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Review Article

Safety and efficacy of pediatric liver transplantation in Saudi Arabia

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ABSTRACT

Evidence shows that liver transplantation is a good management choice for pediatric patients with severe hepatic disorders. In addition, the approach can be used for managing different hepatic disorders, including metabolic and familial ones. Therefore, liver transplantation is indicated and should be urgently conducted to intervene against further deterioration in the health status of the affected patients and enhance their prognosis. Various investigations in the literature validated the efficacy of the modality for different age groups, although many of them reported the incidence of different related complications. In Saudi Arabia, not many studies reported the safety and efficacy of liver transplantation for pediatric patients. The present literature review provided insight regarding the safety and efficacy of the procedure for this population group. We can conclude that liver transplantation in pediatric settings is a safe and productive approach that can be successfully conducted with a favorable prognosis. Moreover, it has been shown that living-related liver transplantation is more favorable than cadaveric-related liver transplantation in these settings, especially when there is a graft shortage, as reported in Saudi Arabia. Despite the favorable outcomes, further reports are still needed for validating the current evidence.

Keywords: Pediatrics, Children, Liver transplantation, Safety, Complications, Efficacy

INTRODUCTION

Evidence shows that various etiologies can affect liver functions in the pediatric population, leading to significant morbidities and life-threatening conditions.[1] These include metabolic, familial, and infectious disorders that might lead to liver failure and subsequent complications resulting in death. Thus, conservative management might be a valid therapeutic approach in many cases. However, in some cases, liver transplantation is indicated and should be urgently conducted to intervene against further deterioration in the health status of the affected patients and enhance their prognosis.[1-3] In addition, various investigations in the literature validated the efficacy of the modality for different age groups, although many of them reported the incidence of different related complications.[4,5]

In Saudi Arabia, not many studies reported the safety and efficacy of liver transplantation for pediatric patients. However, reports show that Saudi Arabia is one of the earliest countries in the Middle East to perform this procedure.[6-9] Therefore, we aim to discuss the efficacy and safety of liver transplantation for pediatric patients in Saudi Arabia based on data from relevant studies in the literature. We also aim to discuss the indications, shed some light on the indications and advantages of the procedure, and provide a brief comparison of the superiority of living-and deceased-donor liver transplantation procedures.

LITERATURE REVIEW

This literature review is based on an extensive literature search in Medline, Cochrane, and EMBASE databases which was performed on 27th November 2021 using the medical subject headings (MeSH) or a combination of all possible related terms, according to the database. To avoid missing potential studies, a further manual search for papers was done through Google Scholar while the reference lists of the initially included papers. Papers discussing safety and efficacy of pediatric liver transplantation in Saudi Arabia were screened for useful information. No limitations were posed on date, language, age of participants, or publication type.

DISCUSSION

The practice of liver transplantation has been described for decades in the scientific literature for managing different conditions. In the current practice guidelines, liver transplantation is considered a main therapeutic approach for many liver-related diseases and neoplasms that might be life-threatening. Furthermore, evidence indicates the efficacy and safety of the condition. Therefore, it might be prioritized in many settings based on the management criteria of each country.[10] The present section discusses the reported efficacy of liver transplantation among pediatric patients in Saudi Arabia. Moreover, we will shed light on the safety of the procedure and the main reported complications based on evidence from studies in the literature.

It has been shown that the great success in liver transplantation has been attributed to the remarkable advances in the surgical field and techniques enhancing the outcomes of the procedure. This also led to the significant outcomes of liver transplantation, even among pediatric patients and very young infants. However, reports still indicate a significant gap between the number of suitable liver donors and the number of patients indicated to have a liver transplantation procedure. Therefore, living-related liver transplantation has been described in the literature as a valid approach to overcome the unavailability of suitable human liver donors needed to conduct cadaveric liver transplantation. Furthermore, evidence from studies in Saudi Arabia shows that cadaveric liver transplantation is hard to perform for children with end-stage liver diseases due to the remarkable shortage and limitations in organ quality and organ shortage. Accordingly, it has been demonstrated that using living-related liver transplantation is acceptable in the different settings across the Kingdom, being the most suitable life-saving approach in different pediatric settings. Studies also aimed to develop modalities that can successfully predict the presence of suitable liver donors to manage patients undergoing liver transplantation. For instance, studies showed that Model for End-stage Liver Disease (MELD)-Na and the pediatric end-stage liver disease (PELD) score are valid tools for assessment and allocation of the health status of donor liver among patients suffering from end-stage liver diseases.[11] However, it has been shown that these scores are not adequately applied in Saudi Arabia for the pediatric population. Instead, most centers perform liver transplantation procedures irrespective of their estimated scores. Moreover, it has been shown that such processes are adequately conducted based on a specified waiting list for the indicated children. Accordingly, accurately estimating these scores cannot be conducted in these settings for the reasons mentioned above.[12-14]

