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International Liver Transplantation Society Global Census

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INTRODUCTION

Pediatric liver transplantation (PLT) was first attempted in 1963 and successfully performed in 1967 using a whole liver graft.¹ Over time, techniques for reduced-, split-, and living donor liver transplantation (LDLT) were developed to address organ shortage, improve organ utilization, and

decrease waitlist mortality. Despite initial concerns regarding the safety of partial grafts for transplantation, recent evidence suggests that excellent graft and pediatric survival can be achieved with any type of graft.^{2,3} In fact, the current literature shows better outcomes for children when using LDLT compared with transplanting deceased donor grafts.⁴

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M.I.R.-D and F.L.-V. were involved in project design, data acquisition, data analysis and interpretation, manuscript preparation, critical manuscript revision, and final approval of the version to be published. M. K. was involved in designing the project, acquisition of data, interpretation of data, critical revision of the manuscript, and final approval of the version to be published. P. M., Q.X., J.C.H., C.U.N., N.-J.Y., V.N., C.O.E., and J.L. were involved in interpretation of data, critical revision of the manuscript, and final approval of the version to be published. M.S.R. designed the project, acquired the data, interpreted the data, prepared the manuscript, critically revised the manuscript, and approved the final version to be published. A.F.-H. M. and J.S.-N. were involved in acquisition of data, critical revision of the manuscript, and final approval of the version to be published. M.R. was involved in conception and design of the work, interpretation of data, critical revision of manuscript, final approval of the version to be published.

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De-identified data and a data dictionary that underlie the results reported in this article will be available upon request. Researchers who provide a methodologically sound proposal should contact Manuel Rodriguez-Davalos (manuel.rodriguez-davalos@gmail.org). Access is granted after a signed data-access agreement is attained.

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In addition to improved surgical techniques, advancements in organ preservation, early postoperative care, and immunosuppression protocols have transformed PLT, which has become the standard of care for children with end-stage liver disease, selected unresectable liver tumors, a number of genetic/metabolic diseases, and cases of acute liver failure.⁵ This remarkable progress in early post-transplant outcomes has allowed some PLT programs to shift their focus to improving quality of life after transplantation, as 10- and 15-y survival rates approach 80%.⁶ However, pediatric liver disease remains a major health problem, and it is estimated that >16 000 children under the age of 15 y died worldwide in 2017 because of end-stage liver disease.⁷

In a number of countries where organ transplantation is well established and regulated, central national or international registries enable transparency, quality control, and collaboration between PLT centers at national⁵⁻¹² and international levels.¹³⁻¹⁵ However, the majority of these international collaborations have only included PLT centers from high-income countries with a focus on deceased donor liver transplantation. The last 10–15 y have seen a major expansion of PLT in middle-income countries in Asia and South America, with a focus on LDLT.¹⁶⁻¹⁹ However, most of these countries do not have comprehensive registries to document the work being performed. Bringing together the activity of these recently established centers with established centers in high-income countries is essential to provide a global picture of PLT. This association will also help all centers learn from each other's experiences to improve outcomes for children with liver disease around the world. The aim of this census, undertaken under the aegis of the International Liver Transplantation Society (ILTS), was to develop a comprehensive picture of global PLT activity, with an emphasis on recently developing regions and identifying potential similarities and differences in PLT practices between regions.

MATERIALS AND METHODS

Study Design

A web-based survey was conducted between May 2018 and August 2019. A focus group was created within the pediatric committee of the ILTS, as well as the Executive Committee. Members of this focus group proposed questions to include in the survey. This being the first global census, the main goal was to enroll as many centers as possible around the world. For this reason, questions focused on demographic data and the type of transplants performed. Likewise, we avoided questions regarding outcomes for this first census. All questions were proposed to the focus group and were included in the survey only after they had been approved by the majority of members. The final survey was developed in English using a cloud-based survey software (SurveyMonkey, San Mateo, CA) and consisted of 15 items, including open-ended, multiple-choice, and questions needing responses on a Likert rating scale. The survey focused on the following areas:

(a) Number of pediatric liver transplants performed in the past year and in the last 5 y; (b) common etiology of liver disease encountered in their program; (c) age and weight of the recipient at the time of transplant; (d) types of grafts used; and (e) the existence of training opportunities

at their center. For descriptive analysis, countries were separated into 6 different regions: Africa, North Central America, South America, Asia, Australia-Oceania, and Europe. The number of transplants for each country was adjusted by pediatric population = $(\text{PLT} \times 1\,000\,000 / \text{pediatric population})$.²⁰

The distributed questionnaire is available as **Supplementary Material (SDC, <http://links.lww.com/TP/C764>)**. Briefly, whole numbers were asked for number of PLT performed in the past year and in the last 5 y. Ranges were used for demographic variables (ie, 0%, 0%–10%, 11%–20%, 21%–30%, 31%–50%, 51%–75%, and 76%–100%) and for the number of cases where specific type of grafts were used (ie, <25, 25–50, 50–100, 100–250, and >250).

