INBORN ERRORS OF METABOLISM - II

ROLE OF LIVER TRANSPLANT IN CHILDREN WITH INBORN ERRORS OF METABOLISM - INDICATIONS AND OUTCOMES

***Rajkali Rajendiran**
****Jagadeesh Menon**
*****Naresh Shanmugam**

Abstract: *Inborn errors of metabolism (IEMs) represent one of the major indications for pediatric liver transplantation, particularly when conventional dietary and medical therapies fail to prevent metabolic instability or progressive organ damage. Liver transplant not only replaces failing hepatic function but also corrects specific enzyme deficiencies central to disorders such as urea cycle defects, maple syrup urine disease, tyrosinemia, organic acidemias, Wilson disease, glycogen storage disorders, Crigler-Najjar syndrome, progressive familial intrahepatic cholestasis and primary hyperoxaluria. Evidence demonstrates that liver transplant provides durable metabolic control, eliminates life-threatening decompensation and permits dietary liberalization, with survival outcomes comparable to non-metabolic indications. Early transplantation mitigates irreversible neurological, cardiac or renal injury and markedly improves growth and quality of life. This review summarizes the pathophysiology, indications and outcomes of liver transplant across major pediatric metabolic disorders, emphasizing its pivotal role in long-term metabolic stabilization.*

Keywords: *Inborn errors of metabolism (IEM), Pediatric liver transplantation, Metabolic stabilization, Long-term outcomes.*

Points to Remember

- ***Liver transplantation serves as a metabolic cure, correcting enzyme deficiencies in liver-related metabolic disorders.***
- ***Early liver transplant improves outcomes, preventing irreversible neurological, cardiac, or renal injury in disorders such as UCDs, MSUD, and organic acidemias.***
- ***Post-transplant metabolic stability helps in elimination of life-threatening decompensations and normalization of key biochemical parameters.***
- ***Quality of life improves substantially, as children can often discontinue strict dietary restrictions and specialized metabolic therapies.***
- ***Overall survival and graft outcomes are comparable to non-metabolic transplant indications, supporting LT as a safe and effective long-term solution for selected metabolic diseases.***

References

1. Eldredge JA, Hardikar W. Current status and future directions of liver transplantation for metabolic liver disease in children. Pediatr Transplant. 2024 Feb; 28(1): e14625.
2. Miller W, Wothe J, Wang Q, Vock D, Bhatt H, Salunke A, et al. Long-term Outcomes of Liver Transplantation for Inborn Errors of Metabolism in Children. Transplant Proc. 2024; 56(6):1359-64.
3. Menon J, Vij M, Sachan D, Rammohan A, Shanmugam N, Kaliamoorthy I, et al. Pediatric metabolic liver diseases: Evolving role of liver transplantation. World J Transplant. 2021 Jun 18; 11(6):161-79.
4. Liver Transplantation and Health Outcomes in Urea Cycle Disorders | Urea Cycle Disorders Consortium

* Consultant (Associate),
email : r.rajkali@yahoo.in
** Consultant,
Department of Pediatric Gastroenterology,
Hepatology and Transplantation.
*** Director - Women and Child Health,
Consultant Pediatric Hepatologist and
Gastroenterologist,
Institute of Advanced Pediatrics,
Dr Rela Institute and Medical Centre,
Chennai.

Cite as: Rajkali Rajendiran, Jagadeesh Menon, Naresh Shanmugam. Role of liver transplant in children with inborn errors of metabolism - Indications and outcomes, Indian J Pract Pediatr. 2025; 27(4):360-365.

[Internet]. [cited 2025 Dec 11]. Available from: https://ucdc.rarediseasesnetwork.org/news/liver-transplantation-and-health-outcomes-urea-cycle-disorders.

