Meta-analysis of donor–recipient gender profile in paediatric living donor liver transplantation

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ABSTRACT

Objective Paediatric living donor liver transplantation (LDLT) has gained popularity due to limited deceased donor organ supply. Some studies report inequalities in donor and recipient gender profiles, but data are sparse. We evaluated LDLT donor–recipient gender profiles, comparing country income categories and gender disparity level.

Design We performed a systematic review, searching PubMed, Embase and Cochrane databases for publications dated January 2006–September 2021. We included full-text English articles reporting gender in ≥40 universally sampled donor–recipient pairs. Search terms were permutations of 'liver transplant', 'living donor' and 'paediatric'. Countries were grouped as high/middle/low-income economies based on World Bank criteria and into groups based on deviation from gender parity in Gender Development Index (GDI) values (group 1 indicating closest to gender parity, group 5 indicating furthest). Proportions analysis with corresponding 95% CI were used for analysis of dichotomous variables, with significance when 95% CI did not cross 0.5. Data are reported as female proportion (%) and 95% CI.

Results Of 12 525 studies identified, 14 retrospective studies (12 countries; 6152 recipients and 6138 donors) fulfilled study inclusion criteria. Male recipient preponderance was seen in lower middle-income countries (all were also GDI group 5) (39.3 (95% CI 34.7 to 44.0)) and female recipient preponderance in GDI groups 1 and 3. Female donor preponderance was seen overall (57.4% (95% CI 55.1 to 59.6)), in middle income countries and in three of four GDI groups represented.

Conclusion There are significant imbalances in recipient-donor gender profiles in paediatric LDLT that are not well explained. The reasons for overall female donor preponderance across income tiers must be scrutinised.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ There are some studies in the published literature reporting gender inequalities among donors and recipients in solid organ transplantation.
⇒ Cultural and societal pressures are thought to be associated with healthcare access disparities between genders.
⇒ Data are sparse in paediatric living donor liver transplantation.

WHAT THIS STUDY ADDS

⇒ Male recipient preponderance was seen in lower middle-income countries (all of which were also Gender Development Index (GDI) group 5) and female recipient preponderance in GDI groups 1 and 3.
⇒ Female donor preponderance was seen overall, in middle-income countries, and in three of four GDI groups represented.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Differences in recipient–donor gender profile in paediatric living donor liver transplantation warrant further study to determine contributing factors.
⇒ Research and publication policies should mandate the reporting of sex to prevent gaps in data that may further entrench disparities.

INTRODUCTION

Since the success of paediatric living donor liver transplantation (LDLT) described by Strong *et al* in 1989, this technique has gained popularity in treating end-stage liver disease in children, particularly in settings with limited deceased donor organ supply.[1] According to a report from the Global Observatory on Donation and Transplantation, 35 784 liver transplants were done in 2019 alone, of which 21.3% consisted of living donor transplantation.[2]

LDLT acts as an alternative to cadaveric liver transplantation in many countries and has many reported benefits. Wait times for organs are shortened as donors are usually parents or relatives who are emotionally invested in the recipients' well-being. Surgeries are performed in a scheduled manner, which reduces the risks inherent in emergency transplantation, such as extended donor organ ischaemic time. Nevertheless, there are ethical issues specific to LDLT, including the small but important risk of donor complications, and subconscious emotional and social pressures donors may face.[3]

In addition, a growing number of reports in the published literature have described gender disparities in healthcare resources, particularly donor and recipient profiles for LDLT.[4] Macintyre and Hunt highlighted the importance of examining the correlation between socioeconomic status and

