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Evaluation of Health-Related Quality of Life Post-Liver Transplantation in Paediatrics

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ABSTRACT

Objective: For liver failure patients, liver transplantation is the only effective therapy option. With higher postoperative survival rates, more focus is required on patient quality of life as a marker of successful liver transplantation. This research evaluates the quality of life following surgery in juvenile liver transplant patients. Methodology: This study was designed as a prospective cross-sectional survey to assess the quality of life of patients. It was conducted at the Pakistan Kidney and Liver Institute and Research Centre (PKLI&RC) over a period spanning from July 2021 to February 2023. Liver transplant recipients, under 15 years, visited OPD at least 6 months after surgery were considered in the study. Quality of life was measured using WHOQOL-BREF. As per scoring guide the scores were converted to 100 sclae. **Results:** In this study, 41 liver recipients participated in the study. Out of 30 alive, most of the 24(80%) liver transplant recipients were aged between 1 to 10 years. Among them 22(73.3%) were male. Overall mean quality of life and general health was 92.33±11.65 (range 60 to 100), mean physical health score was 79.05±5.22 (range 68.57 to 88.57), mean psychological health was 86.22±5.08(range 76.67 to 96.67), Social relationships was 97.33±6.91 (range 70 to 100) and environment was 88.33±5.51 (range 80 to 100). Conclusions: Liver transplantation leads to an improvement in quality of life as compared to the pre-transplant state. This study will aid in better defining expectations for patients and their families, as well as directing the clinical course following liver transplantation. Transplant teams may also target early interventions.

INTRODUCTION

For individuals with a range of end-stage liver diseases, liver transplantation (LT) is the only effective course of treatment. [1] However, this procedure is not without complications. The surgical procedure is complex, and post-operative long-term immunosuppression is also a double-edged sword that is responsible for many of the medical conditions that transplant recipients develop. [2] The availability of donor organs is also a major limitation.

After going through its early stages, living donor liver transplantation (LDLT) has become recognised as a valid option for treating situations when a deceased donor liver graft is either unavailable or not accessible at all. However, the technological intricacy and ethical concern surrounding LDLT are its defining characteristics. On April 30, 2012, Pakistan performed its first living donor paediatric liver transplant on a nine-year-old boy. While on June 18, 2014, first auxiliary

liver transplant on a six-year-old child suffering with Crigler-Najjar Syndrome was performed in Pakistan.

Only highly skilled transplant surgeons and specialists can undertake this strictly controlled procedure at specifically certified transplant centres.

According to the European Association for the Study of the Liver, quality of life(QoL) should be taken into account as an LT outcome metric [2] To date, most of the research has focused on survival rates and physical wellbeing after liver transplantation, with recent studies showing improvements in the post-transplant survival rate at 1 year and 5 years post-surgery (90% to 70%). [4] The traditional idea of survival rate is now considered a false measure of the effectiveness of liver transplantation.

Health-related quality of life (HRQL) is an evolving concept that includes physical, psychological, and social

wellbeing after surgery. [2] An appropriate assessment of HRQL includes parents' perspectives in five domains: physical health, mental health, social functioning, role functioning, and general health perception. Researchers has now developed various well recognized tools for assessment of health-related quality of life.

This is significant because quality of life, as opposed to longevity, is increasingly a major issue for parents. Assessing post-liver transplant quality of life will provide a wider picture of the overall health of transplant patients and will encourage parents to opt for this modern treatment option. [4]

In a growing number of medical specialties, including organ transplantation research, the emphasis is shifting from life expectancy to quality of life. Regaining health to a level that is at least comparable to pre-liver transplantation is the aim of the procedure. Gathering and contrasting fresh perspectives in this field of study was our aim.

METHODOLOGY

The eligibility criteria for this study included pediatric patients under the age of 15 years who underwent liver transplantation at Pakistan Kidney and Liver Institute (PKLI). Only recipients of primary single-organ transplantation were included, specifically those who underwent living donor transplantation and had a minimum follow-up period of six months between July 2021 and February 2023. The exclusion criteria comprised patients who underwent combined or sequential liver and kidney transplantation and those who did not survive beyond six months post-liver transplantation.

