

Paediatric living-donor liver and kidney transplantation during COVID-19

Dear Editor,

The coronavirus disease 2019 (COVID-19) pandemic has impacted global healthcare including paediatric solid organ transplantation (SOT). We report our experience of resuming paediatric living-donor SOT during COVID-19, which took into account safety considerations for living donors, paediatric recipients and the transplant healthcare team. The US Centers for Disease Control and Prevention has categorised SOT recipients at high-risk for COVID-19.¹ During this period, transplantation programmes worldwide were either suspended or curtailed.^{2,3} In Singapore, all non-urgent deceased-donor transplants were temporarily suspended; living-donor transplants could only proceed if medically urgent.^{4,5}

The paediatric solid organ transplant programme at the National University Centre for Organ Transplantation is a small but essential one. Since the start of the paediatric liver and kidney transplant programmes in 1991 and 1989, respectively, a total of 140 liver and 98 kidney transplants have been performed. Living-donor transplantations account for nearly 86% of the paediatric liver transplants and 58% of the paediatric kidney transplants.⁶ In the early years, the wait-list mortality for paediatric liver transplant was 15%.⁷ However, with increasing availability of living donors, the wait-list mortality in the last decade is nearly zero. Particularly for children with acute liver failure or chronic end-stage liver disease, there would be no option for survival without liver transplant, unlike children with renal failure where dialysis is an option. At the time of the nationwide partial lockdown in Singapore known as the circuit breaker (7 April–1 June 2020), there were 22 paediatric patients with kidney failure on long-term dialysis, of whom 4 were on the waiting list for a deceased donor kidney transplant. However, unlike the severe acute respiratory syndrome in 2003, the COVID-19 pandemic was prolonged.⁸ As the paediatric dialysis programme had only 4 dialysis nurses running the national programme, this was almost at full capacity. The mandatory requirement to split medical teams into 2 groups further aggravated the manpower shortage. Therefore, deferring fully worked-up living-related-donor kidney transplants for a prolonged duration would have added to the strain on the dialysis services. Further to the gradual and

tiered re-opening of healthcare services after the circuit breaker, we resumed our paediatric SOT activity from June 2020 with a living-donor kidney transplant. With the transition to phase 2 of gradual re-opening, the paediatric living-donor liver transplants were resumed from August 2020 (Fig. S1 of Supplementary Material in the online version of this article).

In order to safely resume the solid organ transplant programme, a number of measures (including established protocols in Fig. S1 of Supplementary Material) were put in place to ensure safety of living donors, paediatric recipients as well as the healthcare team. These included:

- (1) Requiring donors and recipients to restrict their movement and contact with other people in the 30 days preceding the scheduled transplant date. They were not allowed to travel out of the country, to come into contact with a COVID-19 positive or suspect patient, or come into contact with people considered at “high-risk” in the preceding 14 days.
- (2) Pre-admission COVID-19 nasopharyngeal swab testing using reverse transcription-polymerase chain reaction (RT-PCR) 7 days and 48 hours prior to the transplant date.
- (3) Mandatory full vaccination for the entire healthcare team once the COVID-19 vaccine became available.

The transplantation proceeded only if the donors and recipients were clinically well, adherent to (1) and tested negative in (2).

Prior to transplant, outpatient transplant candidates and caregivers were seen in separate isolation bays in case of any respiratory symptoms or exposure to confirmed COVID-19 cases; with the healthcare personnel having to wear full personal protective equipment (PPE) (comprising N95 mask, gown, gloves, shoe covers and goggles). Transplants would be deferred to beyond 3 weeks post-resolution of respiratory symptoms.

None of the donors or recipients received COVID-19 vaccines because the vaccination efforts in Singapore were initially focused on the elderly and personnel in high-risk occupations.

We performed a total of 8 paediatric transplants (5 kidneys and 3 livers between June 2020 and May 2021), all from living donors only (Table 1).

