# بسم الله الرحمن الرحيم

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تم رفع هذه الرسالة بواسطة / سامية زكى يوسف

بقسم التوثيق الإلكتروني بمركز الشبكات وتكنولوجيا المعلومات دون أدنى مسئولية عن محتوى هذه الرسالة.

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# Renal Assessment in the Setting of Pediatric Living Related Liver Transplantation

**Thesis**

*Submitted for Partial Fulfillment of Master Degree in Pediatrics*

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**Marianne Atef Shaker Shenouda**

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# List of Abbreviations

| Abb. | Full term |
|---|---|

**AKIN**.....Acute Kidney Injury Network
**ALT**.....Alanine amino transferase
**ANOVA**.....Analysis of variance
**APOLT**.....Auxilliary partial orthotopic LT
**ARIC**.....Atherosclerosis Risks in Communities
**ARPKD**.....Autosomal recessive polycystic kidney disease
**AST**.....Aspartate amino transferase
**B2M**.....Beta-2-microglobulin
**BTP**.....Beta-trace protein
**CHS**.....Cardiovascular Health Study
**CKD**.....Chronic kidney disease
**CMS**.....Center for Medicaid and Medicare Services
**CMV**.....Cytomegalovirus
**CNI**.....Calcineurin inhibitors
**CNIs**.....Calcineurin inhibitors
**CTS**.....Collaborative transplant study
**DDLT**.....Countries deceased-donor liver transplant
**e**.....Estimated
**EBV**.....Epstein-Barr virus
**ECM**.....Extracellular matrix
**eGFR**.....Estimated GFR
**eGFR**.....Estimated glomerular filtration rate
**ELISA**.....Enzyme-linked immunosorbent assay
**ESLD**.....End-stage liver disease
**FDA**.....Food and Drug Administration
**GD**.....Graves' Disease
**GFR**.....Glomerular filtration rate

# List of Abbreviations Cont...

| Abb. | Full term |
|---|---|

**GGTP** .....Gamma-glutamyl trans peptidase
**GLDH** .....Glutamate dehydrogenase
**GRWR** .....Graft-recipient body weight ratio
**HAS**.....HA stenosis
**HAT** .....HA thrombosis
**HS** .....Highly significant
**HTN** .....Hypertension
**ICU** .....Intensive Care Unit
**IDMS** .....Isotope dilution mass spectroscopy
**IgAN** .....Immunoglobulin A nephropathy
**KDIGO** .....Kidney Disease Improving Global Outcomes
**LDLT** .....Living-donor-LT
**LFTs** .....Liver function tests
**LOS**.....Length of stay
**LRLT** .....Liver transplanted children
**LT**.....Liver transplantation
**LTx** .....Liver transplantation
**MCTs** .....Medium-chain triglycerides
**MDRD** .....Modification of Diet in Renal Disease
**MELD**.....Model for End Stage Liver Disease
**mGFR**.....Measured GFR
**MHC** .....Major histocompatibility complex
**MMF** .....Mycophenolate mofetil
**mTOR**.....Mammalian target of rapamycin
**NS** .....Non-significant
**PCR** .....Polymerase chain reaction
**PELD**.....Pediatric Model for End Stage Liver Disease

# List of Abbreviations Cont...

| Abb. | Full term |
|---|---|
| **PKC-β** | Protein kinase C beta |
| **pLT** | Pediatric LT |
| **pRIFLE** | Pediatric RIFLE |
| **PTA** | Percutaneous transluminal angioplasty |
| **PTLD** | Post transplant lymphoproliferative disorder |
| **ptlds** | Post-transplant lymphoproliferative disorders |
| **RIFLE** | Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease |
| **ROC** | Receiver-operating characteristics |
| **RRT** | Replacement therapy |
| **S** | Significant |
| **SD** | Standard deviation |
| **SFS** | Small for size graft syndrome |
| **SPLIT** | Studies of Pediatric LT |
| **SPSS** | Statistical Package for the Social Science |
| **TAC** | Tacrolimus |
| **TGF-β1** | Transforming growth factor beta 1 |
| **UCD** | Urea cycle defect |
| **UCLA** | University of California, Los Angeles |

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# Introduction

Liver transplantation in the pediatric age group has become the last resort and yet the preferred option for many end stage liver disorders. This field has shown a great improvement and is considered a breakthrough achievement for previously fatal liver diseases.

In view of the fact that survival rate following liver transplantation has greatly improved over the past three decades, chronic renal insufficiency has become a vital and crucial problem, which increases the complexity of patient management and may in turn influence the survival rate ***(Wenger et al., 2013; Basiratnia et al., 2020).***

The data available regarding the assessment of renal function in the setting of pediatric LRLT are limited unlike that of the adults. Moreover, a variety of studies have demonstrated that a calculated glomerular filtration rate (GFR) based on serum creatinine is inaccurate, especially in pediatric age group ***(Anastaze et al., 2012).*** Hence, this study will be used to determine the incidence of chronic renal insufficiency using more reliable renal testing techniques such as Cystatin C which was shown to be a better marker of GFR than creatinine, creatinine clearance, or eGFR for assessment of renal impairment ***(Seronie-Vivien et al., 2008).***

# Aim of the Work

- **Primary:** To determine the incidence of renal dysfunction among pediatric LT recipients using more reliable renal testing methods.
- **Secondary:** To determine the risk factors of renal dysfunction.