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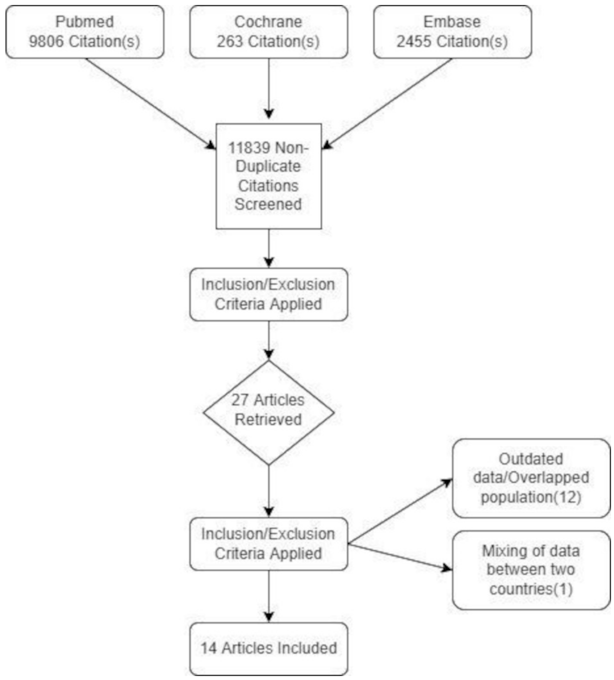

Figure 1 PRISMA diagram. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analyses.

gender disparity in order to understand the mechanism underlying this issue.[5]

In this study, we aimed to evaluate paediatric LDLT donor and recipient gender profiles. A secondary objective was to compare donor–recipient profiles among country income categories and between levels of gender disparity.

METHODS

Literature search

Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines were followed. We performed a systematic review, searching PubMed, Embase and Cochrane databases for publications dated January 2006–September 2021. Search terms used were permutations of 'liver transplant', 'living donor' and 'paediatric'. The reference lists of the full articles were also manually searched to identify additional eligible studies. All studies included in this meta-analysis were published in English.

Study selection and data extraction

Once the database search was completed, all duplicates were removed, and the titles/abstracts of the remaining studies were screened independently by two reviewers (ZYW and ZRL). Selected studies were assessed, and the following data were retrieved from each article and tabulated: first author, year of publication, study period and the gender for both donor and recipient of paediatric living related liver transplantation. If multiple studies drew patients from the same database, the largest one was selected for our review. The reviewers verified the selections and reached consensus at each stage of the screening process.

Inclusion criteria

Studies selected for our meta-analysis had to fulfil the following criteria:

1. Reported the sex for both donors and recipients.
2. Universally sampled data, that is, authors had to report all the patients in their series. For example, if studies reported only on the outcomes for a specific diagnosis, thereby excluding LDLT patients with a different diagnosis, these studies were removed from our analysis.
3. Written in the English language.
4. Published as a full paper in a journal, not as a meeting abstract or review.
5. Contained at least 40 pairs of LDLT paediatric donor–recipient pairs—this minimum sample size was set to improve the efficiency of the work without an appreciable loss of power and to minimise small study bias.

We defined 'paediatric' as patients aged below 18 years. Where studies included both adult and paediatric data, only the paediatric data were extracted and used for analysis.

We recognise that sex and gender, while not mutually exclusive, cannot be used interchangeably. Sex is a biological variable based on chromosomal assignment, while gender is a socially constructed variable that may differ according to the expectations of a given society. As such, we have amended the manuscript so that 'sex' is used where the term clearly refers to biological sex and have maintained the use of the term 'gender' otherwise. This is also in line with one of the key indices used in our data analysis, that is, the gender disparity index.

Exclusion criteria

The following criteria were used to exclude studies:

1. Studies in which it was not clear whether donors were deceased or living.
2. Overlapping studies from the same institution or registry.
3. Studies in which country of origin could not be clearly distinguished. For example, when data were combined from more than one country.

Categories and definitions

We used the following categories and definitions:

Income

Countries were classified into income tiers (high-income countries (HICs), upper middle-income countries (UMICs), lower middle-income countries (LMICs) and low-income countries (LICs)), using World Bank criteria, which is based on gross national income per capita.[6]

Gender disparity

We used Gender Development Index (GDI) grouping, which is based on calculation of disparities between both genders in health, education and economy, in the Human Development Report by the United Nations Development Programme.[7] The GDI categorises countries into five groups (groups 1–5) based on absolute deviation from gender parity. Countries in group 1 are closest in gender parity, while those in group 5 are furthest from gender parity.