A previous investigation at King Faisal specialist hospital and research center estimated that the overall graft and recipient survival rates were 89% and 93%, respectively. However, medical complications were reported among 18% of the recipients, while 17% developed surgical complications. Moreover, during the hospital stay, it has been shown that biopsy-proven rejection was estimated in 7% of the included population, and 5% died after hospital discharge.[15] It should be noted that the relatively high rates of adverse events are attributable to the fact that the procedures were conducted at a high-volume center, in addition to the potential barriers regarding patients' demographics and quality of care. Another investigation in Saudi Arabia also indicated the efficacy of liver transplantation in the pediatric population. However, some complications were also reported among them. The most common complications include hepatic artery thrombosis, biliary strictures, portal vein stenosis, portal vein thrombosis, and hepatic vein stenosis. Overall, the estimated graft and patient survival rates were 86.8% and 89%, respectively. In this study, it has been reported that 15 patients died, and three allografts were lost postoperatively. However, the authors concluded that these reported complications are acceptable in their settings due to different factors related to the availability of resources.[16] Holdar et al also concluded that liver transplantation was associated with enhanced outcomes among patients undergoing Kasai portoenterostomy to manage biliary atresia.[17] The efficacy of liver transplantation was furtherly reported among investigations in Saudi Arabia compared between living and deceased-donor liver transplantation outcomes. Al-Sebayel et al estimated that the total graft and patient survival rates were 80% and 90%, respectively.[18] Besides, no significant differences were noticed between the two groups. However, it has been shown that vascular and biliary complications were significantly higher among patients receiving living-donor liver transplantation. Bassas et al also conducted an investigation at the Armed Forces hospital in Saudi Arabia to investigate the outcomes of liver transplantation in the pediatric population.[19] The authors reported that the procedure is very efficient in general, with estimated rates of 93% and 96% for graft and patient survival rates. However, many complications were reported. The most common ones include positive cytomegalovirus PP65 antigen (38%), acute cellular injury and rejection (38%), systemic infections (14%), vascular occlusion (13%), biliary leaks (10%), and wound infections (3.4%). Accordingly, the

findings of these investigations indicate the validity of liver transplantation for managing different hepatic disorders in the pediatric population with favorable outcomes and minimal adverse events.

Metabolic and familial liver diseases are the most common reasons for conducting liver transplantation in the pediatric population in Saudi Arabia.[15] The most significant endpoint for conducting liver transplantation for these patients was 30-day mortality regardless of the PELD scores for these children. This has been validated for different metabolic and familiar liver diseases, including glycogen storage disease type 4 and progressive familial intrahepatic cholestasis type 3. Recommendations for liver transplantation include having a decompensated hepatic disorder, and the estimated life expectancy of the affected patients is <four weeks according to the assessed liver function tests and clinical manifestations of the affected patients. Other indications include unresectable hepatoblastoma associated with other comorbid hepatic conditions and disorders, liver tumors, and acute liver failure. Evidence shows that the first reported living-related liver transplantation procedure was conducted in the Riyadh Armed Forces hospital and Saudi Arabia in 1998 for a two-year-old girl with favorable outcomes and safety profile.[19] Since the first case was conducted, evidence shows that similar liver transplantation procedures were conducted for adults and pediatric patients.

Many advantages and favorable outcomes were reported for living-related liver transplantation over cadaveric liver transplantation. The first advantage is that patients and donors indicated to living-related liver transplantation are usually well-prepared, and the procedure is considered an elective one. Moreover, living-related liver transplantation is also superior to the other modality. It produces more favorable outcomes by offering enhanced organ quality, favorable timing, and decreased pressure on the waiting list of patients requiring liver transplantation procedures. The incidence of hepatocellular ischemic damage has also been less frequent among patients undergoing living-related liver transplantation procedures.[20,21] This is usually associated with reduced secondary poorly or non-functioning grafts postoperatively. A previous investigation also demonstrated the low prevalence of acute cellular rejection events among pediatric patients receiving living-related liver transplantation.[22] The need to receive immunosuppression modalities has also been lower among patients receiving living-related liver transplantation.[22,23] In this context, it has been demonstrated that the outcomes (regarding patients and graft survival) are superior with living-related liver transplantation.[24-26]

The safety of living transplantation should also be evaluated based on the incidence of related morbidities on donors. Evidence shows that the incidence of these morbidities is not high in these settings. A previous investigation in Saudi Arabia demonstrated that only 8% of the included donors had biliary leakage from the cut surface.[27] All of these cases were successfully managed by relaparotomy procedures. The authors concluded that the estimated rate is more favorable than the findings reported by other investigations in the literature following conducting living-related liver transplantation.[7,28] Incisional hernia might also be a long-term complication among donors. However, evidence indicates that such cases can be easily managed with a favorable prognosis. After 3-4 weeks following the surgical operation, normal hepatic functions were also reported for donors. Moreover, it has been reported that there were no mortalities among this relevant population.[27,29] Accordingly, these findings indicate the validity and safety of the procedure among the different settings in Saudi Arabia.

