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Paediatric Liver Transplant at Army Liver Transplant Unit, Pakistan; A Four-Year Data

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ABSTRACT

Objective: To re-examine the data about survival, prognosis, and complications of twenty-five paediatric liver transplant procedures carried out at Army Liver Transplant Unit, Pak Emirates Military Hospital Rawalpindi, Pakistan.

Study Design: Retrospective longitudinal study.

Place and Duration of Study: Army Liver Transplant Unit, Pak Emirates Military Hospital, Rawalpindi, Pakistan, from Jan 2016 to Feb 2020.

Methodology: The procedural and follow-up data regarding twenty-five pediatric liver transplants was reviewed, and demographic variables, transplant indications and outcomes were documented.

Results: The donation was entirely from living donors. Recipients included 12 boys and 13 girls of mean age 5.8±2.00 years. The stay at the hospital averaged 18±5.6 days. Indications in the order of frequency of encounter included 9(36%) cases of Cryptogenic liver cirrhosis, 4(16%) cases of progressive familial intrahepatic cholestasis, 3(12%) cases of Wilson's disease, 2(8%) cases of Tyrosinemia, congenital hepatic fibrosis and biliary atresia each and one patient (4%) of Criggler-Najjar syndrome, glycogen storage diseases and autoimmune liver disease each. Major complications included viral infections, thrombosis of the portal vein and hepatic artery, bile leak and post-transplant diaphragmatic hernia. 20(80%) recipients were recorded to have survived during the follow-up.

Conclusion: Encouraging results are noted, particularly a high survival rate (20 out of 25) and low complications (few and only well-known in this age group).

Keywords: Liver transplantation, Child, Preschool, End Stage Liver Disease, Liver Cirrhosis, Cholestasis, Progressive familial intrahepatic 1, Hepatic Insufficiency, Mortality

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INTRODUCTION

Paediatric Liver transplantation has improved the lives of many patients who would be in a poor state of health and prognosis otherwise.[1] It has become a solid option for the treatment of children with endstage liver disease, promising good recovery and longer survival than ever before.[2] Modern surgical techniques have made it easy to harvest donations and solved the problem of organ scarcity.[3] This has led to a dramatic decrease in waiting list mortality. In this regard, advances in Split-liver and living-donor transplantation have been particularly beneficial. Nowadays, clinicians focus on ensuring normal growth in children and prevention of complications related to immune suppression instead of looking for a donor or transplant centre. The success of paediatric liver transplant is a bright example of teamwork.[4]

Biliary atresia remains the most frequent indication for liver transplant in paediatric age group.[5] Additionally, cholestasis, pruritis and/or ascites that are untreatable from a clinical point of view; portal hypertension with bleeding from varices that is unresponsive to treatment; multiple episodes of cholangitis or episodes of spontaneous bacterial peritonitis; progressively deficient hepatic synthesis; impact on somatic growth and hepatic encephalopathy are also among the important indication for the procedure.[6]

Paediatric liver transplantation in third-world countries is still in its infancy. Despite the excellent outcomes in established centres, third-world countries must overcome many problems to attain excellence.[7] They include lack of government support, lack of lifelong commitment, organ trafficking, absence of truly multidisciplinary teams, absence of research and continuing education programs.[8]

The current study was the first progress bookmark in the newly established liver transplantation centre at the Army Liver Transplant Unit, Military Hospital, Rawalpindi Pakistan. We aimed to describe the demographics, causes that indicated the

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transplant procedure, transplant-related complications, survival, and length of hospital stay.

METHODOLOGY

The retrospective longitudinal study was carried out to review the data of Paediatric Liver Transplant patients' data at the Army Liver Transplant Unit, Pak Emirates Military Hospital Rawalpindi Pakistan, from January 2016 and February 2020. The study protocol was approved by the Ethical Committee of the Pak Emirates Military Hospital (Ref: A/28/EC/225/2020).

Inclusion Criteria: The first twenty-five liver transplant procedures carried out at Army Liver Transplant Unit were included in the study.

Exclusion Criteria: Transplantation procedures carried out after February 2020 were excluded.

The liver transplant procedures were included in the study through consecutive sampling. Detailed consent was taken at the time of the procedure.

Blood group-compatible donors were selected from the patient's relatives. Then, the decision to carry out the transplant was made in a multidisciplinary team meeting that included the ethics committee. The surgical team performed the operations for LDLT. A group of radiologists and hepatobiliary surgeons devised a surgical plan to facilitate surgery through imaging reconstruction. Simultaneous surgery was started for the donor and recipient to minimize cold ischemia time. The left lobes of the donor were used in all cases.