Design

This was a prospective, cross-sectional study conducted at Pakistan Kidney and Liver Institute and Research Center. An adaptation of the WHOQOL-BREF in paediatric post-liver transplant patients to assess quality of life. It is evaluated using a 26-item questionnaire designed to assess quality of life, which is broadly divided into four domains: physical, social. psychological, and environmental health. All items are scored from 0 to 5, with 0 representing the worst degree of personal satisfaction and 5 the best. The scores are then modified into a score with a range of 0 to 100, with 0 being the lowest score and 100 being the highest. [10,11] Various aspects of life are evaluated using this tool, broadly categorized into physical, environmental, and social. Physical health is represented by 7 items and contains questions pertaining to physical mobility, sleep, and daily activities. Psychological health is assessed through six items, including questions on self-image, attitudes, thoughts, learning ability, and concentration. 8 items assess environmental health in the form of the general and living environment, available services and

resources, and finances, whereas social health is assessed via 3 items focusing on social support and relationships. [10] The study was approved by the hospital research committee. The transplanted patients were approached during their follow-up outpatient visits. questionnaires were given to the parents by the investigators after obtaining consent and providing relevant instruction. The data was entered in IBM SPSS version 27. Age, Gender, Diagnosis was presented in the form of Frequency and percentages. Responses of HRQOL were normally distributed according to Shapiro wilk test (p-value 0.140). Analysis of Variance (ANOVA) was applied to determine the difference between physical, social, and psychological and environmental health according to different age groups. P-value of 0.05 or less was considered as significant.

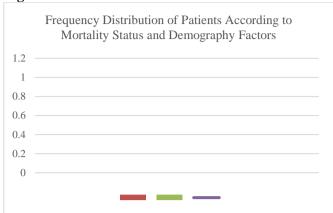
RESULTS

Out of 41 patients aged 15 years or below, who underwent liver transplantation11(26.8%) expired. Among alive male predominance was observed 22(73.3%). Overall mean age of patients was 5.33±3.42 years.

Table 1: Frequency Distribution of Patients According to Mortality Status and Demography Factors

		Status at after s	Total	
Demographics	Categories	Alive 30(73.2%)	Death 11(26.8%)	n=41
Age at transplant	<1 year	3(10.0%)	1(9.1%)	4(9.8%)
	1 -5years	12(40.0%)	6(54.5%)	18(43.9%)
	5-10years	12(40.0%)	3(27.3%)	15(36.6%)
	10-15 years	3(10.0%)	1(9.1%)	4(9.8%)
Gender	Male	22(73.3%)	8(72.7%)	30(73.2%)
	Female	8(26.7%)	3(27.3%)	11(26.8%)
	Biliary atresia	6(20.0%)	4(36.4%)	10(24.4%)
	Biliary Atresia (Missed Kasai)	4(13.3%)		4(9.8%)
	PFIC	6(20.0%)	5(45.5%)	11(26.8%)
	PFIC with HCC	1(3.3%)	1(9.1%)	2(4.9%)
	Cryptogenic liver cirrhosis	2(6.7%)		2(4.9%)
Aetiologia	Primary Hyperoxaluria Type 1	2(6.7%)		2(4.9%)
renotogia	Budd Chiari syndrome	1(3.3%)		1(2.4%)
	Crigler-Najjar Syndrome	5(16.7%)		5(12.2%)
	Familial Hypercholestremia	1(3.3%)		1(2.4%)
	Hepatoblastoma	1(3.3%)		1(2.4%)
	Wilson's disease	1(3.3%)		1(2.4%)
	Hepatic adenoma		1(9.1%)	1(2.4%)

Figure: 1



PFIC: Progressive Familial Intrahepatic Cholestasis

The causes of end-stage chronic liver disease were varied and included Biliary atresia and progressive familial intrahepatic cholestasis as the two most common reasons for liver transplantation at our centre. The youngest child who was operated for liver transplant at PKLI was 7 months old at the time of surgery. Of the patients with Biliary atresia, 71.4% (10 out of 14 patients) had the Kasai procedure which reciprocally suggests that 28.6% Biliary atresia cases were picked at later age and missed the opportunity of Kasai Procedure. Only 14.2% (2 out of 14 patients) patients with progressive familial intrahepatic cholestasis reported to have hepatocellular carcinoma and both had PFIC type 2. Crigler-Najjar Syndrome is reported as a new most common indication for liver transplantation after Biliary atresia and PFIC at our centre, this reflects better handling and understanding of unconjugated neonatal cholestasis in our country. Hence 5 out of 41(12%) patients underwent auxiliary liver transplantation due to Crigler-Najjar Syndrome. (Table 1)

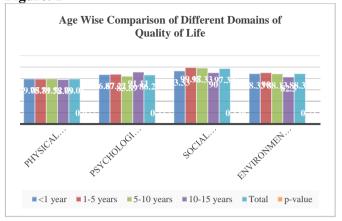
We reported HRQL in patients after liver transplantation secondary to chronic liver disease due to different etiologies, but this could potentially be biased since different etiologies may have distinct effects on quality of life.

