Cohort Study

Pediatric living donor liver transplantation (LDLT): Short- and long-term outcomes during sixteen years period at a single centre- A retrospective cohort study

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ABSTRACT

Background and objectives: Pediatric living donor liver transplantation (LDLT) is an effective tool for managing pediatric patients with end-stage liver disease (ESLD) with good long-term graft and patient survival, especially after improvement in peri-operative care, surgical tools and techniques; however, the morbidity and mortality after such a procedure are still a challenging matter. The study aimed to analyze short-and long-term outcomes after pediatric LDLT in a single centre.

Methods: We retrospectively analyzed 67 pediatric patients who underwent LDLT in the period from April 2003 to July 2018. The overall male/female ratio was 40/27.

Results: Forty-one (61.2%) of patients had ≥1 early and/or late morbidities; the early (less than 3months) and late (≥3months) ones affected 36(53.7%) and 12(17.9%) of them respectively. The 16-year graft and patient survivals were 35(52.2%) while early and late mortalities were 23(34.3%) and 9(13.4%) respectively. Sepsis and chronic rejection were the most frequent causes of early and late mortalities respectively. Moreover, more packed RBCs transfusion units, bacterial infections, and pulmonary complications were independent predictors of poor patient survival.

Conclusions: More packed RBCs transfusion units intra-operatively, and post-liver transplant (LT) bacterial infection, sepsis, chronic rejection, as well as pulmonary complications had a negative insult on our patients’ outcomes, so proper management of them is mandatory for improving outcomes after pediatric LDLT.

1. Introduction

Living donor liver transplantation (LDLT) has become the gold standard treatment option for paediatrics with end-stage liver disease (ESLD), especially after improved patient selection, increased experience, advancement in (pediatric anaesthesia, surgical techniques, graft preservation, peri-operative and intensive care, medical management, antimicrobial medications as well as immunosuppressive agents) [1–4]. However, the complication rate after such a pediatric procedure is still high with a negative insult on transplanted grafts, pediatric recipient morbidities and mortalities [5–7].

Those complications can be categorized into short-term (early; less than 3months) and long-term (late; ≥3months) ones [4,8–12]. Moreover, they include post-transplant pulmonary, vascular, biliary, neurological, and infectious complications, as well as acute rejection, chronic rejection, renal dysfunction, etc [1,12–21].

They should be prevented, and if occurred; should be diagnosed and managed early to improve graft and patient outcomes, however, those outcomes are affected also by additional variables (i.e. Large for size graft (LFSG), pediatric end-stage liver disease (PELD)/model for end-stage liver disease (MELD) scores, centre experience/volume, operative time, operative blood loss, blood transfusion units, etc); those variables should be modulated also for getting better short-and long-term outcomes [8,22–26].

To our knowledge; the short- and long-term outcomes after pediatric
LDLT is few in literature studies, so we analyzed this issue in a single tertiary Egyptian centre for 16 years period.

2. Pediatric recipients and methods

We did this cohort study that analyzed short- and long-term outcomes after pediatric LDLT after being approved by our institutional review board and after obtaining written informed consent regarding surgeries and research from both the recipients’ parents/Guardians and the donors. It was performed in the department of hepato-pancreato-biliary surgery, National liver institute, University of Menoufiya, Menoufiya, Egypt during the period from April 2003 to June 2019 (the liver transplantation (LT) operations were done between April 2003 and July 2018 and the follow-up started from POD1 until June 2019 or until patient loss(median: 18 months; range(0.03–194 months)).

Our series involved 67 pediatric recipients (less than 18 years) after exclusion of adults, recipients with data loss, and cases who refused research. Our work was registered in the research registry with registration NO of researchregistry4593 (wwwresearchregistry.com) and it was reported in line with the STROCSS criteria [27].

All donors were ≥19.5 years old and their assessment included clinical assessment, psychological assessment, lab studies (liver function tests (LFT), virology, etc), abdominal ultrasound (US), computed tomography (CT) angiography and CT volumetric studies, magnetic resonance cholangiopancreatography (MRCP), liver biopsy, etc. In late cases; we did CT with hepatic protocol and 3d imaging reconstruction showing: A: Hepatic vein thrombosis (HVT) B: Inferior vena cava (IVC)

The study parameters were collected from a prospectively maintained database in our LT unit and were analyzed retrospectively. Those parameters included pediatric recipients’ pre-and intra-operative variables, their donors’ variables, primary liver diseases, and postoperative measures.

The details of donors’ and recipients’ surgical techniques including recipients’ vascular and biliary reconstructions have been described previously [28–30]. In short; in the donor surgery; the graft type was chosen concerning the estimated GRWR, and the ratio of the graft volume to the recipient’s standard liver volume (GV/SLV), furthermore, the heptectomy was done using Cavitron ultrasonic surgical aspirator (CUSA) device. The donor biliary anatomy was determined according to both the pre-operative MRCP, and the intra-operative cholangiography (IOC), while the vascular anatomy depended upon pre-operative CT angiography ± intra-operative Doppler US. On the other hand, in the recipient surgery, the total heptectomy phase was done with meticulous dissection and good hemostasis especially in cases with PHN to decrease blood loss, moreover; the hilar portal structures dissection was performed near the liver for obtaining the maximum length of those structures for better future reconstruction, also, the inferior vena cava (IVC) was carefully preserved with temporary portocaval shunts in some cases.

On the other hand; on the back table, Hydroxyl tryptophan ketoglutarate solution was used for graft preservation with vascular manipulations of its hepatic veins (HV)/portal veins (PV) in some cases;
Fig. 3. Then in the implantation phase; HV and PV anastomoses were performed with the aid of surgical loupes using continuous 5/0 and 6/0 prolene sutures respectively; Fig. 4: A, B; moreover, PV anastomosis was done with a growth factor. Then, the hepatic artery (HA) anastomosis was achieved with the help of surgical loupes or microscopy using interrupted 8/0 prolene stitches; Fig. 4: C. The biliary anastomoses were done with the aid of surgical loupes using interrupted 6–0 prolene/Polydioxanone(PDS) stitches; Fig. 5. Doppler US was done routinely after vascular reconstruction and after abdominal closure to determine the pattern and velocity of blood flow. Finally, all our recipients’ abdomens were closed primarily without the occurrence of any abdominal compartment syndrome (ACS).

The post-operative measures have been described previously [28–30]. In brief; they included: 1- Immunosuppression therapy and protocol; it consisted of tacrolimus(FK506) and prednisolone, however, some cases were given cyclosporine when side effects (i.e. neurotoxicity or nephrotoxicity) developed with tacrolimus. Mycophenolate mofetil (MMF) was given for multiple episodes of acute rejection, chronic rejection, and for decreasing tacrolimus dose to prevent or treat renal impairment. On the other hand, sirolimus and/or everolimus were given to some patients to replace tacrolimus if side effects developed and to treat chronic rejection. Lastly, an interleukin-2 receptor blocker was given in late cases at POD 0 and 4 for minimizing the tacrolimus dose.

2- To prevent infection; antibacterial (pre-operative 3rd generation cephalosporine, then intra-/post-operative Imepanem + metronidazole until culture result), antifungal (fluconazole), and antiviral (acyclovir) were given. 3- For prophylaxis of vascular thromboses; Heparin infusion was given (dose; 180–200units/kg/day) adjusted according to activated partial thromboplastin time (APTT) (target levels; 50–70 s), then acetylsalicylate and dipyridamole were given at POD8 at doses of 2 mg/kg/d and 4 mg/kg/d respectively for 3 months.