Post-operatively, recipients were kept in the intensive care unit (ICU) after surgery on a ventilator. MDT was convened to overview the clinical course and decided on extubating under the guidance of extensive vasculature imaging. Immunosuppression was ensured with Infliximab, steroids, Tacrolimus, and Mycophenolate mofetil. All patients with INR <2 and platelets >100x10^9 were given Aspirin. Steroids were tapered off as recommended, and tacrolimus levels were checked during follow-up. After discharge, recipients were followed up in the outpatient department. Routine labs were also done on follow-up.

Demographic details of the liver transplant recipients, indications for the procedure, medical and surgical complications, duration of stay in the hospital and survival were documented.

Statistical Package for Social Sciences (SPSS) version 20.0 was used for the data analysis. Quantitative variables were expressed as Mean±SD and qualitative variables were expressed as frequency and percentages.

RESULTS

Twenty-five cases of paediatric liver transplantation carried out between January 2016 and February 2020 were included in the study, with a minimum follow-up of six months. Out of 25, 20(80%) were alive and healthy till the filing of this manuscript. The liver transplant recipients were aged 6 months to 8 years (mean 5.8±2.00 years). The group included 12 boys (48%) and 13 girls (52%). The mean weight of the recipients was calculated to be 13±6.006 (5.5-30) and a mean hospital stay of 18±4.81 (14-29) (Table-I).

Table-I: Demographics of the Recipients of Liver Transplant (n=25)

Characteristics	n(%)
Age, Mean±SD (range) in years	5.8±2.00 (0.6-8 years)
Sex girls/boys	12(48%)/13(52%)
Blood Group	
A	10(40%)
B	5(20%)
AB	1(4%)
O	9(36%)
Weight, Mean±SD (range) in kilograms	13±6.006 (5.5-30)
Duration of stay, Mean±SD (range) in days	18±4.81 (14-29)
Pediatric End-Stage Liver Disease (PELD) Score, Mean±SD (range)	18.12±5.6(10-27)

There were 9 cases (36%) of cryptogenic liver cirrhosis; the most frequently recognized cause of liver transplant in the patients reviewed in this study. This was followed by progressive familial intrahepatic cholestasis 4(16%) and Wilson's disease 3(12%). Tyrosinemia, congenital hepatic fibrosis and biliary atresia accounted for two patients each (8%), while one patient belonged to Criggler-Najjar syndrome, glycogen storage diseases and autoimmune liver disease each (4%) (Figure).

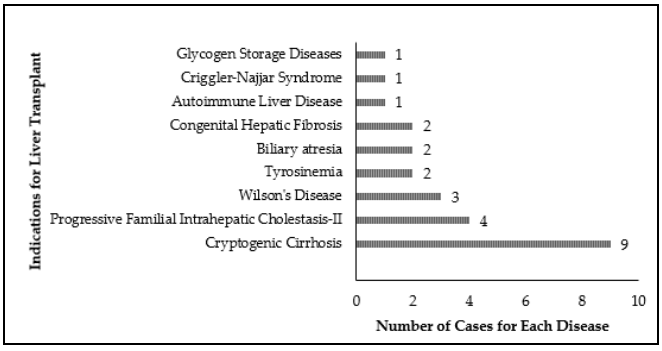

Figure: Frequency of Various Diseases/ Indications that led to the decision of Liver (n=25)

Medical complications encountered during the follow-up are listed in Table-II. They include 1 case of Epstein bar Virus infection (EBV), Cytomegalovirus infection (CMV), Hepatitis B, Budd Chiari syndrome, and nephrocalcinosis. Two of the recipients developed diabetes mellitus (DM). Among the surgical complications encountered, Hepatic artery stenosis, portal vein thrombosis and Bile leak happened once. Five recipients (20%) expired due to various complications, while 20(80%) were alive and healthy until their follow-up was recorded.

Table-II: Medical and Surgical Complications and Survival (n=25)

Parameters	Frequency
Medical Complications	
Epstein Bar Virus	1
Cytomegalovirus + Varicella Zoster	1
Hepatitis B	1
Diabetes mellitus	2
Surgical Complications	
Hepatic Artery thrombosis	1
Portal vein thrombosis	1
Bile Leak + Biliary stricture	1
Other Complications	
Post-transplant diaphragmatic hernia	1
BUDD CHIARI syndrome	1
Tremors, dystonia, dysarthria in Wilson's disease	1
Nephrocalcinosis	1
Survival	
Survived	20
Expired	5

DISCUSSION

We at the Army Liver Transplant Unit received patients at different stages of diseases that needed liver transplants. This is the first data review of this centre regarding the first 25 cases of a paediatric liver transplant. The findings and outcome reported here have important implications for the future of liver transplantation in the Third World, particularly Pakistan.

