[*†]Daphna T. Katz, [*]Miguel Saps, [*]Alejandro Llanos-Chea, and [*]Liz Febo-Rodriguez
[*]*Division of Pediatric Gastroenterology, Hepatology, and Nutrition, University of Miami Miller School of Medicine*
[†]*Department of Pediatrics, Jackson Memorial Hospital, Miami, FL*

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SARS-CoV-2 in Pediatric Liver Transplant Recipients: The European Experience

To the Editor: We read the article by Kehar et al (1) with great interest, in which the authors suggest that pediatric liver transplant (LT) recipients in North America were not at risk of worse outcomes compared to chronic liver disease patients (CLD). We hereby present our data from three international registries on coronavirus disease 2019 (COVID-19) in pediatric liver patients (CovidHep, SECURE-Liver, ERN RARE-LIVER), which offer a different viewpoint.

Twenty-one LT recipients and 16 CLD pediatric patients from 10 European centres developed confirmed severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection (Table 1). LT recipients were more frequently hospitalized (38% vs 19%; relative risk [RR] 2.03; 95% confidence interval [CI] 0.7–6.4; $P = 0.20$) and presented more complications (19%) in comparison to CLD (0%). Two LT children required intensive care, one requiring non-invasive ventilation. There were no deaths. Inpatient LT recipients were more frequently on combined immunosuppression, specifically prednisone and mycophenolate mofetil (MMF) compared to outpatients (87.5% vs 7.7%; RR 0.09; 95% CI 0.02–0.41; $P = 0.0003$). Unlike what has been reported in adults, time since LT was probably not a factor, given that follow up spanned 1–8 years.

The relative contributions of immunosuppression, comorbidity, age and other variables to host vulnerability to SARS-CoV2 infection remain unclear. It is possible that combined immunosuppression led to increased hospitalization of LT recipients. MMF discontinuation has recently been recommended to curb the risk of lymphopenia (2). Although this is a small cohort, we suggest that pediatric LT recipients under combined immunosuppression, especially using MMF, should be monitored carefully in case of SARS-CoV-2 infection and prioritized for vaccine studies.

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Ruth De Bruyne, Department of Pediatric Gastroenterology, Hepatology and Nutrition, Ghent University Hospital, Ghent University, Ghent, Belgium
Sandra Ferreira, Paediatric Hepatology and Liver Transplant Unit, Paediatric Department of Coimbra Hospital and University Center (CHUC)
Loreto Hierro, Department of Pediatric Hepatology, La Paz University Hospital, Madrid, Spain
Martin Jankofsky, Department of Pediatric Hepatology and Liver Transplantation, University Medical Centre Hamburg-Eppendorf, Hamburg, Germany
Matea Kovačić, University of Zagreb School of Medicine, Zagreb, Croatia
Mathias Ruiz, Hépatologie, Gastroentérologie et Nutrition pédiatriques, Centre de référence de l'atrésie des voies biliaires et cholestases génétiques, Hôpital Femme Mère Enfant, Hospices Civils de Lyon, Lyon, France
Natalie Van den Ende, Department of Gastroenterology and Hepatology, University Hospitals KU Leuven, Leuven, Belgium

[*†]Gustav Buescher, [*†]Marcial Sebode, [‡]Thomas Marjot, [§]Gwilym J. Webb, [||]Andrew M. Moon, [‡]Eleanor Barnes, [||]Alfred S. BarrittIV, [†¶]Mara Cananzi, [*†]Ansgar W. Lohse, [†#]Marianne H. Jørgensen and [**]Valérie McLin
[*]*I. Department of Medicine, University Medical Centre Hamburg-Eppendorf, Hamburg, Germany*
[†]*European Reference Network on Hepatological Diseases (ERN RARE-LIVER)*
[‡]*Oxford Liver Unit, Translational Gastroenterology Unit, Oxford University Hospitals NHS Foundation Trust, University of Oxford, Oxford, UK*
[§]*Cambridge Liver Unit, Addenbrooke's Hospital, Cambridge University Hospitals, Cambridge, UK*
[||]*Division of Gastroenterology and Hepatology, University of North Carolina, Chapel Hill, NC*
[¶]*Unit of Pediatric Gastroenterology, Digestive Endoscopy, Hepatology and Care of the Child with Liver Transplantation, Department of Women's and Children's Health, University Hospital of Padova, Padova, Italy*
[#]*Department of Paediatric and Adolescent Medicine, Rigshospitalet, Copenhagen, Denmark*
[**]*Swiss Pediatric Liver Center, Department of Pediatrics, Gynecology and Obstetrics, University of Geneva and University Hospitals Geneva, Geneva, Switzerland*