4-The follow-up of pediatric recipients (i.e. by transplant surgeons, pediatric hepatologists, pediatric endoscopists, and pediatric intervention radiologists) was done daily until hospital discharge, then weekly until the end of the 1st 3 months then monthly until the end of the 1st year, then yearly until the end of the follow-up period to detect: a-Early (short-term; less than 3months), and late (Long-term; ≥3months) morbidities (i.e. infection, pulmonary, vascular, biliary, renal, rejection, etc); they were graded according to Clavien grading. b- Early (less than 3months), and late (≥3months) mortalities, as well as mortality causes. c- Graft and patient survival outcomes.

The statistical analysis was done by SPSS 21 software (SSPS Inc, Chicago, IL, USA). Nominal variables were expressed in frequencies and percentages and analyzed using Fisher exact or Chi-square tests. Continuous variables were expressed as medians (ranges) or means ± SDs and were compared using the t- or Mann-Whitney U tests. Univariate and then multivariate analyses were performed to detect predictors of early and/or late morbidities as well as predictors of patients’ survival. The Kaplan–Meier method was applied for analysis of the survival of recipients and was compared using log-rank tests. In all tests, a P-value of <0.05 was significant.

3. Results

3.1. Pediatric recipients’ characteristics

Regarding pre-operative recipients’ and their donors’ details; they were classified as 40(59.7%) males and 27(40.3%) females. Their median age and weight reached 2.8 (range; 0.7–17) years and 13 (range; 6.4–74) kg respectively. Their donors were categorized into 29(43.3%) males and 38(56.7%) females, where, their median age and body mass
The median recipient age was 30 (range; 19.5–43) years and 26 (range; 18–35) respectively. Table 1.

The 1st-degree donor to recipient relation was the most frequent (77.6%). The recipients’ median MELD and PELD scores were 16 (range; 11–26) and 13.5 (range; 2–34) respectively, moreover, their most frequent Child-Turcotte-Pugh (CTP) score was C 27 (40.3%). Pre LT Portal hypertension (PHN) affected 40 (59.7%) of them, in whom; oesophageal varices (OV) grade I was the most frequent endoscopic finding 15 (22.4%). The identical donor to recipient blood group matching was more frequent 48 (71.6%). Lastly, the median NO of LT/ year was 4 (range; 0–13) cases; Table 1. The most frequent primary liver disease that has led to LT was biliary atresia (34.3%), followed by Byler’s disease (17.9%); Table 2.

As regards recipients’ operative variables details; 56 (83.6%), 6 (9%), 4 (6%), and 1 (1.5%) of patients were given left lateral, left lobe + middle hepatic vein (LL + MHV), (right lobe (RL)-MHV), and mono-segment II liver grafts respectively. The single HV, PV, HA and biliary anastomoses were done in 64 (95.5%), 67 (100%), 61 (91%) and 59 (82.1%) patients respectively while < 1 anastomosis of the HV, HA and bile duct were performed in 3 (4.5%), 6 (9%) and 12 (18%) of them respectively. The duct to duct (D-D) and hepaticojejunostomy (HJ) biliary reconstructions were performed in 29.9% and 70.1% of our recipients respectively, furthermore, biliary stents were put in 88.1% of them. The median actual graft weight and GRWR were 300 (range; 110–900) gm and 2 (range; 0.7–4.3) respectively. However, actual GRWR ≥3, GRWR <4 (LFSG), and GRWR <0.8 (SFSG) were 15 (22.4%), 2 (3%), and 1 (1.5%) of patients respectively. The median cold and warm ischemia times (CIT and WIT) were 45 (range; 10–105) mins and 35 (range; 25–80) mins respectively. The median intra-operative packed Red blood cells (RBCs) and plasma transfusions were 1.5 (range; 0–5) units and 3 (range; 0–12) units respectively. The median operative time and postoperative hospital stay were 9 (range; 5–14) hours and 23 (range; 1–135) days respectively. Table 3.

3.2. Postoperative morbidities

Forty-one (61.2%) of our pediatric recipients had ≥1 early (less than 3 months) and/or late (≥3 months) morbidities. Regarding early morbidities; they affected 36 (53.7%) of patients where early bacterial infections were the most frequent ones; they affected 21 (31.3%) of patients (24 infections involved 21 patients). They were classified into chest infection (11 (16.4%)), biliary infection (5 (7.5%)), wound infection (7 (10.5%)) and infected abdominal collection (1 (1.5%)); moreover, they were categorized into Clavien grades II, III, and V in 9, 2 and 13 of them respectively. They were managed by antibiotics according to culture and sensitivity, by intervention radiology and/or surgically. The treatment was successful in 11 of those infections. Table 4.

Early pulmonary complications affected 13 (19.4%) of our recipients and were categorized into chest infection (11 (16.4%)), pulmonary
Table 1
The pre-operative recipients’ and their donors’ details.

| Category                                      | No (%)       |
|-----------------------------------------------|--------------|
| Donor age(years) (Median(range))             | 67(100%)     |
| Donor gender                                  |              |
| males                                         | 30(19.5–43)  |
| females                                       | 38(56.7%)    |
| BMI of the donor (Median(range))              | 26(18–35)    |
| Donor to recipient relation                   |              |
| 1st degree                                    | 52(77.6%)    |
| 2nd degree                                    | 3(4.5%)      |
| 3rd degree                                    | 2(3%)        |
| 4th degree                                    | 2(3%)        |
| Unrelated                                     | 8(11.9%)     |
| Recipient age(years) (Median(range))          | 2.8(0.7–17)  |
| Recipient weight (Median(range))              | 5(7.5%)      |
| Recipient weight >10 Kg                       | 19(28.4%)    |
| Recipient gender                              |              |
| males                                         | 40(59.7%)    |
| females                                       | 27(40.3%)    |
| Metabolic disease as indication for LT        | 25(37.3%)    |
| BA as indication for LT                       | 23(34.3%)    |
| MELD score(12years) (Median(range))           | 16(11–26)    |
| PELD score(12years) (Median(range))           | 13.5(2–34)   |
| PELD or MELD scores (Median(range))           | 14(2–34)     |
| CTP score                                     |              |
| A                                             | 18(26.9%)    |
| B                                             | 22(32.8%)    |
| C                                             | 27(40.3%)    |
| Pre LT PHN                                    | 40(59.7%)    |
| Upper endoscopy result                        |              |
| Not done                                      | 18(26.9%)    |
| Free                                          | 9(13.4%)     |
| PHG                                           | 10(14.9%)    |
| OV grade I                                    | 15(22.4%)    |
| OV grade II                                   | 8(11.9%)     |
| OV grade III                                  | 4(6%)        |
| OV grade IV                                   | 3(4.5%)      |
| Bl. Group                                     |              |
| Compatible                                    | 19(28.4%)    |
| Identical                                     | 48(71.6%)    |
| No of LT/year (Median(range))                 | 4(0.13)      |

BMI: Body mass index, LT: Liver transplantation, BA: Biliary atresia, MELD: Model for end-stage liver disease, PELD: Pediatric end-stage liver disease, CTP: Child-Turcotte-Pugh, PHN: Portal hypertension, PHG: Portal hypertensive gastropathy, OV: Esophageal varices.