For comparative analysis, transplant centers were categorized into quintile categories according to the year when they performed their first PLT, with the oldest quintile (before 1988) allocated in an “established centers” group, whereas an “emerging centers” group consisted of the most recent quintile (after 2010). Countries were also classified according to their gross national income (GNI) per capita in (a) low, (b) lower-middle, (c) upper-middle, and (d) high-income groups, as defined by The World Bank.²¹

An exploratory analysis was performed comparing the United States and India because they had the highest number of participating centers (the United States [$n = 30$] and India [$n = 11$]) and represented opposite ends of GNI per capita, as well as of the spectrum of established to emerging centers.

Survey Administration

The list of PLT centers to contact was finalized by including centers in the Society of Pediatric Liver Transplantation (SPLIT), European Liver Transplant Registry (ELTR), and the Japanese Liver Transplantation Society registry. Centers in other countries were identified by communicating with ILTS representatives from those regions, or through a literature review searching for centers publishing on PLT.

The questionnaire was distributed by email to 157 pediatric liver transplant centers around the world and was also made available through the official ILTS website. The first email was sent in May 2018, shortly after the ILTS meeting took place. Two wk before the end of the study period (August 2019), a reminder email was sent to those centers that had not answered the survey at that time and those that responded with partial data. Program directors were contacted by our corresponding author and coauthors, but any team member was able to complete the survey. Survey answers were limited to 1 per center. Three centers answered to the questionnaire more than one time. In these cases, we reached out to the program director to corroborate the data. Only active programs performing PLT in the previous 5 y were included in this study. Active programs were defined as those performing at least 1 PLT in the previous 5 y and pediatric population was defined as age 17 or less at the time of transplant. Cross-referencing the obtained answers was unable to be done because of the unavailability of databases for some regions.

Data Analysis

Descriptive statistics for liver transplant volume are reported as mean \pm standard deviation for normally

distributed data and median interquartile range (IQR) for non-normally distributed variables. Results from multiple-choice questions were reported as numbers and proportions. Finally, answers from rating scale questions were categorized as ordinal variables and reported as numbers and proportions.

Student's t-test was performed for variables with normal distribution, and the Mann-Whitney U test was performed for non-normally distributed continuous variables. Categorical variables were compared using the χ^2 test or Fisher exact test when indicated. A two-tailed *P* value <0.05 was considered statistically significant. Analysis was performed using SPSS version 25.0 (SPSS, Chicago, IL) and R software, version 3.4.4 (R Core Team, 2018).

RESULTS

Response Rate and Participants' Demographic Data

A total of 108 (69%) centers answered the survey, ranging from 60.6% in North Central America to 100% in Africa and Australia-Oceania. Among the responding programs, North Central America accounted for the maximum responses with 34.2% (37 of 108), followed by Asia (29.6% [32 of 108]) and Europe (20.3% [22 of 108]). Eleven percent (12 of 108) were from South America, 2.7% (3 of 108) from Australia-Oceania, and 1.8% (2 of 108) from Africa (Table 1). The United States (30) and India (11) had the highest number of participating centers. The remaining 36 countries had ≤ 5 participating centers, and 22 of them had only one participating program.

Number of PLTs Performed

The overall characteristics of PLT programs per region are depicted in Table 2. Results are shown as median (range). Within 12 mo before survey administration, a total of 2615 PLTs were performed worldwide with a median of 11.5 (IQR: 6–25.7) per center. The center with the highest volume in the previous year (443) was from China. One center from North Central America did not perform PLT during the past year but was active within the last 5 y. Overall, Asia performed the most PLT during that period with 1279 (48.9%) cases, followed by Europe with 526 (20.1%) and North Central America with 505 (19.3%) PLT. South America, Australia-Oceania, and Africa accounted for 231 (8.8%), 47 (1.7%), and 27 (1.0%) PLT, respectively. The volume of PLT per million pediatric population (pmpp) performed last year in each country is illustrated in Figure 1.

During the last 5 y, a total of 10,619 PLTs were performed around the world (Figure 2). PLT programs performed a median of 50 (IQR: 30–112.5) PLT during this time period. Throughout the last 5 y, the center with the highest volume (1078) was from China. Two centers, 1 from South America and 1 from Asia, had performed only one PLT in this time frame; both centers started their PLT activities last year. Distribution of PLTs within each region was similar to that described above. Asia, Europe, and North Central America performed most of the PLT during the last 5 y, with 4617 (43.4%), 2362 (22.2%), and 2318 (21.8%) procedures, respectively. Conversely, South America performed 965 (9.0%), Australia-Oceania 202 (1.9%), and Africa 155 (1.4%) PLT during the same time

period. The number of PLT/pmpp performed within the last 5 y in each country is illustrated in Figure 1.

Type of Grafts

Worldwide, 32 (29.6%) centers had performed greater than 50 LDLT over the last 5 y, compared to 13.8% performing >50 split/reduced, and 13.8% doing >50 LTs with whole grafts (Figure 3A). When looking at the regional trends over the last 5 y (Figure 3B), LDLT was highly prevalent in Asia and Africa, likely because of the low number of deceased donors in these countries. Centers from Australia-Oceania appear to prefer split or reduced grafts from deceased donors, and European centers report the use of living donors, deceased whole, and deceased split/reduced grafts. Finally, North Central America is the only continental region that most frequently uses whole liver grafts. A higher proportion of lower-middle-income countries (68.7%) performed ≥ 25 living donor liver transplants over the last 5 ye compared to high-income countries (36%; *P* = 0.019). A greater proportion of programs from high-income countries have performed ≥ 25 whole liver transplants (WLTs) (52.4% versus 6.2%; *P* = 0.001) and ≥ 25 split/reduced liver transplants (53.2% versus 6.2%; *P* < 0.001) compared to centers from lower-middle-income countries.