TABLE 1. Patient characteristics and clinical parameters of pediatric liver transplant recipients and patients non-transplanted with chronic liver disease with SARS-CoV-2 infection

	Liver transplant recipients (LT)	Non-transplanted, chronic liver disease patients (CLD)
n	21	16
Female	12 (57%)	7 (44%)
Median age (interquartile range)	10 (6–14)	12 (1–15)
Liver cirrhosis	4 (19%)	8 (50%)
Median years from transplantation (interquartile range)	4 (1–8)	n.a.
Liver disease aetiology		
Biliary atresia	9 (43%)	3 (19%)
Autoimmune hepatitis	1 (5%)	4 (25%)
Alagille syndrome	2 (10%)	2 (13%)
Progressive familial intrahepatic cholestasis	3 (14%)	1 (6%)
Other entities*	5 (24%)	6 (38%)
Comorbidities		
Overweight (BMI > 25)	0	2 (13%)
Arterial hypertension	2 (10%)	1 (6%)
Pulmonary disease	1 (5%)	2 (13%)
Chronic kidney disease	2 (10%)	1 (6%)
Other chronic diseases	5 (24%)	5 (31%)
Symptoms of SARS-CoV-2 infection		
Fever	8 (38%)	4 (25%)
Coughing	8 (38%)	5 (31%)
Shortness of breath	3 (14%)	3 (19%)
Fatigue	4 (19%)	0
Myalgia	0	1 (6%)
Outcome		
Severe complications (exacerbation of chronic diarrhea, melena and hematochezia†, hemodialysis)	3 (14%)	0
Multisystem inflammatory syndrome (MISC) with bacterial superinfection	1 (5%)	0
Inpatient care	8 (38%)	3 (19%)
Intensive care (ICU admission)	2 (10%)	0
Non-invasive ventilation	1 (5%)	0
Invasive ventilation	0	0
Death	0	0
Immunosuppressive regimen of non-hospitalized patients		
Tacrolimus mono	11 (52%)	
Ciclosporin mono	1 (5%)	
Tacrolimus + ciclosporin	1 (5%)	
Prednisolone mono		2 (13%)
Azathioprine mono		1 (6%)
Adalimumab mono		1 (6%)
Prednisolone + azathioprine		3 (19%)
None		6 (38%)
Immunosuppressive regimen of hospitalized patients		
Tacrolimus mono	2 (10%)	
Tacrolimus + prednisolone	2 (10%)	
Tacrolimus + mycophenolate mofetil	1 (5%)	
Mycophenolate mofetil + prednisolone	1 (5%)	
Ciclosporin + prednisolone	1 (5%)	
Ciclosporin + mycophenolate mofetil + prednisolone	1 (5%)	
None		3 (19%)

BMI = body mass index; CLD = chronic liver disease patients; ICU = intensive care unit; LT = liver transplant recipients; SARS-CoV-2 = severe acute respiratory syndrome coronavirus-2. * LT recipients: glycogen storage disease, methylmalonic aciduria, acute liver failure, neonatal sclerosing cholangitis, cholestasis and malnutrition, hepatoblastoma; CLD: IgG4-associated disease, PSC, Joubert syndrome, biliary cirrhosis, neonatal cholestasis, ARPKD.
† Due to underlying liver disease.

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