Table 2
The primary pediatric liver disease.

| Category                                      | No (%)       |
|-----------------------------------------------|--------------|
| BA                                            | 23(34.3%)    |
| Byler’s disease                               | 12(17.9%)    |
| Cryptogenic liver cirrhosis                   | 6(9%)        |
| Criptar Najjar syndrome                       | 5(7.5%)      |
| AIH                                           | 3(4.5%)      |
| BCS                                           | 3(4.5%)      |
| Wilson’s disease                              | 2(3%)        |
| Secondary biliary cirrhosis from choledochal cyst | 2(3%)    |
| Congenital hepatic fibrosis                   | 2(3%)        |
| HCV                                           | 2(3%)        |
| Tyrosinemia                                   | 2(3%)        |
| Hepatoblastoma                                | 2(3%)        |
| cavernous haemangiomas                        | 1(1.5%)      |
| Bile Ducts Pauclity                           | 1(1.5%)      |
| Primary Hyperoxaluria                         | 1(1.5%)      |

BA: Biliary atresia, AIH: Autoimmune hepatitis, BCS: Budd Chiari syndrome, HCV: Hepatitis C virus.

Table 3
The intra-, and post-operative details.

| Category                                      | No (%)       |
|-----------------------------------------------|--------------|
| Category                                      |              |
| No (%)                                        | 67(100%)     |
| Or Median(range)                              |              |
| Donor gender                                  |              |
| males                                         | 56(83.6%)    |
| females                                       | 6(9%)        |
| BMI of the donor                              | 4(6%)        |
| Donor to recipient relation                   |              |
| 1st degree                                    | 1(1.5%)      |
| 2nd degree                                    | 64(95.5%)    |
| 3rd degree                                    | 2(3%)        |
| 4th degree                                    | 1(1.5%)      |
| Unrelated                                     | 67(100%)     |
| Recipient age(years)                          | 2(3%)        |
| Recipient weight (Median(range))              | 61(91%)      |
| Recipient weight >10 Kg                       | 2(6%)        |
| Recipient gender                              |              |
| males                                         | 20(29.9%)    |
| females                                       | 47(70.1%)    |
| Metabolic disease as indication for LT        |              |
| BA as indication for LT                       |              |
| MELD score(12years) (Median(range))           |              |
| PELD score(12years) (Median(range))           |              |
| PELD or MELD scores (Median(range))           |              |
| CTP score                                     |              |
| A                                             | 20(29.9%)    |
| B                                             | 4(6%)        |
| C                                             | 1(1.5%)      |
| Pre LT PHN                                    | 3(4.5%)      |
| Upper endoscopy result                        |              |
| Not done                                      | 20(29.9%)    |
| Free                                          | 10(14.9%)    |
| PHG                                           | 15(22.4%)    |
| OV grade I                                    | 8(11.9%)     |
| OV grade II                                   | 4(6%)        |
| OV grade III                                  | 3(4.5%)      |
| Bl. Group                                     |              |
| Compatible                                    | 23(34.3%)    |
| Identical                                     | 47(69%)      |
| No of LT/year (Median(range))                 | 4(0.13)      |
| BMI: Body mass index                          |              |
| LT                                             | 67(100%)     |
| Or Median(range)                               |              |
| Donor gender                                  |              |
| males                                         | 56(83.6%)    |
| females                                       | 6(9%)        |
| BMI of the donor                              | 4(6%)        |
| Donor to recipient relation                   |              |
| 1st degree                                    | 1(1.5%)      |
| 2nd degree                                    | 64(95.5%)    |
| 3rd degree                                    | 2(3%)        |
| 4th degree                                    | 1(1.5%)      |
| Unrelated                                     | 67(100%)     |
| Recipient age(years)                          | 2(3%)        |
| Recipient weight (Median(range))              | 61(91%)      |
| Recipient weight >10 Kg                       | 2(6%)        |
| Recipient gender                              |              |
| males                                         | 20(29.9%)    |
| females                                       | 47(70.1%)    |
| Metabolic disease as indication for LT        |              |
| BA as indication for LT                       |              |
| MELD score(12years) (Median(range))           |              |
| PELD score(12years) (Median(range))           |              |
| PELD or MELD scores (Median(range))           |              |
| CTP score                                     |              |
| A                                             | 20(29.9%)    |
| B                                             | 4(6%)        |
| C                                             | 1(1.5%)      |
| Pre LT PHN                                    | 3(4.5%)      |
| Upper endoscopy result                        |              |
| Not done                                      | 20(29.9%)    |
| Free                                          | 10(14.9%)    |
| PHG                                           | 15(22.4%)    |
| OV grade I                                    | 8(11.9%)     |
| OV grade II                                   | 4(6%)        |
| OV grade III                                  | 3(4.5%)      |
| Bl. Group                                     |              |
| Compatible                                    | 23(34.3%)    |
| Identical                                     | 47(69%)      |
| No of LT/year (Median(range))                 | 4(0.13)      |

BMI: Body mass index, LT: Liver transplantation, BA: Biliary atresia, MELD: Model for end-stage liver disease, PELD: Pediatric end-stage liver disease, CTP: Child-Turcotte-Pugh, PHN: Portal hypertension, PHG: Portal hypertensive gastropathy, OV: Esophageal varices.

Table 4
The incidence of early biliary complications.

| Category                                      | No (%)       |
|-----------------------------------------------|--------------|
| Spontaneous haemorrhage                       | 7(10.5%)     |
| Early acute rejection                         | 10(14.9%)    |
| HCV                                           | 2(3%)        |
| BA                                            | 1(1.5%)      |
| AIH                                           | 1(1.5%)      |
| BCS                                           | 3(4.5%)      |
| HCV                                           | 2(3%)        |
| Tyrosinemia                                   | 2(3%)        |
| Hepatoblastoma                                | 2(3%)        |
| cavernous haemangiomas                        | 1(1.5%)      |
| Bile Ducts Pauclity                           | 1(1.5%)      |
| Primary Hyperoxaluria                         | 1(1.5%)      |

LL: Left lobe, MHV: Middle hepatic vein, RL: Right lobe, HV: Hepatic vein, NO: Number, PV: Portal vein, HA: Hepatic artery, D-D: Duct to duct, HJ: Hepaticojejunostomy, GRWR: Graft recipient weight ratio, SFSG: Large for size graft, SFSG: Small for small graft, CIT: Cold ischemia time, WIT: Warm ischemia time, RBCS: Red blood cells, FK: Tacrolimus, MMF: Mycophenolate mofetil.
grades II, III and V involved 2, 2 and 3 of them respectively. The cases with biliary leak ± biloma were managed conservatively, by percutaneous drainage, endoscopic retrograde cholangeopancreatography (ERCP) and/or surgery (Open drainage, and/or external biliary diversion) under antibiotic coverage; however cholangitis cases were managed by antibiotics with a good result in 4 of the 7 patients.