Table 1. Paediatric liver and kidney transplantations performed between June 2020 and May 2021 in Singapore

Age, months/ Sex/ Weight, kg	Primary disease	PELD for liver recipient	Pre-transplant COVID-19 swab (donor and recipient) ^a	Blood products given, mL	ICU/Hospital stay, days		Immunosuppression regime		Follow-up, months	Graft survival/ Patient survival (%)	Transplant-related complications in recipient	
					Donor	Recipient	Induction	Maintenance				
K1 207/M/54	Bilateral dysplastic kidneys	-	Neg	Neg	Nil	0/5	5/38	Methylpred Basiliximab ^b MMF	Prednisolone Tacrolimus MMF	15	100/100	Nil
K2 230/F/50.9	FSGS	-	Neg	Neg	Nil	0/7	5/28	Methylpred Basiliximab ^b MMF	Prednisolone Tacrolimus MMF	14	100/100	Antibody-mediated rejection (non-HLA)
K3 114/F/19.8	Congenital solitary cystic dysplastic kidney	-	Neg	Neg	Nil	0/5	5/42	Methylpred Basiliximab ^b MMF	Prednisolone Tacrolimus MMF	12	100/100	Nil
K4 63/F/14.9	Denys-Drash syndrome	-	Neg	Neg	980	0/5	8/44	Methylpred Basiliximab ^b MMF	Prednisolone Tacrolimus MMF	8	100/100	Intraoperative bleeding from graft gonadal vein/hilar fat
K5 222/M/53.2	Alport syndrome	-	Neg	Neg	Nil	0/6	5/10	Methylpred Basiliximab ^b MMF	Prednisolone Tacrolimus MMF	4	100/100	Nil
L1 33/M/11	Biliary atresia	13	Neg	Neg	255	0/6	4/26	-	Prednisolone Tacrolimus	12	100/100	Nil
L2 14/F/10.25	Biliary atresia	20.4	Neg	Neg	415	0/6	5/24	-	Prednisolone Tacrolimus	11	100/100	Pneumothorax Mild ACR
L3 16/F/9.31	Biliary atresia	25.6	Neg	Neg	1275	0/7	7/79	-	MMF Prednisolone Tacrolimus	8	100/100	PV thrombosis Abdominal abscess EBV-hepatitis

ACR: acute cellular rejection; D-2: within 48 hours prior to transplant; D-7: 7 days prior to transplant; EBV: Epstein Barr virus; FSGS: focal segmental glomerulosclerosis; ICU: intensive care unit;

HLA: human leukocyte antigen; K1–5: kidney transplant numbers 1–5; L1–3: liver transplant numbers 1–3; Methylpred: methylprednisolone; MMF: mycophenolic mofetil; Neg: negative;

PELD: paediatric end-stage liver disease score

^a Swab from nasopharynx and oropharynx for SARS-CoV-2-RT-PCR

^b Basiliximab was given on day 0 and day 4

Notes:

None of the donors or recipients received any COVID-19 vaccine.

Among the kidney transplant recipients, case K3 was a pre-emptive transplant.

The immunosuppression practice remained the same pre-COVID-19 and during COVID-19.

Intraoperative measures included the use of PPE whereas the immediate post-transplant protocols were not altered. In the immediate post-transplant period, we did not see an increase in ventilation need or respiratory infections. This meant that the precautions taken pre-transplant coupled with the negative PCR testing prior to transplant were sufficient measures until the immediate post-transplant period.

Following discharge, in addition to standard post-transplant advice, recipients were instructed to report respiratory symptoms or any symptoms attributable to COVID-19. They were also advised to mostly stay at home, wear mask when going out and avoid crowded places for 3–6 months in the post-transplant period. At a median follow-up of 11.5 months (range 4–15 months), all patients are alive and well with good graft function. Screening for COVID-19 was not routine. However, there was a low threshold for testing for COVID-19 using the SARS-CoV-2 PCR based on clinical indications. While it is possible that asymptomatic COVID-19 could have been missed, there was no evidence of increased respiratory or other morbidity attributable to COVID-19 in the immediate post-transplant period and for the duration of the follow-up.

Living-donor organ transplantation allows for directed organ donation. During a pandemic, the transplants could be scheduled, balancing the clinical acuity of the transplant candidates with the resource constraints on the healthcare system. Furthermore, the patients and their families could adhere to the safe-management measures in place.

Going forward, we have made pre-transplant COVID-19 vaccination mandatory for age-eligible transplant candidates.⁹ Pre-transplant COVID-19 vaccines are administered 2–4 weeks apart from other live vaccines; based on common paediatric practice to separate live vaccines from other vaccines. For the eligible organ recipients, COVID-19 vaccination is being mandated 3–6 months after their transplantation.¹⁰

In the course of the past 15 months, we have demonstrated that paediatric living-donor liver and kidney transplantation could be resumed safely during COVID-19 under strict pre-transplant isolation and screening protocols, peri-transplant infectious precautions and standard post-transplant immunosuppression and management.

Acknowledgment

We would like to thank Ms Dimple Rajgor for helping with formatting and submission of the manuscript.

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