey.

We are closely monitoring transplant patients in our centers across Turkey. If a patient can reach one of our institutes, they are evaluated in-person, otherwise, they are evaluated by telemedicine. We have not observed any negative effects in the treatment and follow-up of patients to date. In case of COVID-19 positivity, our immunosuppressive protocol is modified: we discontinue antiproliferative agents (both, mycophenolate mofetil and azathioprine); CNIs are continued, however, if patients require ventilation with a severe pneumonia, we either reduce, or in severe cases discontinue CNIs. The interleukin-6 inhibitor, tocilizumab is considered to treat severe cytokine release symptoms. According to the Ministry of Health, there are

no reported COVID-positive transplant patients in Ankara at this time.

Our center in Istanbul performed 91 liver transplant and 101 kidney transplants in 2019 with only 17 liver and 13 kidney transplants from February 1 to April 1, 2020, formed. Istanbul is the epicenter of COVID-19 pandemic with 60% of all detected cases in the country. Almost 90% of the transplant centers in Istanbul have stopped liver transplantation except for urgent cases. There have been no deceased donor offers since March 15. Deceased donor testing has been challenging with prolonged turnaround times for COVID tests. Living donor liver transplants were placed on hold at the end of March, and only emergency procedures have been considered. Outpatient clinics are conducted through telemedicine, with very occasional face-to-face meetings.

Six transplant recipients (4 liver, 2 kidney) are known to have tested positive for COVID-19 in our center. All presented with low-grade fever, cough, and fatigue and were treated with hydroxychloroquine, oseltamivir, and azithromycin; antiproliferative immunosuppressants were discontinued, and the dosage of CNIs was reduced. Favipiravir was used in 1 liver transplant patient.

EGYPT

Transplant activities in Egypt are limited to live donor liver and kidney procedures. During the pandemic, the ministry of health raised the medical health service capacity and assigned 23 hospitals for the management of COVID-19 in each governorate as quarantine hospitals. The Air Force Specialized Hospital liver transplant program performed 101 living donor liver transplants in 2019; however, from February to April 2020, only 14 live donor liver transplants were performed, representing a 50% projected annual. Ain Shams University Hospital and Cairo Fatemic Center performed 74 liver transplants in 2019 and only 10 from February to April. Most Governmental and University Centers have temporarily discontinued transplant activities based on an unacceptable donor risk, uncertain data on the impact of COVID-19 on recipients and to reserve resources for the management of the pandemic. The proposed precautions adopted for those who are going for transplant are home isolation for donor and recipient for 14 days before transplant, to perform COVID-19 PCR twice at 48 hours intervals before transplant, and to admit recipient 3 days and donors 1 day before transplant. In the outpatient clinic, most of the patients are managed through telemedicine; few patients, particularly recently transplanted patients those with abnormal laboratory and radiological findings continue to be seen in our clinics.

The national protocol for management of transplantation during the COVID pandemic is implemented. (i) The waiting list prioritizes advanced liver status, rapid clinical deterioration, acute fulminant liver failure, and hepatocellular carcinoma; (ii) postliver transplant clinic follow-up has been suspended and transferred to teleconference with patients sending their laboratory results, imaging, current medications, and questions to our senior medical staff. Seriously and acutely ill patients get admitted. (ii) Planned transplant recipients are admitted 2 days before a scheduled procedure for clinical assessment, initial COVID-19 questionnaire, COVID testing, blood work, arterial blood

gases, and chest CT scan. Living donors are admitted 24 hours before surgery using the same protocol. A separate isolated ICU is dedicated to posttransplant care of 1 donor and recipient pair at a time. (iv) Posttransplant COVID-19 positive cases will be transferred to the hospital assigned by the Ministry of Health for isolation, treatment, and confirmation of seroconversion. Immunosuppressive changes for COVID-19 positive transplant patients include discontinuation of mycophenolate mofetil and a reduction of CNIs by 30%–50% in clinically mild to moderate cases with a discontinuation in patients with severe symptoms or those on ventilators.

Live donor kidney transplants have been reduced to about 10% of the rate of 2019. Most of governmental hospitals have stopped kidney transplants. There has been no confirmed COVID-19 positive kidney transplant recipient to date. Procedures have been adopted to ensure social distancing during follow-up relying on electronic communication and an extended supply of medications to reduce visits. When seen physically in the clinic precautions include face masks, protective gloves, and spacing of schedules to avoid waiting room crowding.

KUWAIT

In 2019, Kuwait has performed 6 liver transplant and 103 kidney transplants. In contrast, from February 1 to April 1, 2020, there have been no liver transplants and only 12 kidney transplants. Deceased donor transplants continue, though the numbers have dropped. All donors are tested for COVID-19. Accepting criteria for deceased donors have been more restricted leading to reject 2 potential deceased donors with unclear clinical symptoms,

despite negative PCR test living donor transplants were placed on hold by February 19 with 1 exception to avoid the need for dialysis. Outpatient clinics focus currently on the dispersion of medication to be picked up in-person or dispatched by the police.

CONCLUSIONS

The impact of the COVID-19 pandemic on transplantation in the Middle East has common features:

- (1) Transplant activities have been significantly reduced across the region.
- (2) Deceased donor transplantation (where available) continue in lower frequencies with less available donors that are tested for COVID before procurement.
- (3) The region depends on living donation for kidney and liver transplantation; tight regulation with early preoperative admissions of donor and recipients, testing for COVID-19 and strict intraoperative protective measures have been implemented; nevertheless numbers have declined drastically and living donor transplants have been restricted to the sickest patients who are at substantial risk if the procedure is postponed.
- (4) Physical attendance at the outpatient clinic is being kept to a minimum with extensive use of telemedicine and virtual clinics. No immediate negative impacts have been reported to date, but the long-term impact needs to be studied.

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