Table 4

| Category                      | Clavien grade I | Clavien grade IIIa or b | Clavien grade V | Treatment result (Success) | Treatment result (Failure) | Total No (%) |
|-------------------------------|------------------|-------------------------|----------------|-----------------------------|---------------------------|---------------|
| **Early complications (<3 months)**   |                  |                         |                |                             |                           | 67(100%)      |
| **Bacterial infection**        |                  |                         |                |                             |                           | 36(53.7%)     |
| 1-Chest infection              | 1                | 0                       | 10             | 1                           | 10                        | 11            |
| 2-Biliary infection            | 2                | 0                       | 3              | 2                           | 3                         | 5(7.5%)       |
| 4-Wound infection              | 6                | 1                       | 0              | 7                           | 0                         | 7(10.5%)      |
| 5-Infected abdominal collection(perforated colon) | 0                | 1                       | 0              | 1                           | 0                         | 1(1.5%)       |
| **Pulmonary complications**    |                  |                         |                |                             |                           | 13            |
| 1-Chest infection              | 1                | 0                       | 10             | 1                           | 10                        | 11            |
| 2-Pulmonary embolism           | 0                | 0                       | 1              | 0                           | 1                         | 1(1.5%)       |
| 3-Hemothorax                   | 0                | 1                       | 0              | 1                           | 0                         | 1(1.5%)       |
| **Acute rejection**            | 9                | 0                       | 1              | 9                           | 1                         | 10            |
| **Vascular**                   |                  |                         |                |                             |                           | 8(12%)        |
| 1-HA stenosis                 | 0                | 0                       | 1              | 0                           | 1                         | 1(1.5%)       |
| 2- HAT                        | 0                | 0                       | 1              | 0                           | 1                         | 1(1.5%)       |
| 3- PVT                        | 1                | 0                       | 1              | 1                           | 1                         | 2(3%)         |
| 4-HV stenosis                 | 0                | 1                       | 0              | 1                           | 0                         | 1(1.5%)       |
| 5-PVT + HVT                   | 0                | 0                       | 2              | 0                           | 2                         | 2(3%)         |
| 6-IVC stenosis                | 0                | 0                       | 1              | 0                           | 1                         | 1(1.5%)       |
| **Biliary**                   |                  |                         |                |                             |                           | 7(10.5%)      |
| 1-Bile leak + biloma           | 0                | 1                       | 1              | 1                           | 1                         | 2(3%)         |
| 2- Bile leak                  | 0                | 1                       | 2              | 1                           | 2                         | 3(4.5%)       |
| 3-Cholangitis                  | 2                | 0                       | 0              | 2                           | 0                         | 2(3%)         |
| **Wound complications**        |                  |                         |                |                             |                           | 7(10.5%)      |
| 1-Wound infection + burst abdomen | 0              | 1                       | 0              | 1                           | 0                         | 1(1.5%)       |
| 2-Wound infection              | 6                | 0                       | 0              | 6                           | 0                         | 6(9%)         |
| **Renal impairment**           | 3                | 0                       | 2              | 3                           | 2                         | 5(7.5%)       |
| **GIT complications**          |                  |                         |                |                             |                           | 4(6%)         |
| 1-Haematemesis                | 0                | 2                       | 0              | 2                           | 0                         | 2(3%)         |
| 2-Colonic perforation         | 0                | 1                       | 0              | 1                           | 0                         | 1(1.5%)       |
| 3-Hepatic encephalopathy      | 0                | 0                       | 1              | 0                           | 1                         | 1(1.5%)       |
| **Neurological complications** |                  |                         |                |                             |                           | 4(6%)         |
| 1-Neurological complications  | 1                | 0                       | 0              | 1                           | 0                         | 1(1.5%)       |
| 2-Recurrent BCS               | 0                | 0                       | 1              | 0                           | 1                         | 1(1.5%)       |
| 3-Early graft failure          | 0                | 0                       | 1              | 0                           | 1                         | 1(1.5%)       |

HA: Hepatic artery, HAT: Hepatic artery thrombosis, PVT: Portal vein thrombosis, HV: Hepatic vein, HVT: Hepatic vein thrombosis, IVC: Inferior vena cava, GIT: Gastrointestinal, BCS: Budd Chiari syndrome.

As regards late morbidities; they affected 12(17.9%) of our patients. Late bacterial infections involved 4(6%) of our smart recipients; those infections were classified into chest, and biliary infections that affected 3(4.5%) and 1(1.5%) of patients respectively, furthermore, they were sorted regarding Clavien grading into grades II, III and V in 1, 2 and 2 of them respectively. They were managed by antibiotics; moreover, the cholangitis case was managed surgically. The outcome was successful in 2 of the 4 cases.

The incidence of chronic rejection was 4(6%) that occurred in the 11th, 12th, 16th and 18th post-transplant months. It was diagnosed histologically according to updated Banff criteria [31]. Patients were given MMF beside FK for its management, furthermore, when FK toxicity occurred they were shifted to Sirolimus or Everolimus, however, the 4 patients, unfortunately, died (Clavien grade V).

In our series, the late pulmonary complications involved 4(6%) of recipients, they were divided into chest infections (3(4.5%) and pleural effusions (1(1.5%) moreover, they were categorized into Clavien grades II, III and V in 1, 1 and 2 of them respectively; they were managed by antibiotics for infection and chest tube for effusion with 2 mortalities; one from sepsis and the other from acute respiratory distress syndrome (ARDS).
Late complications (≥3months) were common, involving 1(1.5%), 1(1.5%) and 2(3%) of them respectively; they were all Clavien grade III as they were managed by ERCP, percutaneous transhepatic drainage (PTD) and/or surgical reconstruction under antibiotic coverage with final improvement in all of them. Table 5.

As regards late vascular complications; they were 3 cases (4.5%) and were classified into HAT and HV stenosis in 1(1.5%) and 2(3%) of them respectively. Clavien grades II, III and V involved 1, 1 and 1 of them; they were managed by anticoagulants and fibrinolytic for HAT as well as by angiographic dilatation and stenting for HV stenosis with successful results in 2 of the 3 cases. Table 5.

Lastly, late acute rejection, renal impairment and recurrent BCS affected 2(3%), 2(3%) and 1(1.5%) of patients respectively; they were managed by pulse steroids for rejection, renal supportive treatment for renal impairment and angiographic dilatation and stenting for BCS with a successful outcome in 2, 1 and 1 of them respectively. Table 5.

### 3.3. Predictors of early and/or late morbidity

On univariate analysis, CTP class C, higher PELD/MELD scores, biliary stents, more intra-operative packed RBCs transfusion units and longer duration of operation were predictors of early and/or late morbidities, however, on multivariate analysis, there was no independent predictor of those morbidities. Table 6.

### 3.4. Survival outcomes of pediatric patients

In our work; the 6months, 1-year, 3-year, 5-year, 10-year and 16-year graft and patient survivals were 42(62.7%), 39(58.2%), 36 (53.7%), 35(52.2%), 35(52.2%) and 35(52.2%), and 43(64.2%), 41 (61.2%), 36(53.7%), 35(52.2%), 35(52.2%) and 35(52.2%) respectively. The mortality in the 1st LT period (from 2003 to 2013); 38 patients reached 63.2%, however it was significantly less (27.6%; p = 0.004) in the 2nd LT period (from 2014 to 2018); 29 patients. The early (less than 3months) mortality reached 34.3% mostly due to sepsis, renal impairment and LFSGs; however, the late (≥3months) mortality was 13.4% mostly from chronic rejection and late sepsis. Table 7; Fig. 6.