Etiology of Liver Disease

Worldwide, 44 (40.6%) centers responded that >50% of their PLT are performed because of biliary atresia (Figure S1A, SDC, <http://links.lww.com/TP/C764>). This pattern was maintained when analyzing individual regions (Figure S1B, SDC, <http://links.lww.com/TP/C764>).

Age and Weight at the Time of Transplant

The most common age groups at the time of transplantation were <12 mo, and 1–5 y, as 13 (12.5%), and 12 (11.4%) centers answered that >50% of their PLT are performed in these age groups (Figure S2A, SDC, <http://links.lww.com/TP/C764>). Regional variance can be observed in Figure S2B (SDC, <http://links.lww.com/TP/C764>). Worldwide, 24 (23.0%) of centers answered that >50% of their PLT are performed on patients weighing ≤ 10 kg at the time of transplantation (Figure S3A SDC, <http://links.lww.com/TP/C764>). Regional trends can be observed in Figure S3B (SDC <http://links.lww.com/TP/C764>).

Training Opportunities

From the participating programs, 74.8% (80 of 108) reported having training opportunities in their transplant centers. The two participating programs from Africa (2 of 2, 100%) had training opportunities, followed by Europe (19 of 22, 86.3%), and Asia (26 of 31, 83.8%). Two-thirds of the centers from North Central America (25 of 37, 67.5%) and Australia-Oceania (2 of 3, 66.7%) reported having training opportunities. South America had the lowest proportion of programs with training opportunities (6 of 12, 50%). As expected, programs with training opportunities have performed more pediatric liver transplants both over the last year and within the last 5 y compared to programs without training opportunities (Table 3).

TABLE 1.**Participating centers**

North Central America
 Intermountain Primary Children's Hospital, Salt Lake City
 Medical College of Wisconsin, Milwaukee
 The Hospital for Sick Children (SickKids), Toronto, Canada
 Lucile Packard Children's Hospital Stanford, Palo Alto
 Hospital Angeles, Chihuahua, Mexico
 Ann and Robert H. Lurie Children's Hospital, Chicago
 Centro de Trasplante Hepatico y Cirugia Hepatobiliar, San Jose, Costa Rica Memorial Hermann TMC, Houston
 Centro Medico Puerta de Hierro, Guadalajara, Mexico University of Nebraska, Omaha
 Jackson Memorial Hospital, Miami
 Montefiore Medical Center, Bronx
 Indiana University Health, Indianapolis
 Cleveland Clinic, Cleveland
 MedStar Georgetown, Washington
 Phoenix Children's Hospital, Scottsdale
 Duke University Medical Center, Durham
 Mount Sinai Hospital, New York City
 Christus Muguerza Sur, Ciudad Guadalupe, Mexico
 Boston Children's Hospital, Boston
 Children's Medical Center Dallas, Dallas
 University of Minnesota Masonic Children's Hospital, Minnesota
 Seattle Children's Hospital, Burien
 Yale New Haven Children's Hospital, New Haven
 Texas Children's Hospital, Houston
 Children's Mercy Hospital, Kansas City, United States of America Hospital Auxilio Mutuo, San Juan
 Hospital Infantil de Mexico Federico Gomez, Ciudad de Mexico, Mexico
 Unidad de Hepatologia y Trasplante Infantil, Guadalajara, Mexico University of North Carolina, Chapel Hill
 Children's Hospital Colorado, Aurora
 Medical University of South Carolina, Charleston
 UPMC Children's Hospital, Pittsburgh
 Children's Hospital Los Angeles, Los Angeles
 Mattel Children's Hospital UCLA, Los Angeles
 UCSF, San Francisco
 Children's Hospital of Philadelphia, Philadelphia

Asia
 National Center for Child Health and Development, Tokyo, Japan
 The Institute of Liver Disease and Transplantation, Dr. Rela Institute and Medical Centre, Chennai, India
 Gleneagles Global Health City, Chennai, India
 Renji Hospital, Shanghai, China
 Seoul National University College of Medicine, Seoul, Republic of Korea
 Sir Ganga Ram Hospital, New Delhi, India
 Shifa International Hospital, Islamabad, Pakistan Kauvery Hospital, Chennai, India
 Nagoya University Hospital, Nagoya, Japan
 Syzganov's National Scientific Center of Surgery, Almaty, Kazakhstan
 Siriraj Hospital Mahidol University, Bangkok, Thailand
 KEM Hospital, Pune, India
 Wockhardt Hospitals Ltd, Mumbai, India
 Beijing Friendship Hospital, Beijing, China
 Jichi Medical University, Tochigi, Japan
 Tianjin First Center Hospital, Tianjin, China
 Cipto Mangunkusumo General Hospital, Jakarta, Indonesia
 Shiraz Transplant Center, Shiraz, Iran
 Ramathibodi Hospital, Bangkok, Thailand Fortis Hospitals, Noida and Delhi, India
 Okayama University Hospital, Okayama, Japan Global Hospital, Hyderabad, India
 Kyoto University Hospital, Kyoto, Japan
 Mongolian First Central Hospital, Ulaanbaatar, Mongolia
 Apollo Hospitals Mumbai, Mumbai, India
 Asan Medical Center, Seoul, South Korea
 National University Hospital, Singapore, Singapore