Certain conditions might also impact the outcomes and safety of liver transplantation. For instance, reports based on statistics from the COVID-19 pandemic show that the surgical outcomes of patients with and without COVID-19 infections might be affected based on the various circumstances and pandemic-related stress. However, various investigations have indicated that children with COVID-19 usually have milder forms of the disease and do not have any serious manifestations or life-threatening complications compared to adults.[30,31] This has been attributed to various reasons among the relevant reports in the literature. Some of the reasons include the low prevalence of associated comorbidities in children, healthier respiratory tracts because of the reduced exposure to smoking and air pollutants, and having a more active and intense immune response that can deal with the various forms of threatening organisms.[32] Furthermore, it has been shown that developing an intensive immune response in adults might also explain the association between severe disease and developing respiratory distress syndrome in this population. As it is widely known, patients with liver transplantation are usually immunocompromised and are prone to catching various types of infections. However, there is no evidence estimating or documenting the rate of COVID-19 infections among these patients. In this context, evidence from global investigations during the pandemic indicated that the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus causing COVID-19 pandemic, does not usually lead to an immunocompromised state in the affected patients. This has also been validated for other coronaviruses causing similar infections. In this context, evidence shows that the immune response to the infection is the main cause responsible for initiating tissue damage in the affected patients and not due to the viral infection itself. Accordingly, it has been reported that weaker immune responses among immunocompromised patients might be protective in these situations against developing serious tissue damage and major complications.[33] However, such evidence is not supported by adequate studies in the literature and needs further validation before making solid conclusions.

CONCLUSION

Evidence shows that liver transplantation is a good management choice for pediatric patients with severe hepatic disorders. In addition, the approach can be used for managing different hepatic disorders, including metabolic and familial ones. Liver transplantation in pediatric settings is a safe and productive approach that can be successfully conducted with a favorable prognosis. Moreover, it has been shown that living-related liver transplantation is more favorable than cadaveric-related liver transplantation in these settings, especially when there is a graft shortage, as reported in Saudi Arabia. Despite the favorable outcomes, further reports are still needed for validating the current evidence.