### 3.5. Pre- and intra-operative parameters as predictors of patient survival outcome

On univariate analysis, CTP class C, Pre LT PHN, biliary stents, more

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**Table 5**

Late morbidities.

| Category                        | Clavien grade II | Clavien grade III or b | Clavien grade V | Treatment result (Success) | Treatment result (Failure) | Total |
|---------------------------------|------------------|------------------------|----------------|-----------------------------|---------------------------|-------|
| **Late complications (≥3months)**|                  |                        |                |                             |                           |       |
| Bacterial infection             |                  |                        |                |                             |                           | 12    |
| 1-Chest infection               | 1                | 0                      | 2              | 1                           | 2                         | 4     |
| 2-Biliary                       | 0                | 1                      | 0              | 1                           | 0                         | 1     |
| Chronic rejection               |                  |                        |                |                             |                           | 4     |
| Pulmonary complications         |                  |                        |                |                             |                           | 4     |
| 1-Chest infection               | 1                | 0                      | 2              | 1                           | 2                         | 4     |
| 2-Pleural effusion              | 0                | 1                      | 0              | 1                           | 0                         | 1     |
| Biliary                         |                  |                        |                |                             |                           | 0     |
| 1-HJ stricture + recurrent cholangitis | 0                      | 1                      | 0              | 1                           | 0                         | 1     |
| 2-HJ stricture                  | 0                | 1                      | 0              | 1                           | 0                         | 1     |
| 3-D-D stricture                 | 0                | 2                      | 0              | 2                           | 0                         | 2     |
| Vascular                        |                  |                        |                |                             |                           | 3     |
| 1-HAT                           | 1                | 0                      | 0              | 1                           | 0                         | 1     |
| 2-HV stenosis                   | 0                | 1                      | 1              | 1                           | 1                         | 2     |
| Acute rejection                 | 2                | 0                      | 0              | 2                           | 0                         | 2     |
| Renal impairment                | 1                | 0                      | 1              | 1                           | 1                         | 2     |
| Recurrent BCS                   | 0                | 1                      | 0              | 1                           | 0                         | 1     |

HJ: Hepaticojejunostomy, D-D: Duct to duct, HAT: Hepatic artery thrombosis, HV: Hepatic vein, BCS: Budd Chiari syndrome.

**Table 6**

Predictors of early and/or late morbidities.

| Category                        | Early and/or late morbidity No (%) | No morbidity No (%) 26/100 (Mean ± SD) | P-value Univariate analysis | P-value Multivariate analysis |
|---------------------------------|-----------------------------------|-----------------------------------------|----------------------------|-----------------------------|
| Recipient age (year)            | 5.1 ± 5.2                         | 6.2 ± 5.6                               | 0.4                        |                             |
| Recipient age ≥1 year           | 4(9.8%)                           | 1(3.8%)                                 | 0.4                        |                             |
| Recipient weight(kg)            | 18.6 ± 15.6                       | 22.2 ± 18.7                             | 0.4                        |                             |
| Recipient weight <10 kg         | 13(31.7%)                         | 6(23.1%)                                | 0.4                        |                             |
| CTP score                       |                                   |                                         |                            |                             |
| A                               | 7(17.1%)                          | 11(42.3%)                               | 0.2                        |                             |
| B                               | 13(31.7%)                         | 9(34.6%)                                |                            |                             |
| C                               | 3(7.3%)                           | 6(23.1%)                                |                            |                             |
| PELD or MELD scores             |                                   |                                         |                            |                             |
| Pre LT PHN                      | 26(63.4%)                         | 14(53.8%)                               | 0.3                        |                             |
| Actual graft weight(g)          | 311.9 ± 137.8                     | 378.1 ± 197.8                           |                            |                             |
| Actual GRWR                      | 2.2 ± 0.9                         | 2.1 ± 0.8                               | 0.7                        |                             |
| Actual GRWR ≥3                  | 10(24.4%)                         | 5(19.2%)                                | 0.4                        |                             |
| Biliary stent                   | 39(95.1%)                         | 20(76.9%)                               | 0.033                      |                             |
| CIT(min)                        | 54.4 ± 27                         | 50 ± 22.6                               | 0.5                        |                             |
| WIT (min)                       | 38.1 ± 10                         | 402.2 ± 14.1                            | 0.5                        |                             |
| Intraoperative packed RBCs transfusion (units) | 1.7 ± 1              | 1.1 ± 1.2                               | 0.003                      |                             |
| Intraoperative plasma transfusion (units) | 3.6 ± 3                                 | 2.4 ± 2.3                               | 0.1                        |                             |
| Operative time (hours)          | 9.4 ± 2                           | 8 ± 1.9                                 | 0.006                      |                             |

CTP: Child-Turcotte-Pugh, PELD: Pediatric end-stage liver disease, MELD: Model for end-stage liver disease, LT: Liver transplantation, PHN: Portal hypertension, GRWR: Graft recipient weight ratio, CIT: Cold ischemia time, WIT: Warm ischemia time, RBCs: Red blood cells.
had an independent association with patient mortality. Table 8; Fig. 7.

Table 7

| Category                      | No (%)  |
|-------------------------------|---------|
| Graft survival                | 42(62.7%)|
| 6 months survival             | 39(58.2%)|
| 1-year survival               | 36(53.7%)|
| 3-year survival               | 35(52.2%)|
| 5-year survival               | 35(52.2%)|
| 10-year survival              | 35(52.2%)|
| 16-year survival              | 35(52.2%)|
| Patient survival              | 43(64.2%)|
| 6 months survival             | 41(61.2%)|
| 1-year survival               | 36(53.7%)|
| 3-year survival               | 35(52.2%)|
| 5-year survival               | 35(52.2%)|
| 10-year survival              | 35(52.2%)|
| Survival per months Median(Range) | 18(0.03-194) |

*1st-period mortality 24/38(63.2%)
2nd-period mortality 8/29(27.6%)
Early mortality(3months) 23(34.3%)

Main causes:
- Sepsis 12(17.9%)
- Renal impairment 2(3%)
- LFSG 2(3%)
- Hepatic encephalopathy 1(1.5%)
- Acute rejection 1(1.5%)
- Early graft failure 1(1.5%)
- HAT 1(1.5%)
- PVT 1(1.5%)
- IVC stenosis 1(1.5%)
- Pulmonary embolism 1(1.5%)
- Late mortality 9(13.4%)

Main causes:
- Chronic rejection 4(6%)
- Sepsis 2(3%)
- ARDS 1(1.5%)
- HV stenosis 1(1.5%)
- Renal impairment 1(1.5%)

* Difference is significant, 1st-period mortality: From (2003–2013), 2nd-period mortality (from 2014 to 2018), LFSG: Large for size graft, HAT: Hepatic artery thrombosis, PVT: Portal vein thrombosis, IVC: Inferior vena cava, ARDS: Acute respiratory distress syndrome, HV: Hepatic vein.

Fig. 6. Kaplan-Meier patient survival curve: Period of LT and survival; 1st (2003–2013), 2nd (2014–2018) (Log rank = 0.013).

3.6. Early and/or late morbidities as predictors of patient survival outcomes

On univariate analysis, the overall early and/or late morbidities, bacterial infections, pulmonary complications, acute rejection, chronic rejection, vascular complications, and renal impairment were significant risks of patient mortality, on the other hand, on multivariate analysis, bacterial infections and pulmonary complications were independent predictors of poor patient outcome. Table 9; Fig. 7.

4. Discussion

Despite being a challenging procedure; pediatric LDLT is a life-saving option for paediatrics with ESLD, and other catastrophic liver conditions like tumours especially in countries like Egypt that don’t have a deceased donor liver transplantation (DDLT); however, the complications after it are still a big problem with devastating effects despite the recent improvement in such a field of pediatric LDLT [32].