Continued next page

TABLE 1. (Continued)

Medanta, The Medicity Hospital, Delhi, India Indraprastha Apollo Hospital, Delhi, India
 Amritha Institute of Medical Science and Research Centre, Cherthala, India Schneider Children Medical Center, Petach Tikva, Israel
 Kaohsiung Chang Gung Memorial Hospital, Niao Sung, Taiwan
 The Medical City, Pasig, Philippines

Europe
 University Medical Center Groningen, Groningen, The Netherlands
 King's College Hospital, London, United Kingdom
 Ankara University, Ankara, Turkey
 Paul Brosse Hospital, Lyon, France
 Medipol University Hospital, Istanbul, Turkey
 National Medical Research Center of Transplantation and Artificial Organs, Moscow, Russia
 Memorial Atasehir Hospital, Istanbul, Turkey
 Bambino Gesù Children's Hospital, Rome, Italy
 Hospital Vall d'Hebron, Barcelona, Spain
 Karolinska University Hospital, Stockholm, Sweden
 University Padova, Padua, Italy
 Baskent University, Ankara, Turkey
 ASST Papa Giovanni XXIII, Bergamo, Italy
 ISMETT, Palermo, Italy
 IKEM Hospital, Prague, Czech Republic
 AOU Citta della Salute e della Scienza, Torino, Italy
 Necker University Hospital, Paris, France
 Istanbul Univesity, Istanbul, Turkey
 University Hospital Ghent, Ghent, Belgium
 Children's Memorial Health Institute, Warszawa, Poland
 Hospital Infantil La Paz, Madrid, Spain
 Birmingham Children's Hospital NHS Foundation Trust, Birmingham, UK

South America
 Hospital Sirio-Libanes, Sao Paulo, Brazil
 Hospital Edgardo Rebagliati Martins, Lima, Perú
 Hospital de Pediatria Juan P. Garrahan, Buenos Aires, Argentina
 Fundacion Cardiointantil IC, Bogota, Colombia
 Hospital de Criança Santo Antonio, Porto Alegre, Brazil
 Sanatorio Parque de Rosario, Rosario, Argentina
 Pontifica Universidad Catolica de Chile, Santiago, Chile
 Hospital Pablo Tobon Uribe, Medellin, Colombia
 Centro Medico Imbanaco de Cali, Cali, Colombia
 Hospital de Clinicas de Porto Alegre, Porto Alegre, Brazil
 Hospital Ricardo Gutierrez, Buenos Aires, Argentina
 Fundacion Favalaro, Buenos Aires, Argentina

Australia-Oceania
 Lady Cilento Children's Hospital, Queensland, Australia
 Auckland City Hospital, Auckland, New Zealand
 The Children's Hospital at Westmead, Sydney, Australia

Africa
 Wits Donald Gordon Medical Centre, Johannesburg, South Africa
 Menoufia University, Cairo, Egypt

Emerging Versus Established PLT programs

Established centers ($n = 20$) started their PLT activity before 1988, and the majority of these were located in North Central America (11 of 20, 55%). On the other hand, emerging centers ($n = 20$) performed their first PLT after 2010. Asia had the highest number (10 of 20, 50%) of the emerging programs. All established centers are located in high-income countries (100%), compared to only 2 (10%) emerging centers ($P < 0.001$). It is worth noting that 40% of emerging centers are located in lower-middle-income countries. Established centers performed a median of 15 (IQR: 9.2–29) PLT last year compared to 5 (1.2–10)

in emerging centers ($P = 0.002$). Most established centers (90%) reported having training opportunities, compared to 47% (9 of 19) of emerging centers ($P = 0.006$).

The United States had the highest number of established centers ($n = 10$). Conversely, India was the country with the most emerging centers ($n = 5$).

PLT programs from India had their first transplant more recently (median: 2010, IQR: 2006–2017) than programs from the United States (median: 1988, IQR: 1984–1996.2; $P < 0.001$). Despite this, centers from India have performed a similar number of PLT during the last year (median: 16 versus 13.5, $P = 0.942$) and within the last 5 y (median: 40

TABLE 2.**Characteristics of PLT activity across world regions**

Region	Participating countries, n (%)	PLT centers, n (%)	Year of first PLT, median (range)	PLT per center last year, median (range)	PLT per center last 5 y, median (range)	Total PLT last year	Total PLT last 5 y	High-volume centers, n (%)
North Central America	4 (10.5)	37 (34.2)	1991 (1967–2018)	11 (0–44)	50 (2–180)	505	2318	26 (70)
Asia	14 (36.8)	32 (29.6)	2006 (1988–2018)	12.5 (1–443)	47.5 (1–1078)	1279	4617	7 (58)
South America	5 (13.1)	12 (11.1)	2006 (1991–2018)	9 (1–106)	32.5 (1–407)	231	965	10 (31)
Europe	11 (28.9)	22 (20.3)	1995 (1981–2014)	19.5 (2–97)	80.5 (22–403)	526	2362	10 (45)
Australia-Oceania	2 (5.2)	3 (2.7)	1986 (1984–2002)	9 (8–30)	50 (42–110)	47	202	3 (100)
Africa	2 (5.2)	2 (1.8)	2004 (2003–2005)	13.5 (5–22)	77.5 (25–130)	27	155	1 (50)
Total	38 (100)	108 (100)	1998 (1967–2018)	11 (0–443)	50 (1–1078)	2615	10 619	57 (52)

PLT, pediatric liver transplantation.