Table 2Age Wise Comparison of Different Domains of Quality of Life

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	<1 year	1 -5years	5-10years	10-15 years	Total	p-value
Physical health	79.05 ±7.19	78.81 ±4.94	79.52 ±4.85	78.09 ±8.73	79.05 ±5.22	0.977
Psychological health	86.67 ± 0.00	87.22 ±5.48	83.89 ±4.46	91.11 ±5.09	86.22 ± 5.08	0.117
Social relationships (Out of 100%)	93.33 ±11.55	99.17 ±2.89	98.33 ±3.89	90.00 ±17.32	97.33 ±6.91	0.136
Environment (Out of 100%)	88.33 ±6.29	90.00 ±5.44	88.13 ±5.45	82.50 ±2.50	88.33 ±5.51	0.217

ANOVA, p-value not significant at 0.05

Figure: 2



Overall quality of life and general health were assessed by two questions, and 56.1% of parents marked them as very good, 12.2% as good, and only 4.9% as neither good nor bad. The mean score of parent-reported HRQL in different domains, i.e., Overall mean quality of life and general health was 92.33±11.65 (range 60 to 100), mean physical health score was 79.05±5.22 (range 68.57 88.57), mean psychological health 86.22±5.08(range 76.67 to 96.67), Social relationships was 97.33±6.91 (range 70 to 100) and environment was 88.33±5.51 (range 80 to 100). There was no relationship between QOL in various areas and any of the factors aside from general wellbeing. In all areas, QOL following transplantation increased liver when compared to the patients' preoperative Transplantation had several positive effects on physical function. Patients reported feeling less alone, anxious, and despairing, which improved their ability to interact socially. Pre- and post-transplant items in longitudinal data demonstrated a notable improvement in indices of personal satisfaction.

DISCUSSION

The WHO conceptualizes HRQL as "individuals' perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns". Health-related quality of life (HRQL) is hence a patient-centered clinical outcome that is used globally for patients with diverse conditions. The study discovered that the indices used to assess quality of life, which examined the physical, psychological, social, and environmental domains as well as overall quality of life, were significantly impacted by living donor liver transplantation.

We present the first prospective living donor liver transplantation centre analysis of quality of life after paediatric liver transplantation in Pakistan. The exploration looked at the effect it created and uncovered a positive and huge impact on all domains of HRQL. The

results corroborate the theory that, in comparison to pretransplant health, overall HRQL significantly increases following liver transplantation [14] [17] [22]. This study demonstrates how the experience of living with a new liver altered the participants' perspectives on life in a modest way [17, 22]. The main reason for the liver transplantation was chronic liver disease due to various etiologies. We report no pediatric liver recipient secondary to acute liver failure during this time period. All the patients received split liver graft from living donor after taking approval from Punjab Human Organ Transplant Authority (PHOTA).

Parents have reported that there has been a noticeable improvement in their children's quality of life, but comparison to age-matched peers should also be sought ^[26]. Although male predominance (73.2%) was noted ^[6], the total quality of life score showed no clear relationship with age, gender, or the main reason for liver transplantation ^[6]. In concordance with research conducted worldwide, biliary atresia continues to be the most frequent cause of paediatric liver transplant ^[19] ^[21] Surprisingly our data revealed that progressive familial intrahepatic cholestasis equally contributes to the burden of chronic liver disease in our country.

The strong religious beliefs, close-knit family relationships, and well-established family structure in our society may be the reasons for the high domain scores. Some of the existing literature also suggests that HRQL improves in a specific pattern, with the highest scores in the first year followed by a decline, but to demonstrate such an effect in our study requires a longer follow-up [20]. Longitudinal HRQL monitoring might reveal more about the dynamics of HRQL following LT and help identify patients who need more intensive, customized follow-up [20]. This in turn will shift the focus of researchers and clinicians from survival rate to a more realistic approach of HRQL. This in future may aid in defining long term management of post liver transplant patients.