Table 8

| Pre- and intra-operative variables as predictors of patient survival outcome. |
|---------------------------------|-----------------|------------------|-----------------|-----------------|
| Category                        | Patient survival No (%) | Patient mortality No (%) | P-value Univariate analysis | P-value Multivariate analysis |
|                                 | (Mean ± SD)       | (Mean ± SD)       |                               |                               |
|                                 |                   |                   |                               |                               |
| Pre LT PHN                      |                  |                   |                               |                               |
| Biliatry stent                  | 27(77.1%)        | 32(100%)          | 0.004                         | 1                             |
| CIT (min)                       | 50.8 ± 21.7      | 54.8 ± 28.9       | 0.5                           |                               |
| WIT (min)                       | 40.3 ± 13.4      | 37.3 ± 9.4        | 0.3                           |                               |
| Intraoperative packed RBCs transfusion (units) | 1.2 ± 1.2 | 1.7 ± 0.8 | 0.001 | 0.04 |
| Intraoperative plasma transfusion (units) | 2.8 ± 27 | 3.5 ± 28 | 0.3 | |
| Operative time (hours)          | 8.3 ± 1.8        | 9.4 ± 2           | 0.02                          | 0.7                           |

BA: Biliary atresia, CTP: Child-Turcotte-Pugh, MELD: Model for end-stage liver disease, PELD: Pediatric end-stage liver disease, PHN: Portal hypertension, GRWR: Graft recipient weight ratio, CIT: Cold ischemia time, WIT: Warm ischemia time, RBCs: red blood cells.
prophylaxis; bacterial infections that cause remarkable morbidities and mortalities in the early and late periods after pediatric LT are still common due to poor patient general condition, being ultra major operation, using immunosuppressants, etc \([16,39]\). They ranged from 39.1% to 67% in the previous literature \([39,42,47]\), however, they were less in our series (34.3%); and this is due to our improved infection control policies, especially in our later cases.

Higher PELD/MELD scores were associated with morbidities in our work, in the same line; they were significant or independent predictors of morbidities in Kitajima et al., 2017 \([2]\), Raices, et al., 2019 \([8]\), and Chung et al., 2020 \([48]\) studies. However, PELD/MELD scores were not associated with relaparotomy due to morbidities in Okada et al., 2019 \([49]\) study.

Longer operative time was a significant predictor of morbidity in our present work, also, it was associated with relaparotomies due to morbidities in Yoeli et al., 2018 \([6]\) and Okada et al., 2019 \([49]\) studies.

Increased amounts of intra-operative packed RBCs transfusion was a predictor of morbidity in the present series, in similar, it was correlated with relaparotomy due to morbidities in Yoeli et al., 2018 \([6]\) work.

Our 5-, 10-, and 16-year post-transplant patient survival were 52.2%, 52.2%, and 52.2% respectively, however, the literature ranges of post pediatric LDLT 5-, 10-, and 20-year patient survivals were 69%-97% \([23,43,50-52]\), 77.2%-94% \([32,42,51,53,54]\), and 79.6%-84.2% \([51,55]\) respectively. On the other hand, our patient mortality reached 47.8%; however, it ranged in the pediatric LDLT literature between 4.2% and 13% \([2,32,34,56,57]\). Our lower survival and higher mortalities in comparison to the literature come from several reasons: 1- most mortalities occurred within the 1st 3months post LT (23/32; 72%) due to sepsis that decreased in later cases after improving infection control policies. 2- We are a mixed adult/pediatric LT centre with few pediatric LT cases/year (median 4; range 0-13 cases; low volume pediatric LT centre) 3- The mortality was higher in the earlier periods of LT due to less experience but improved in later periods.

Higher PELD/MELD scores had a trend towards significant correlation with poor patient survival in our work, also, a higher PELD score was an independent predictor of poor patient survival in Pan et al., 2020 \([22]\), Lu et al., 2020 \([25]\) and Kehar et al., 2019 \([32]\) studies, moreover, it was a significant predictor of patient loss in Oh et al., 2010 \([42]\); study, in contrast, it did not affect survival in Kitajima et al., 2017 \([2]\), Raices, et al., 2019 \([8]\), Chung et al., 2020 \([48]\) or Shehata et al., 2012 \([58]\) studies respectively. However, it was not a significant predictor of morbidity in our present study.

Despite advanced infection control policies and antibacterial
mortality in Alam et al., 2017 [45] study. Also, they were independently associated with pulmonary complications; they were associated with patient mortality in our work; it was an independent predictor of poor patient survival in Shehata et al., 2012 [58] study.

Longer operative time was a significant predictor of patient mortality in our study, also, it was an independent predictor of poor patient survival in Pan et al., 2020 [22] study, however; it was not associated with survival in Boillot et al., 2021 [24] or Shehata et al., 2012 [58] studies. Due to accumulating experience, surgical techniques advancement, and pre-and post-transplant care improvement; the later periods of LT have been better than the earlier ones regarding patient survival, in similar, later periods of LT were significant predictors of better survival in ours, Pan, et al., 2020 [22], Pu, et al., 2020 [23], Boillot, et al., 2021 [24] and Venick et al., 2018 [59] studies, but they did not affect survival in Raices et al., 2019 [8] or Shehata et al., 2012 [58] studies.

The overall post-transplant complications were associated with patient mortality in the recent study, also, complications were significant predictors of mortality in Ho et al., 2004 [7] study, and early relaparotomy from early morbidities was significantly associated with poor patient survival in Okada et al., 2019 [49] study.

LFSG affects post LT outcomes by reducing oxygen and blood supplies of the liver graft, increasing vascular complications rate, inducing allograft dysfunction and/or loss and/or necrosis, inducing renal dysfunctions, as well as the occurrence of ACS and large for size syndrome [8,23]. In a similar line in our work; The 2 cases with LFGs died from their sequels, and GRWR≥3 had a trend towards independent correlation with patient mortality, also; LFSG was an independent predictor of poor patient survival in Lu et al., 2020 [25] study. However, it did not affect survival in Kitajima et al., 2017 [2], Goldaracena, et al., 2020 [33], Ersoy, et al., 2017 [56], Shehata, et al., 2012 [58] or Akdur et al., 2015 [60] studies.

Despite being a cause of morbidity and mortality after LT; biliary complications did not affect mortality in ours, Liao, et al., 2019 [18] or Sanada et al., 2019 [37] studies. Post pediatric LDLT vascular complications are common causes of morbidity and mortality [39]. Also, they were predictors of patients’ mortality in ours, Steinbrück, et al., 2011 [61] and Sieders et al., 2000 [62] studies. But they did not affect survival in Shehata et al., 2012 [58] study.

Post LT acute rejection is a known cause of graft dysfunction [63]. It was correlated with patient loss in our series; also, it was a major cause of death in Kitajima et al., 2018 [34] study. However, it did not affect graft or patient survival in Yilmaz et al., 2006 [40] or Shehata et al., 2012 [58] studies.

Despite advanced immunosuppression after LT; chronic rejection remains a major reason for graft and/or patient loss [42,43,59,64]. Also, in our work; it was the major cause of late mortality and a significant predictor of patient loss, similarly, it was an independent predictor of patient loss in Oh et al., 2010 [42] study. In contrast, it did not affect graft or patient survival in Yilmaz et al., 2006 [40] study.

We found a significant correlation between post LT renal impairment and patient mortality, similarly; Post LT hemodialysis was an independent predictor of poor patient survival in Boillot et al., 2021 [24] study. Regarding pulmonary complications; they were associated with patient mortality in Alam et al., 2017 [45] study. Also, they were independently associated with mortality in our work.

Bacterial infection was associated with patient mortality in Pouladfar et al., 2019 [47] and Shepherd et al., 2008 [65] studies. Also, it was an independent predictor of patient loss in our study and in a similar line; sepsis was the major cause of early mortality, and the 2nd most common cause of late mortality in our study, similarly; it was the major cause of mortality in Kitajima et al., 2017 [2], Kehar, et al., 2019 [32], Kitajima, et al., 2018 [34], Mohan, et al., 2017 [43] and Tanaka et al., 2010 [66] pediatric LDLT studies.