5. Oishi K, Arnon R, Wasserstein MP, Diaz GA. Liver transplantation for pediatric inherited metabolic disorders: considerations for indications, complications, perioperative management. Pediatr Transplant. 2016 Sep; 20(6):756-69.
6. Häberle J, Burlina A, Chakrapani A, Dixon M, Karall D, Lindner M, et al. Suggested guidelines for the diagnosis and management of urea cycle disorders: First revision. J Inherit Metab Dis. 2019 Nov; 42(6):1192-230.
7. Department of Pediatrics, Division of Pediatric Gastroenterology, Akdeniz University School of Medicine, Antalya, Turkey, Basturk A, Keceli M, Department of Pediatrics, Division of Pediatric Gastroenterology, Akdeniz University School of Medicine, Antalya, Turkey, Erbis H, Department of General Surgery, Akdeniz University School of Medicine, Transplantation Institute, Antalya, Turkey, et al. Liver transplantation from a live donor to a patient with maple syrup urine disease: Two case reports. Türk Pediatri Ars. 2018 Jul 29; 53(2):113-6.
8. Vasudevan AK, Shanmugam N, Rammohan A, Balakrishnan U, Menon J, Iqbal MAUH, et al. Long-Term Amino Acid Homeostasis, Neurodevelopmental and Growth Profiles Following Liver Transplantation in Maple Syrup Urine Disease. Pediatr Transplant. 2024 Sep; 28(6):e14845.
9. Daou KN, Barhoumi A, Bassyouni A, Karam PE. Diagnostic and Therapeutic Challenges of Hereditary Tyrosinemia Type 1 in Lebanon: A 12-Year Retrospective Review. Front Pediatr. 2021;9:698577.
10. Bolia R, Srivastava A. Liver Transplantation for Tyrosinemia Type 1 in the Developing World: Is It Really the Best We Can Offer? Indian J Pediatr. 2022 May 1; 89(5):427-8.
11. Menon J, Shanmugam N, Valamparampil JJ, Hakeem A, Vij M, Jalan A, et al. Liver Transplantation: A Safe and Definitive Alternative to Lifelong Nitisinone for Tyrosinemia Type 1. Indian J Pediatr. 2022 May;89(5): 438-44.
12. Mc Guire PJ, Lim-Melia E, Diaz GA, Raymond K, Larkin A, Wasserstein MP, et al. Combined liver-kidney transplant for the management of methylmalonic aciduria: a case report and review of the literature. Mol Genet Metab. 2008 Jan; 93(1):22-9.
13. Romano S, Valayannopoulos V, Touati G, Jais JP, Rabier D, de Keyzer Y, et al. Cardiomyopathies in Propionic Aciduria are Reversible After Liver Transplantation. J Pediatr. 2010 Jan 1; 156(1):128-34.
14. Baumgartner MR, Hörster F, Dionisi-Vici C, Haliloglu G, Karall D, Chapman KA, et al. Proposed guidelines for the diagnosis and management of methylmalonic and propionic acidemia. Orphanet J Rare Dis. 2014 Sep 2; 9(1):130.
15. Ferrarese A, Morelli MC, Carrai P, Milana M, Angelico M, Perricone G, et al. Outcomes of Liver Transplant for Adults With Wilson's Disease. Liver Transplant Off Publ Am Assoc Study Liver Dis Int Liver Transplant Soc. 2020 Apr; 26(4):507-16.
16. Shimizu S, Sakamoto S, Horikawa R, Fukuda A, Uchida H, Takeda M, et al. Longterm Outcomes of Living Donor Liver Transplantation for Glycogen Storage Disease Type 1b. Liver Transplant Off Publ Am Assoc Study Liver Dis Int Liver Transplant Soc. 2020 Jan; 26(1):57-67.
17. Liu M, Sun LY. Liver Transplantation for Glycogen Storage Disease Type IV. Front Pediatr. 2021; 9:633822.
18. Sambati V, Laudisio S, Motta M, Esposito S. Therapeutic Options for Crigler-Najjar Syndrome: A Scoping Review. Int J Mol Sci. 2024 Oct 13; 25(20):11006.
19. Menon J, Shanmugam N, Vij M, Veerankutty FH, Rammohan A, Rela M. Simultaneous total internal biliary diversion during liver transplantation for progressive familial intrahepatic cholestasis type 1: Standard of care? Liver Transplant Off Publ Am Assoc Study Liver Dis Int Liver Transplant Soc. 2024 Jul 1; 30(7):699-706.
20. Kubitz R, Dröge C, Kluge S, Stross C, Walter N, Keitel V, et al. Autoimmune BSEP Disease: Disease Recurrence After Liver Transplantation for Progressive Familial Intrahepatic Cholestasis. Clin Rev Allergy Immunol. 2015 Jun 1; 48(2):273-84.
21. Morgan SH, Purkiss P, Watts RWE, Mansell MA. Oxalate Dynamics in Chronic Renal Failure: Comparison with Normal Subjects and Patients with Primary Hyperoxaluria. Nephron. 2008 Dec 5; 46(3):253-7.
22. Cochat P, Schärer K. Should liver transplantation be performed before advanced renal insufficiency in primary hyperoxaluria type 1? Pediatr Nephrol. 1993 Apr 1;7(2): 212-8.