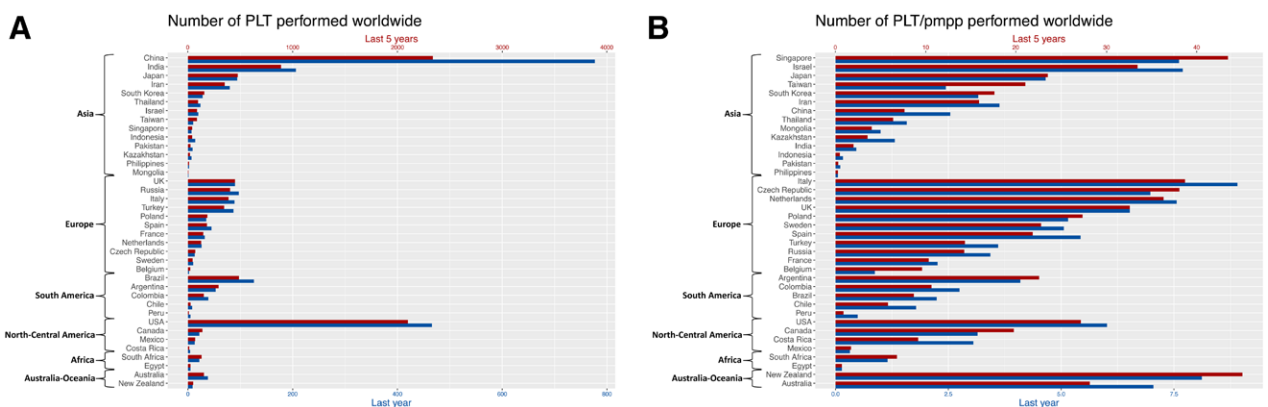


FIGURE 1. Number of pediatric liver transplants performed in each country. A, Total, and (B) adjusted pmpp (only those PLT performed in participating centers are shown). Red bars represent rates over the last 5 y (top x-axis), and blue bars represent transplant rates over the last year (bottom x-axis). PLT, pediatric liver transplantation; pmpp, per million pediatric population.

versus 68, $P = 0.552$) compared to centers in the United States. Important differences were identified when examining the types of grafts used in each country. In India, 72.7% (8 of 11) of the programs have performed at least 25 LDLT over the last 5 y, compared to 13.3% (4 of 30) programs in the United States ($P = 0.001$). On the other hand, over the same time period, a greater proportion of centers from the United States performed ≥ 25 WLT (60% [18 of 30] versus 9.0% [1 of 11]; $P = 0.005$) and ≥ 25 SLT/reduced (56.6% [17 of 30] versus 0% [0 of 11]; $P = 0.001$) compared to centers in India.

GNI and PLT

The majority of PLT programs were located in high-income countries (56.5%), followed by upper-middle- (28.7%), and lower-middle- (15.8%)-income countries. No centers from low-income countries participated in the census. Last year, 1044 (39.9%) liver transplants were performed in high-income countries, 1334 (51%) in upper-middle-income countries, and 237 (9.1%) in lower-middle-income countries. During the last 5 y, high-income countries performed 4992 (46.4%) PLT, followed by upper-middle- and lower-middle-income countries performing 4704 (44.3%) and 993 (9.4%) PLT, respectively. Centers located in lower-middle-income countries started their PLT activities later than centers from high-income

countries (Table 4). A higher proportion of lower-middle-income countries (68.7%) had performed ≥ 25 LDLT over the last 5 y compared to high-income countries (36%; $P = 0.019$). On the contrary, a greater proportion of programs from high-income countries have performed ≥ 25 WLT (52.4% versus 6.2%; $P = 0.001$) and ≥ 25 SLT/reduced (53.2% versus 6.2%; $P < 0.001$) compared to those from lower-middle-income countries.

DISCUSSION

This study represents, to the best of our knowledge, the most geographically comprehensive study reporting on PLT activity, comprising 38 countries from 6 different continental regions that have performed 10 619 PLT in the last 5 y. Additionally, this survey helps clarify the distribution of typical demographic and clinical variables of children at the time of transplantation, as well as the types of grafts used for PLT and how these vary across the globe.