Lastly, to our knowledge; this is one of the unique pediatric LDLT studies mentioning the independent association between both pulmonary complications and bacterial infection and patient mortality, and this is due to sepsis which has led to those catastrophic mortalities. In conclusion; more packed RBCs transfusion units intra-operatively, and post LT bacterial infection, sepsis, chronic rejection, as well as pulmonary complications had a negative insult on our patients’ outcomes, so proper management of them is mandatory for improving outcomes after pediatric LDLT.

Ethical approval

The approval by National liver institute (IRB), Menoufia University that was done retrospectively.

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Author contributions

Emad Hamdy Gad: Surgical procedures, study design, data collection, writing, analysis and publication.

Ahmed Nabil Sallam: Surgical procedures, data collection, and analysis.

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Guarantor

All the authors of this paper accept full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish.

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Declaration of competing interest

No conflict of interest to declare.

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The main limitation of the study is the small NO of patients and being a retrospective one as well as the comparisons of our results were done with previous heterogenous literature studies (prospective or retrospective, small or large volumes, short or long duration studies) despite being pediatric living donor liver transplantation studies; so, we recommend doing further large prospective studies of pediatric LDLT and making the comparison with similar large prospective pediatric LDLT studies.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.103938.
References

[1] C. Aydin, E. Oran, S. Akbulut, S. Karakas, C. Kayadag, S. Karagul, et al., Postoperative pulmonary complications after liver transplantation: assessment of risk factors for mortality, Transplant. Proc. 47 (5) (2015) 1488-1494.

[2] T. Kitajima, S. Sakamoto, K. Sakai, H. Uchiida, S. Narumoto, A. Fudala, et al., Living donor liver transplantation for post-Kasai biliary atresia: analysis of pretransplant predictors of outcomes in infants, Liver Transplant. 23 (9) (2017) 1199-1209.

[3] H. Saing, S.T. Fan, P.K.H. Tam, C.M. Lo, W.I. Wei, K.L. Chan, et al., Surgical complications and outcome of pediatric liver transplantation in Hong Kong, J. Pediatr. Surg. 37 (2002) 1673-1677.

[4] W.A. Ziaziaris, A. Darabi, A.J. Holland, A. Alexander, J. Karimpouli, A. Shun, et al., Delayed primary closure and the incidence of surgical complications in pediatric liver transplant recipients, J. Pediatr. Surg. 50 (12) (2015) 2137-2140.

[5] F.A. Alvarez, R. Sanchez-Charia, J. Ginka, M. de Santibanes, J. Pekoli, E. de Santibanes, et al., Intrahepatic cholangiogiectasymontosity for complex biliary stenosis after pediatric living-donor liver transplantation, Pediatr. Transplant. 21 (5) (2017), https://doi.org/10.1111/ptt.12922.

[6] D. Yoeli, R.L. Ackah, R.B. Sigurdsson, M.I. Kuehl, N.T.N. Galvan, R.T. Cotton, et al., Reoperative complications following pediatric liver transplantation, J. Pediatr. Surg. 53 (11) (2018) 2240-2244.

[7] M.C. Ho, Y.M. Wu, R.H. Ho, W.J. Ko, Y.H. Ni, M.H. Chang, et al., Surgical complications and outcome of living related liver transplantation, Transplant. Proc. 36 (8) (2004) 2249-2251.

[8] M. Raies, M.E. Czerwonski, V. Ardiles, G. Boldrini, D. D’Angostino, J. Marzo Del Pont, et al., Short- and long-term outcomes after live-donor transplantation with hyper-reduced grafts in low-weight pediatric recipients, J. Gastrointest. Surg. 23 (12) (2019) 2411-2420.

[9] C.Y. Hsiao, C.M. Ho, Y.M. Wu, M.C. Ho, R.H. Hu, P.H. Lee, Biliary complication in pediatric liver transplantation: a single-center 15-Year experience, J. Gastrointest. Surg. 23 (4) (2019) 751-759.

[10] C.C. Lin, F.R. Chang, C.C. Wang, Y.S. Chen, C.L. Chen, Y.W. Liu, et al., Early postoperative complications in recipients of living donor liver transplantation, Transplant. Proc. 36 (8) (2004) 2338-2341.

[11] R. Zhang, Z.J. Zhu, L.Y. Sun, L. Wei, W. Xu, Z.G. Zeng, et al., Outcomes of pediatric liver transplantation: deceased donor liver transplantation vs. living donor liver transplantation, Transplant. Proc. 50 (10) (2018) 3601-3605.

[12] J.J. Moon, G.O. Jung, G.S. Choi, J.M. Kim, M. Shin, E.Y. Kim, et al., Risk factors for portal vein complications after pediatric live liver donor transplantation with left-sided grafts, Transplant. Proc. 42 (2010) 871-875.

[13] N.S. Choudhary, S. Saigal, R.K. Bansal, N. Saraf, D. Gautam, A.S. Soin, Chronic and acute rejection after LIV-H graft transplantation: a clinician needs to know, J. Clin. Exp Hepatol. 7 (4) (2017) 358-366.

[14] K. Kanamori, M. Kubota, S. Sakamoto, A. Ishiguro, M. Kasahara, Neurological complications after living-donor liver transplantation in children, Brain Dev. 43 (5) (2021) 637-645.

[15] U.D. Ekong, N.A. Gupta, R. Urban, W.S. Andrews, 20- to 25-year patient and graft survival following a single pediatric liver transplant-Analysis of the united network of organ sharing database: where to go from here, Pediatr. Transplant. 23 (6) (2019) e13523.

[16] A.M. Alcama, L.J. Alessi, S.N. Vehovic, N. Bansal, G.J. Bond, J.A. Carcillo, et al., Delayed primary closure and the incidence of surgical complications in pediatric liver transplant recipients, J. Pediatr. Surg. 37 (2002) 1673-1677.

[17] M. Firoozifar, R. Rasekh, G. Pouladfar, Z. Jafarpour, S.A. Malek Hosseini, M. Kehar, et al., Living donor liver transplantation for post-Kasai biliary atresia: analysis of 100 transplantation procedures, Transplant. Proc. 41 (2009) 2444-2446.

[18] Y. Sanada, T. Kato, Y. Hirata, N. Namada, N. Okada, Y. Ibara, et al., Biliary complications following pediatric living donor liver transplantation: risk factors, treatments, and prognosis, Transplantation 103 (9) (2018) 1683-1870.

[19] J.J. Li, C.H. Zu, S.P. Li, W. Gao, Z.Y. Shen, J.Z. Cai, Effect of graft size matching on pediatric liver-donor transplantation outcomes in a single center, Clin. Transplant. 32 (1) (2018), https://doi.org/10.1111/ctr.13160.

[20] L. Eboli, A.C. Tannuri, N. Gibelli, T. Silva, P. Braga, U. Tannuri, Comparison of the results of living donor liver transplantation due to acute liver failure and biliary atresia in a quaternary center, Transplant. Proc. 49 (4) (2017) 832-835.

[21] F. Yilmaz, U. Aydin, D. Nart, M. Zeytunlu, Z. Karasu, T. Kaya, et al., The incidence and management of acute and chronic rejection after living donor liver transplantation, Transplant. Proc. 35 (2003) 1435-1437.