A dominant number of patients falling in this study were found to be suffering from cryptogenic cirrhosis. A similar study was published by Bhatti *et al*.[9] citing the findings of a living donor liver transplant centre in Al-Shifa Hospital, Islamabad. There were 4 cases of Wilson's disease and cryptogenic fibrosis, 3 cases of Criggler-Najjar syndrome, 2 cases of Budd-Chiari Syndrome and one case of biliary atresia. This is similar to our study, where biliary atresia was not the dominant finding. This can be attributed to the limited diagnostics, especially for metabolic and genetic diseases. Apart from that, progressive familial intrahepatic cholestasis and Wilson's disease were notable, too. The number of patients suffering from biliary atresia who had transplanted liver in this centre stood at 4th number 2(10%). While many other studies from different countries have reported biliary atresia as the most common cause for liver transplant in paediatric patients [4,7,10,11] our centre, and also Bhatti *et al*. did not receive that many patients with this condition. This could be due to a delay in initial diagnosis, lack of facilities for the bridging operation (kasai procedure), and hence fewer children surviving to reach a transplant unit.

While international studies on indications for liver transplant report decompensated liver disease due to hepatitis and cirrhosis as indications of liver transplant in adults.[12,13] One study published on pediatric liver transplant have reported biliary atresia as the most frequently encountered cause.[14] Other causes that contributed to the number of candidates for a liver transplant at our centre included congenital and metabolic disorders, which is understandable for a pediatric population. The fact that only one of the included patients suffered from hepatocellular carcinoma is again attributed to the nature of the population, i.e., paediatric. This HCC was secondary to Tyrosinemia, which is a recognized complication. HCC is supposed to be a late complication of hepatitis, and its incidence in the paediatric population is low as compared to the older population.[15] While our data suggests a slightly different epidemiological distribution of etiological factors, it may change when more data is pooled in the future.

The finding of living donors is important as many international studies from developed countries cite deceased liver donors.[16] In third-world countries, especially in Pakistan, legislation and cultural hindrances often make it hard to get deceased organ harvests and living donors from the families available. This cultural difference is comparable to other countries with similar issues. This burdens the resources double as two instead of one surgical procedures are needed, and the surgery cost is doubled.[17] Without government support and/or medical insurance, this burdens the patient's pocket.

In our study, the major medical complications that we encountered were infections with EBV, CMV, and hepatitis B. A few children developed hyperglycemia needing insulin therapy, which can be attributed to immunomodulatory drugs like steroids and tacrolimus. Surgical complications encountered included Hepatic artery thrombosis, portal vein thrombosis and bile leak. Late complications included HEP B, DM, Bud Chiari syndrome and nephrocalcinosis. One child diagnosed with Wilson disease developed dysarthria and dystonia post-transplant. These symptoms were thought to be related to delayed presentation of neurological Wilson disease. Many other studies have reported similar patterns of complications.[18] Although most of these are manageable in more developed centres with optimized facilities and advanced surgical and medical facilities, we lost a major number of patients to surgical complications 5(20%. However, the patients who survived the initial trauma of surgery remained well over the time of follow-up. The multidisciplinary teams working on establishing and running this endeavour are doing their best, yet room for optimization of effective liaison and communication remains. This is indeed a high percentage of mortality as compared to reports elsewhere. Using the index of poor prognostic factors [PPFs], we can understand that improving outcomes remains an uphill task in our population.[19] Nevertheless, the factors discussed above, including the late presentation and medical comorbidities, explain somehow the relatively high mortality in our data. Given the enormous need to establish a centre for a large paediatric population in the country, we are set to expand our services and improve our results.

A short follow-up of the patients also remains a limitation of the study. However, this is a newly established facility, the best possible follow-up we could make. Of course, future reports on the centre's audit will also be much more evident in this regard.

CONCLUSION

Substantial progress has been made at the Army Liver Transplant Unit, Pak Emirates Military Hospital Rawalpindi Pakistan. Twenty patients out of the 25 included in this study of paediatric liver transplants survived with few complications. Arguably, future numbers will alter the trends found in this audit.

Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

SMC & SH: Data acquisition, data analysis, drafting the manuscript, critical review, approval of the final version to be published.

FI & QM: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

QB: Conception, study design data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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