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REFERENCES

1. Dhawan A, Cheeseman P, Mieli-Vergani G. Approaches to acute liver failure in children. Pediatric Transplantation. 2004;8(6):584-8.
2. Ciocca M, Ramonet M, Cuarterolo M, López S, Cernadas C, Alvarez F. Prognostic factors in paediatric acute liver failure. Arch Disease Childhood. 2008;93(1):48-51.
3. Cochran JB, Losek JD. Acute liver failure in children. Pediatric Emergency Care. 2007;23(2):129-35.
4. Al Sebayel M, Abaalkhail F, Hashim A. Living donor liver transplant versus cadaveric liver transplant survival in relation to model for end-stage liver disease score. Transplantation Proceedings. 2015;47(4):1211-3.
5. Jain A, Singhal A, Kashyap R, Safadjou S, Ryan CK, Orloff MS. Comparative analysis of hepatitis C recurrence and fibrosis progression between deceased-donor and living-donor liver transplantation: 8-year longitudinal follow-up. Transplantation. 2011;92(4):453-60.
6. Al Sebayel MS, Ramirez CB, Abou Ella K. The first 100 liver transplants in Saudi Arabia. Transplantation Proceedings. 2001;33(5):2709.
7. Jawdat M, Qattan N, Bassas A, Al Karawi MA, Mohamed E, Khallil H. The first liver transplant in Saudi Arabia and the Arab world. Hepato-gastroenterology. 1993;40(3):297-300.
8. Jawdat M, Qattan N, al Karawi M, Mohamed AE, Khalil H. The first liver transplant in Saudi Arabia and the Arab world. Transplantation. 1992;54(4):766-7.
9. Al Sebayel M, Kizilisik A, Ramirez C. Liver transplantation at king fahad national guard hospital riyadh, kingdom of saudi arabia. Saudi J Kidney Dis Transplantation. 1996;7(2):173.
10. Pham TS, Reda A, Ngan Nguyen TT. Blood exchange transfusion in viral hepatitis in a small infant: a case report. Transfusion Apheresis Sci. 2020;59(6):102907.
11. Wiesner RH, McDiarmid SV, Kamath PS. MELD and PELD: application of survival models to liver allocation. Liver Transplantation. 2001;7(7):567-80.
12. Al-Judaibi B, Almaghrabi R, Alghamdi M. Saudi association for the study of liver diseases and transplantation position statement on liver transplantation during the COVID-19 pandemic. Saudi J Gastroenterol. 2020;26(5):233-9.
13. Son PT, Reda A, Viet DC. Exchange transfusion in the management of critical pertussis in young infants: a case series. Vox sanguinis. 2021;116(9):976-82.
14. Thieu H, Bach Dat B, Nam NH. Antibiotic resistance of Helicobacter pylori infection in a children's hospital in Vietnam: prevalence and associated factors. Minerva Medica. 2020;111(5):498-501.
15. Fayyad A, Shagrani M, AlGoufi T. Progress and outcomes of the first high-volume pediatric liver transplantation program in Saudi Arabia. Clinical Transplants. 2014:77-83.
16. Khan I, Al-Shaqrani M, Arain Z, Al-Hebbi H, Wali S, Bassas A. One hundred and thirty-seven living donor pediatric liver transplants at Riyadh Military Hospital Results and outlook for future. Saudi Med J. 2009;30:403-8.
17. Holdar S, Alsaleem B, Asery A, Al-Hussaini A. Outcome of biliary atresia among Saudi children: A tertiary care center experience. Saudi J Gastroenterol. 2019;25(3):176-80.
18. Al-Sebayel M, Khalaf H, Al-Sofayan M. Experience with 122 consecutive liver transplant procedures at King Faisal Specialist Hospital and Research Center. Ann Saudi Med. 2007;27(5):333-8.
19. Bassas AF, Chehab MS, Al-Shahed MS. Pediatric living-related liver transplantation in Saudi Arabia. Saudi Med J. 2002;23(6):640-4.
20. El-Qushayri AE, Ghozy S, Reda A, Kamel AMA, Abbas AS, Dmytriw AA. The impact of Parkinson's disease on manifestations and outcomes of Covid-19 patients: A systematic review and meta-analysis. Reviews Med Virol. 2021:e2278.
21. El-Qushayri AE, Dahy A, Reda A. A closer look to the high burden of the psychiatric disorders among health care workers (HCWs) in Egypt during COVID-19 outbreak: A meta-analysis of 3137 HCWs. Epidemiol Health. 2021:e2021045.
22. Marcos A, Ham JM, Fisher RA, Olzinski AT, Posner MP. Single-center analysis of the first 40 adult-to-adult living donor liver transplants using the right lobe. Liver Transplantation. 2000;6(3):296-301.
23. Neuberger J. Incidence, timing, and risk factors for acute and chronic rejection. Liver Transplantation Surgery. 1999;5(4-1):S30-6.
24. Révillon Y, Michel JL, Lacaille F. Living-related liver transplantation in children: the 'Parisian' strategy to safely increase organ availability. J Pediatr Surg. 1999;34(5):851-3.
25. Malagó M, Rogiers X, Wadström J, Burdelski M, Broelsch CE. Optimal clinical regimens for living

related liver transplantation. Transplantation Proceedings. 1994;26(5):2665-8.
26. Emond JC, Renz JF, Ferrell LD. Functional analysis of grafts from living donors. Implications for the treatment of older recipients. Anna Surg. 1996;224(4):544-52.
27. Al-Shurafa H, Jawdat M, Wali S. Donor experience and outcome of pediatric living-related liver transplantation in Saudi Arabia. J Hepato-biliary-pancreatic Surgery. 2003;10(6):428-31.
28. Reichert PR, Renz JF, Rosenthal P. Biliary complications of reduced-organ liver transplantation. Liver Transplantation Surg. 1998;4(5):343-9.
29. Dibas M, Doheim MF, Ghozy S, Ros MH, El-Helw GO, Reda A. Incidence and survival rates and trends of skull Base chondrosarcoma: A Population-Based study. Clin Neurol Neurosurg. 2020;198:106153.
30. Wang G, Zhang Y, Zhao J, Zhang J, Jiang F. Mitigate the effects of home confinement on children during the COVID-19 outbreak. The Lancet. 2020;395(10228):945-7.
31. Lee PI, Hu YL, Chen PY, Huang YC, Hsueh PR. Are children less susceptible to COVID-19? J Microbiol. 2020;53(3):371-2.
32. Behrman RE, Kliegman RM, Jenson HB. Nelson Textbook of Pediatrics. Arch Dis Childhood. 1945;40:338-8.
33. D'Antiga L. Coronaviruses and Immunosuppressed Patients: The Facts During the Third Epidemic. Liver Transplantation. 2020;26(6):832-4.

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