[22] Y. Hirata, Y. Sanada, T. Urushahi, Y. Ibara, N. Yamada, N. Okada, et al., Antibody- drug treatment for steroid-resistant rejection after pediatric living donor liver transplantation: a single-center experience, Transplant. Proc. 50 (1) (2018) 60-65.

[23] S.H. Oh, K.M. Kim, D.Y. Kim, Y.J. Lee, K.W. Rhee, J.Y. Jang, et al., Long-term outcomes of pediatric living donor liver transplantation at a single institution, Pediatr. Transplant. 14 (7) (2010) 870-878.

[24] N. Mohan, S. Sarkar, A. Rastogi, M.S. Dhalwai, V. Raghunath, D. Goyal, et al., Outcome of 200 pediatric live donor liver transplantations in India, Indian Pediatr. 54 (11) (2017) 913-918.

[25] K.M. Campbell, N. Yazigi, P.C. Ryckman, M. Alonso, G. Tiao, W.F. Ballerini, et al., High prevalence of renal dysfunction in long-term survivors after pediatric living donor transplantation, J. Pediatr. Transplant. 14 (2015) 472-477.

[26] S. Alam, A. Sapare, S. Rao, R. Aggarwal, A.L. D’Cruz, Respiratory morbidity following pediatric orthotopic liver transplantation, Indian Pediatr. 54 (3) (2017) 244-246.

[27] I. Buchonnet-Mettrailler, S. Blanchon, S. Luthold, B.E. Wildhaber, P. C. Rinnes, B. Ararazone-Arigofo, et al., Pulmonary complications after liver transplantation in children: risk factors and impact on early post-operative morbidity, Pediatr. Transplant. 22 (2018), e12435.

[28] G. Pouladfar, Z. Jafarpour, S.A. Malek Hosseini, M. Firoozifar, R. Rasekh, L. Khosravifard, Bacterial infections in pediatric patients during early post-liver transplant period: a prospective study in Iran, Transplant. Infect. Dis. 21 (2019), e13001.

[29] P.H.Y. Chang, K.S.H. Chok, K.K.Y. Wong, P.K.H. Tam, C.M. Lo, Determining the optimal timing of liver transplant for pediatric patients after Kasai portoenterostomy based on disease severity scores, J. Pediatr. Surg. 55 (9) (2020) 1899-1906.

[30] N. Okada, Y. Sanada, Y. Oishi, T. Urushahi, Y. Ibara, N. Yamada, et al., The causes and outcomes of early relaparotomy following pediatric liver-donor transplantation, Liver Transplant. 25 (7) (2019) 1066-1073.

[31] Y. Shirouzu, M. Kasahara, D. Morisaka, S. Sakamoto, K. Taira, K. Uryuhara, et al., Vascular reconstruction in living liver donor transplantation in infants weighing less than 6 kilograms: the Kyoto experience, Liver Transplant. 12 (8) (2006) 1224-1232.

[32] M. Kasahara, K. Uryuhara, S. Sakamoto, A. Fukuda, H. Furukawa, S. Sakanisa, et al., Japanese Liver Transplantation Society. Living donor liver transplantation for biliary atresia: an analysis of 2085 cases in the registry of the Japanese Liver Transplantation Society, Am. J. Transplant. 18 (3) (2018) 659-668.

[33] M. Kasahara, Y. Sanada, T. Wדקawa, T. Urushahi, M. Umehara, S. Egami, et al., Outcomes of living donor liver transplantation in 126 patients with biliary atresia: a single-center experience, Transplant. Proc. 42 (10) (2010) 4127-4131.
M. Ueda, F. Oike, Y. Ogura, K. Uryuhara, Y. Fujimoto, M. Kasahara, et al., Long-term outcomes of 600 living donor liver transplants for pediatric patients at a single center, Liver Transplant. 12 (9) (2006) 1326–1336.

M. Kasahara, S. Sakamoto, K. Sasaki, H. Uchida, T. Kitajima, T. Shigeta, et al., Living donor liver transplantation during the first 3 months of life, Liver Transplant. 23 (8) (2017) 1051–1057.

M. Kasahara, K. Umeshita, Y. Inomata, S. Uemoto, Japanese Liver Transplantation Society, Long-term outcomes of pediatric living donor liver transplantation in Japan: an analysis of more than 2200 cases listed in the registry of the Japanese Liver Transplantation Society, Am. J. Transplant. 13 (7) (2013) 1830–1839.

Z. Ersoy, S. Kaplan, A. Ozdemirkan, A. Torgay, G. Arslan, A. Pirat, et al., Effect of graft weight to recipient body weight ratio on hemodynamic and metabolic parameters in pediatric liver transplant: a retrospective analysis, Exp. Clin. Transplant 15 (Suppl 1) (2017) 53–56.

M. Haberal, H. Karakayali, A. Atiq, S. Sevmis, G. Moray, F. Ozcan, et al., Duct-to-duct biliary reconstruction without a stent in pediatric living-donor liver transplantation, Transplant. Proc. 43 (2) (2011) 595–597.

M.M. Shehata, S. Yagi, Y. Okamura, T. Iida, T. Hori, A. Yoshizawa, et al., Pediatric liver transplantation using reduced and hyper-reduced left lateral segment grafts: a 10-year single-center experience, Am. J. Transplant. 12 (12) (2012) 3406–3413.

R.S. Venick, D.G. Farmer, J.R. Soto, J. Vargas, H. Yersiz, F.M. Kaldas, et al., One thousand pediatric liver transplants during thirty years: lessons learned, J. Am. Coll. Surg. 226 (4) (2018) 355–366.

A. Akdur, M. Kirnap, F. Ozcan, A. Sezgin, H.E. Aytavazoglu Soy, F. Karakayali Yarbug, et al., Large-for-size liver transplant: a single-center experience, Exp. Clin. Transplant (Suppl 1) (2015) 108–110.

K. Steinbrück, M. Enne, R. Fernandes, J.M. Martinho, E. Balbi, L. Agoglia, et al., Vascular complications after living donor liver transplantation: a Brazilian, single-center experience, Transplant. Proc. 43 (1) (2011) 196–198.

E. Sieders, P.M. Peeters, E.M. TenVergert, K.P. de Jong, R.J. Porte, J.H. Zwaveling, et al., Early vascular complications after pediatric liver transplantation, Liver Transplant. 6 (3) (2000) 326–332.

K.P. Au, S.C. Chan, K.S. Chok, W.W. Sharr, W.C. Dai, S.L. Sin, et al., Clinical factors affecting rejection rates in liver transplantation, Hepatobiliary Pancreat. Dis. Int. 14 (4) (2015) 367–373.

A.C. Tanmuri, F. Lima, E.S. Mello, R.Y. Tanigawa, U. Tanmuri, Prognostic factors for the evolution and reversibility of chronic rejection in pediatric liver transplantation, Clinics 71 (4) (2016) 216–220.

R.W. Shepherd, Y. Turnelle, M. Nadler, J.A. Lowell, M.R. Narkewicz, S. V. McDiarmid, et al., SPLIT research group, Risk factors for rejection and infection in pediatric liver transplantation, Am. J. Transplant. 8 (2) (2008) 396–403.

H. Tanaka, A. Fukuda, T. Shigeta, T. Kuroda, T. Kimura, S. Sakamoto, et al., Bilary reconstruction in pediatric live donor liver transplantation: duct-to-duct or Roux-en-Y hepaticojejunostomy, J. Pediatr. Surg. 45 (8) (2010) 1668–1675.