Biliary atresia is the most common indication for PLT worldwide. More than half of the children were < 5 y of age at the time of transplantation for up to at least 12% of centers. Most children weighed < 10 kg at the time of transplantation for 23% of all centers. These findings are in accordance with those previously reported by different registries, societies, and multiple transplant centers.^{14,18,20-30} There are countries that, because of resources or experience,

Pediatric Liver Transplants Performed Last 5 years

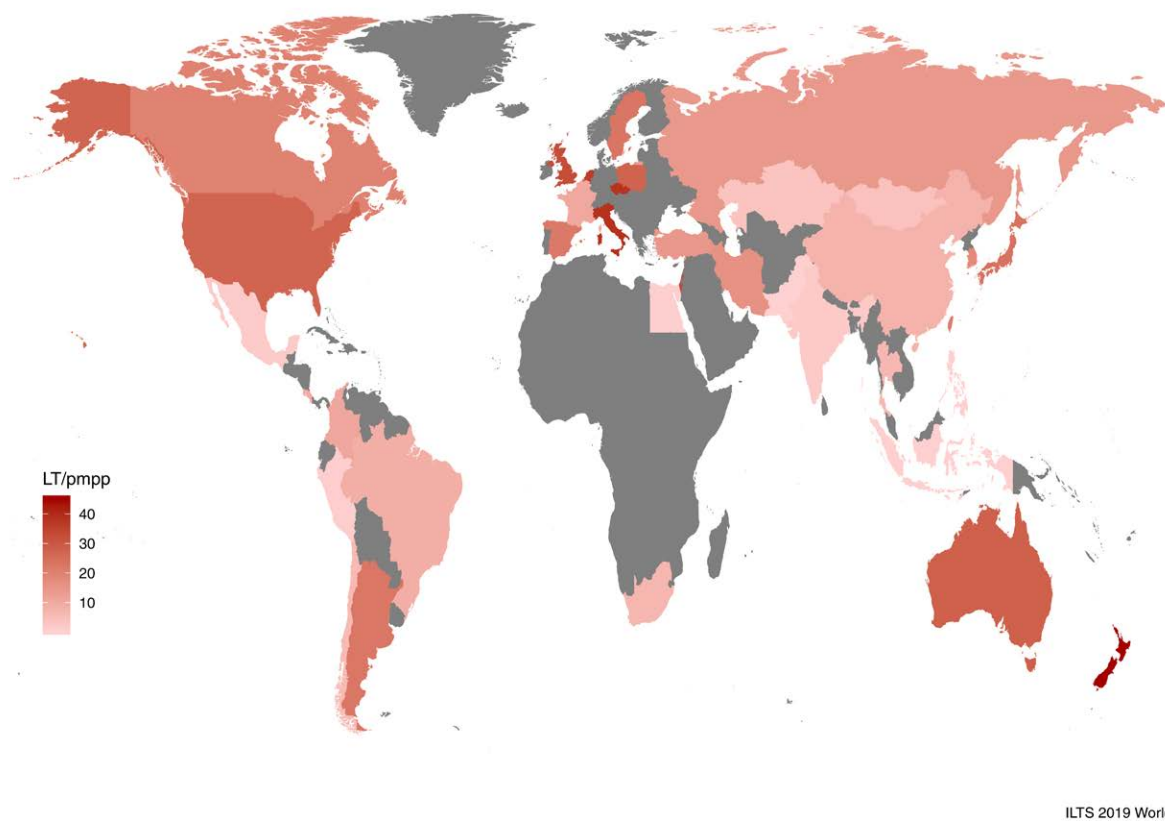


FIGURE 2. World heatmap for PLTs performed pmpp over the last 5 y. ILTS, International Liver Transplantation Society; PLT, pediatric liver transplant; pmpp, per million pediatric population.

may not transplant children weighing <10 kg. The Kasai procedure in BA needs to be performed within a narrow temporal window to be successful. In countries such as India with limited access to specialist pediatric care, most children would have crossed the cutoff age for the Kasai procedure by the time the diagnosis of biliary atresia is made and the child reaches a pediatric surgical specialist. Some of these children are then referred for liver transplantation (LT) after a variable period of time to an LT center. Most LT centers in India are in the private health sector and hence have the infrastructure and expertise. Unfortunately, many children would never be considered for LT because of social and financial reasons. This aspect has been highlighted in publications from India. Safwan et al and Mohan et al have reported primary LT for biliary atresia in 43.1% and 34%, respectively, in their PLT cohorts.^{17,26}

The concept of a liver transplant registry has been previously developed by other nations and societies; the largest published registries are briefly described as follows: The Organ Procurement and Transplantation Network first recorded a PLT on 1988 and has overseen 17 593 PLT to this date, with 49 reported active programs on the last annual report.^{20,27} The ELTR started collecting data on all liver transplants performed in 175 European centers since

1968. In its last published report, ELTR had performed 15 866 PLT >50 y, although its annual report did not mention how many of the 175 centers performed PLT.²² The Japanese Liver Transplantation Society Registry was initiated in 1992 and recently reported outcomes on >3200 PLTs performed in 67 centers since then, with 34 active programs in the last year (including adult programs).¹⁴ The SPLIT started as a multicenter registry in 1995, including centers from the United States and Canada; this registry was relaunched in 2011 and has enrolled 1911 PLT from 39 centers since then. In 2018, SPLIT changed its name and is now known as the Society of PLT, with three international sites outside of the United States and Canada, submitting limited patient data (Table 5).²³ All of which represent PLT centers from high-income countries. This is the first report which incorporates data from multiple lower-middle- and upper-middle-income countries. Furthermore, the majority of PLT included in this census were performed outside high-income countries (60.1% in the last year and 53.6% within the last 5 y). This finding is noteworthy because of the following:

(1) Most participating centers (61 of 108) are located in high-income countries; and (2) 31.2% of the programs from lower-middle-income countries have been active for >5 y, compared to only 1.6% of the high-income

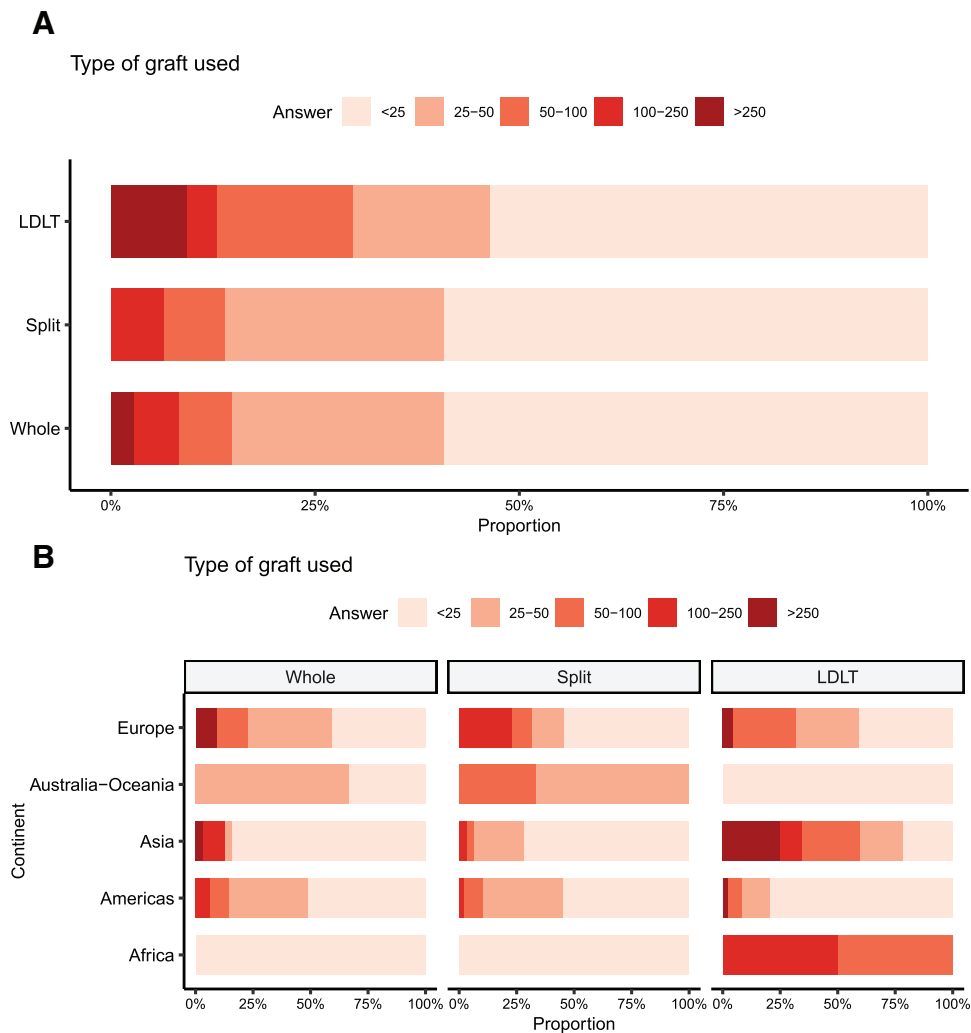


FIGURE 3. Type of graft and average number of PLT performed in the last 5 y. A, Worldwide and B, regional. PLT, pediatric liver transplantation.

TABLE 3.

Comparison of PLT volume between programs with and without training opportunities

Variable	Programs with training opportunities (n = 80)	Programs without training opportunities (n = 27)	P
LT last year, median (IQR)	17.5 (8.25–27.75)	6 (2–9)	<0.001
LT last 5 y, median (IQR)	75 (40–131.5)	30 (8–40)	<0.001

IQR, interquartile range; LT, liver transplantation; PLT, pediatric liver transplantation.

group. This underscores the important contributions of these centers and reveals the urgency to foster truly global collaborations. Ideally, already established international transplant societies such as ILTS, SPLIT, the Transplantation Society, and the International Pediatric Transplant Association would join to promote such potential collaborations.