*Chapter 1*

# Pediatric Liver Transplantation

In 1953, the pioneer of human orthotopic liver transplantation (LT), Thomas E Starzl, was the first to attempt an orthotopic liver transplant into a 3 years old patient suffering from biliary atresia. Thus, the first LT in humans was attempted in a disease, which, up until today, remains the main indication for pediatric LT (pLT). During the last sixty-eight years, refinements in diagnostics and surgical technique, the introduction of new immunosuppressive medications and improvements in perioperative pediatric care have established LT as routine procedure for childhood acute and chronic liver failure as well as inherited liver diseases.

In contrast to adult recipients, pLT differs greatly in indications for LT, allocation practice, surgical technique, immunosuppression and post-operative life-long aftercare. Many aspects are focus of ongoing preclinical and clinical research ***(Christina et al., 2015)***

LT is the only curative treatment option for patients with irrevocable acute or chronic liver failure and, in the last six decades, has developed from an experimental approach with very high mortality to an almost routine procedure with good short and long-term survival rates. In the early years, long-term survival rates after pediatric LT (pLT) were 11% - 39% ***(Pichlmayr et al., 1984)*** and, since then, have improved to up to 90% with long-term graft survival rates of > 80% ***(Yazigi, 2013).***

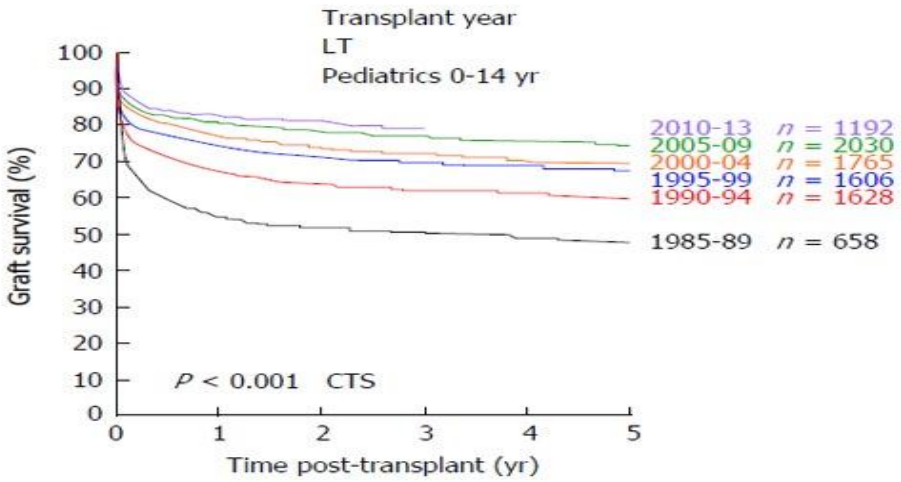


**Figure (1):** Development of graft survival after pediatric liver transplantation from 1985 until 2013 (collaborative transplant study data). CTS: Collaborative transplant study; LT: Liver transplants.

Due to continuing improvements of surgical and interventional techniques as well as perioperative neonatal and pediatric intensive care medicine, the average age of pediatric transplant recipients has steadily declined, with a continuous increase of patients transplanted within the first year of life. As of today, approximately 27% of pLT are performed in recipients younger than 12 months. Patients in this young age, which in former years could not be transplanted (and mostly died before reaching the size and age of transplant ability), today show a long-term survival of almost 90%, which is comparable to older children.

At the same time, long-term survival after pLT implies life-long aftercare in an interdisciplinary team to ensure a life with as little as possible secondary morbidity ***(Christina et al., 2015).***

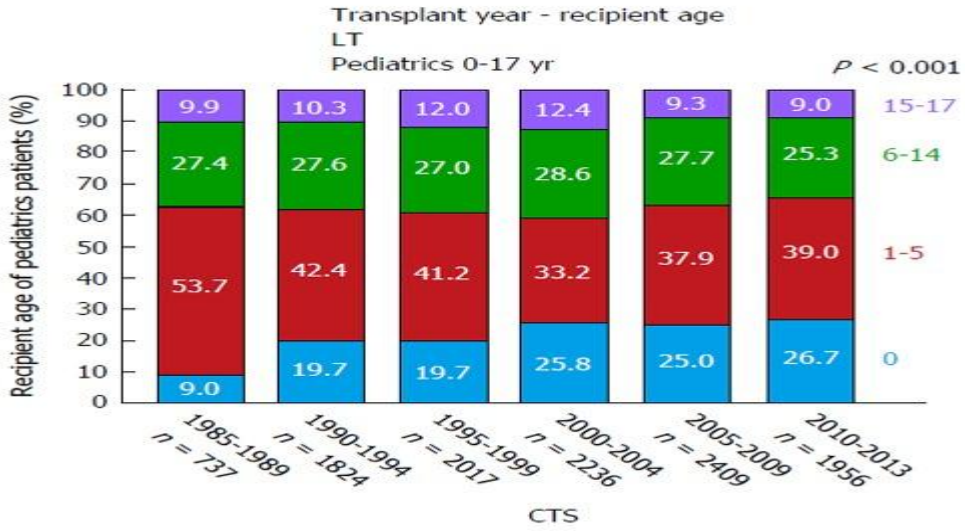


**Figure (2):** Age distribution of pediatric liver transplantation recipients from 1985 until 2013 (collaborative transplant study data). CTS: Collaborative transplant study; LT: Liver transplants.

## Liver transplantation indications:

Indications for LT in pediatric patients are manifold and can be classified into cholestatic disorders, metabolic liver diseases causing liver cirrhosis, metabolic liver diseases without liver cirrhosis, acute liver failure, acute and chronic hepatitis, and liver tumors. With approximately 40%, the main indication for pLT is biliary atresia. Thus, the indications for pLT are significantly different to indications in adult LT recipients ***(Melter et al., 2012).***