Physical functioning improved in 91.4% of our subjects. It usually begins to improve after discharge from the hospital, although variations are common because of the inherent dangers of the surgical procedure, the use of immunosuppressants, the risk of infection, and the possibility of rejection, to name a few major concerns [7]. When compared to the general population, surgical morbidity—both early and late—is probably going to have a significant role in suboptimal physical health. Post-LT children report less fatigue and more physical activity, but they still show decreased levels of motor proficiency and functional capacity [15] Despite this, the patients' notable physical improvement demonstrates the advantages of surgery for this very serious illness [8] [27]. It is a sign that the patient is free of their medical condition.

Long-term liver transplant survivors are said to have deteriorations in physical health more frequently, and this appears to be correlated with the degree of immunosuppressive medication [8].

The World Health Organization characterizes psychological well-being as a condition in which each person is able to reach their full potential, manage everyday stressors, work effectively and efficiently, and contribute to their community ^[6] 93.3% of our study population reported improvement in this domain following liver transplantation. Relief from the stressful wait for a transplant and improved physical health could be a reasonable explanation ^[9].

It has been suggested that receiving a transplant and spending time in the intensive care unit are severe stressors that lower quality of life and increase mental strain. Following liver transplantation, these individuals are more likely to experience a low quality of life and other psychiatric illnesses (such as anxiety and posttraumatic stress disorder) [9] [25]. Hence, support would be required in the psychological health domain in order to further enhance HRQL [16, 23]. Strict medication schedule along with the visual adverse effects of some of the medications and a large scar mark on the abdomen can decrease not only the overall HROL but also psychological wellbeing. Pediatric post liver-transplant population is more vulnerable to psychological stress as they are less expressive and parent reported data may give a false reflection of overall picture.

How much an individual can socialize in comparison to other people of the same age is determined by the social functioning domain. In 2015, a group in Birmingham produced an article titled "It's Hard But You've Gotta Get On With It: The Experiences of Growing Up With a Liver Transplant," which explored the difficulties and struggles that confront young liver transplant patients. The primary issues they encountered stemmed from their scars, their need to take immunosuppressants, and restrictions on certain daily activities, such as participating in contact sports [8] [25]. Mayer et al. also looked at the long-term psychological effects on paediatric transplant recipients at Hannover Medical School who received their surgery prior to 2002. While they transitioned smoothly into adulthood, the majority of patients showed strong levels of self-esteem and social integration. Similar results are obtained from our study, where the greatest improvement was attained in this domain (96.6%).

Because the questionnaire was completed by the parents, there is an inherent restriction to our study: children in the future may be labelled as different and may experience social isolation. This can be avoided by providing patients with psychological support from friends and family [12].

The physical surroundings, financial resources, safety, health, and social services, recreation, general environment, and transportation are all included in the environmental health domain [13] While many children and families feel elated after a successful transplant, our cohort exhibited the least improvement (85.4%) in the environmental category. Living in a resource limited part of the world where financial constraints put a huge burden on healthy people we can assume its effect on liver transplant patients as well. To improve this domain of HRQL national level efforts are required. We as a nation need to facilitate this special population and their caregivers. Transplant centers should also extend their services by opening specially designed sub-centers. These centers should be trained not only in providing medical management but also address other concerns related to HROL.

These kids require extra assistance, care, and attention. This group's environmental factors need to be more thoroughly examined and addressed. The lack of social groups and social services including community nurses in our country needs to be addressed at national level for attaining satisfactory outcomes. Following up with paediatric transplant recipients and their families following their discharge, medical practitioners should take great care to assess and identify any current or potential issues and take appropriate action to address them in detail.

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Strengths and Limitations

The application of a validated HRQL evaluation tool provides strength to the study. We acknowledge the presence of various limitations in the current study. The single-centre design and limited sample size restrict the findings' representativeness and generalizability. Parent-completed surveys introduced response bias. More specifically, our cohort's good outcomes could not be contextualized because there was no matched comparison group made up of non-transplant patients.

CONCLUSION

We find that chronic liver disease significantly lowers HRQL but living donor liver transplant can bring a positive change in child's life. Liver transplant not only increases survival but also quality of life. The significance of the data from this study will aid in better defining expectations for patients and their families, as well as directing the clinical course following liver transplantation. In addition to this it will help in strengthening living donor solid organs transplantation programs in this part of the resource limited region. In future we expect that similar studies will open the doors for deceased donor solid organ transplants as well. The transplant teams now can better answer the questions of parents regarding what should be expected after liver transplantation and we can also show to the rest of the world that our expertise in organ transplantation is on improving trends.

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