The survey clearly demonstrated an essential difference in the practice of PLT across regions. Most transplants performed in high-income countries with established centers

are deceased donor liver transplants, mostly split/reduced grafts. The only exception to this observed trend is the North Central America region, where whole liver grafts from deceased donors are utilized more frequently, according to our results and previous reports.^{15,27} Conversely, centers located in lower-middle-income countries mostly perform LDLT. The utilization of living donors in lieu of deceased donors is multifactorial. Barriers to deceased donations in these countries include low public acceptance of deceased donations because of strong cultural beliefs. Developing a successful deceased donor program also depends on established healthcare infrastructure, extensive healthcare coverage for its population, and a mature system of organ allocation among others.²⁸ This is still not a reality in most of the middle-income countries where children are often referred during late stages of their disease and waiting for a deceased donor carries a high risk of mortality.^{28–30} LDLT is indeed a better option in these circumstances because the child can undergo timely surgery and the donor, usually a parent, undergoes a left lateral segmentectomy. Left lateral segment donation is associated with low morbidity and centers performing living donor PLT have gained good experience in performing the procedure safely.⁸

TABLE 4.**Comparison between lower-middle-income countries and high-income countries**

Variable	Lower-middle income (n = 16)	High income (n = 61)	P
First LT year, median (IQR)	2011 (2006.2–2014)	1990 (1985–1997.5)	<0.001
LT last year, median (IQR)	8 (2.7–23.7)	15 (7.5–25)	0.191
LT last 5 y, median (IQR)	27.5 (8.5–113.7)	71 (37.5–110.5)	0.023
Centers performing ≥ 25 LDLT over last 5 y, n (%)	11 (68.7%)	22 (36.0%)	0.019
Centers performing ≥ 25 WLT over last 5 y, n (%)	1 (6.2%)	32 (52.4%)	0.001
Centers performing ≥ 25 SLT/reduced over last 5 y, n (%)	1 (6.2%)	33 (53.2%)	<0.001
Centers with training opportunities, n (%)	12 (75%)	49 (80.3%)	0.977

IQR, interquartile range; LDLT, living donor liver transplantation; LT, liver transplantation; SLT, split-liver transplant; WLT, whole liver transplant.

TABLE 5.**Characteristics of major current registries collecting data regarding PLT**

Registry	Established (y)	Active pediatric transplant programs	Pediatric liver transplants (till date)	Government/society based
UNOS	1988	49	17 593	Nonprofit organization with government contract
SPLIT	1995	39	1911	Society
ELTR	1968	175 ^a	15 866	Society
JLTS	1992	34 ^a	3200	Society
KONOS	2000	22	1017	Government

^a Both adult and pediatric centers.

ELTR, European Liver Transplant Registry; JLTS, Japanese Liver Transplantation Society; KONOS, Center for Korean Network for Organ Sharing; PLT, pediatric liver transplantation; SPLIT, Society of Pediatric Liver Transplantation; UNOS, United Network for Organ Sharing.

Certainly, this study has some limitations, including those inherent to a survey. Selection bias is a potential problem for this study because high-volume centers with good outcomes might be more open to participation. In addition, although programs were sent an email invitation, personal communication was also needed in a significant number of them to encourage enrollment. Considering previous registries, this census was not exhaustive. Notwithstanding, outcome data were not included in the survey in order to promote participation, and 14.8% of the programs were low-volume centers (<5 PLT last year). Training opportunities were enquired, but details regarding specific training (ie, transplant surgery, hepatology, infectious diseases, etc.) were not collected and need to be addressed in future projects. The accuracy of the data is another limitation, as we cannot guarantee that medical records were consulted while answering the survey, and a majority of this self-reported data are impractical to verify. One additional limitation was the use of a new questionnaire that has not been previously validated in external cohorts. Finally, as a cross-sectional study, we were not able to identify changes over time, especially in the types of grafts used in each center. Legal modifications and cultural changes (eg, modern religious views have recently started to encourage organ donation in the context of a selfless act) may have an impact on donor and graft types.

In conclusion, this study corroborates that indications for PLT are similarly distributed worldwide, with biliary atresia, other cholestatic disorders, and metabolic disorders being the most frequent indications for PLT. In the same way, age and weight at the time of transplantation have a comparable pattern between the different regions around the globe; young (<12 mo) patients weighing <10 kg account for the majority of PLT performed. PLT requires high-level proficiency and cooperation between

hepatology, surgery, anesthesia, intensivists, infectious disease physicians, and paramedical personnel in the context of readily available hospital resources. As such, centers from high-income countries laid the groundwork in the early years. However, as the new era of global surgery begins, the 2030 sustainable development goals demand an effort to generate systemic solutions through broad international collaborations.^{30,31} This international collaboration between PLT centers can hopefully serve as a steppingstone for future development of PLT worldwide and also stimulate collaborative studies and research. We know that important centers, especially from Europe, were not able to send their data in a timely manner, so the census is planned to be repeated every 2 y, along with multisociety collaboration. New questions in terms of education, etiology, and study population will also be addressed. As a society, the importance of a formal world registry versus a registry that could capture data of countries that are not currently part of regional registries such as ELTR, SPLIT, or JLTR will also be assessed to eventually join forces aimed at helping children with liver disease around the world.

In the last decade, advancements in lower-middle and upper-middle income countries in the PLT have been impressive. Some centers from lower-middle-income countries have established adult programs and are planning to start PLT activities in the next few years. For the greater good of children with liver disease, we believe it is imperative that these centers share the lead in PLT. This report is a first step in understanding the need around the world and getting us closer to gathering data on how many children have access to this life-saving procedure.

Once this need is documented, it will be possible to determine how many children actually get listed and transplanted. These efforts should be followed by strategies to decrease waitlist mortality and improve global access.

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