Statistical analysis

Data were collected and pooled from non-overlapping studies. Heterogeneity was assessed using I^2; single-arm meta-analyses were performed using a fixed effect model for low heterogeneity and a random effects model for high heterogeneity. Female proportions were used as the base, and the corresponding 95% CIs were used for analysis of dichotomous variables, with significance when the 95% CI did not cross 0.5. Statistical analysis was performed using MedCalc Statistical Software (MedCalc

Table 1 Summary of studies included

Study	Countries	Period of study	Recipient sex ratio (F:M)	Donor sex ratio (F:M)	Income level	GDI group	Most common indication for transplantation (n (%))	
Darius 2014[22]	Belgium	July 1993–November 2010	95:108	109:94	High income	Group 2	Biliary atresia	132 (65)
Haseli 2013[23]	Iran	April 1999– March 2011	73:118	115:61	Lower middle income	Group 5	Cholestatic disease	81 (42)
Heaton 2008[24]	UK	October 1993–July 2006	17:33	23:27	High income	Group 2	Biliary atresia	23 (46)
Julka 2014[25]	Taiwan	March 2008– September 2010	40:47	49:38	High income	–	Biliary atresia	78 (90)
Kasahara 2021[26]	Japan	November 1989 and December 2018	1858:1413	1809:1462	High income	Group 1	Chronic liver disease	2332 (71)
Lee 2016[27]	Korea	January 2000–June 2014	82: 54	66:70	High income	Group 3	Biliary atresia	98 (72)
Li 2018[28]	China	January 2009– September 2015	123: 129	147:105	Upper middle income	Group 2	Biliary atresia	242 (96)
Mohan 2017[29]	India	September 2004–July 2016	80:120	121:77	Lower middle income	Group 5	Biliary atresia	72 (75)
Montenovo 2018[30]	USA	1 March 2002 and 31 December 2016	408:392	460:340	High income	Group 1	Cholestatic disease	502 (63)
Nikeghbalian 2009[31]	Iran	January 1997–March 2008	20:30	30:20	Lower middle income	Group 5	Wilson's disease	16%
Oh 2010[32]	Korea	1994–2006	64:49	70:46	High income	Group 3	Biliary atresia	70 (61)
Pan 2020[33]	China	October 2006– August 2016	287:257	333:211	Upper middle income	Group 2	Cholestatic disease	488 (90)
Tannuri 2011[34]	Brazil	June 1998– June 2010	72:49	73:48	Upper middle income	Group 1	Biliary atresia	81 (67)
Zhang 2018[35]	China	June 2013– August 2016	70:64	86:48	Upper middle income	Group 2	Biliary atresia	113 (84)

F, female; GDI, Gender Development Index; M, male.

Software Ltd, Ostend, Belgium). Our study was exempted from institutional board review, as it was a systematic review of published papers.

Assessment of methodological quality of included studies

All studies were retrospective observational clinical studies for which the Newcastle–Ottawa Scale (NOS) was used to assess their methodological quality. The NOS has a maximum score of nine stars. Any studies with a low risk of bias were allocated seven or more stars, those of moderate risk with four to six stars and those of high risk with three or less stars.

RESULT

Study characteristics

A total of 12 524 studies were identified based on our search strategy, and 685 duplicates were removed (figure 1). Twenty-seven studies were assessed; 13 studies were removed due to outdated data or when studies combined data from different countries. Thus, 14 retrospective studies (12 countries, total participants 12290) fulfilled our study inclusion criteria (table 1). World Bank Income Group Classification and GDI grouping were used in the analysis. All studies originated from high and middle-income countries. There were none from LICs. With regards to the GDI group, one study from Taiwan was excluded as there was no recent data on GDI, and no studies were from countries classified as GDI group 4. The studies included had low risk of bias when assessed according to the NOS (table 2).

Overall sex profiles for paediatric LDLT donors and recipients

A total of 6152 recipients and 6138 donors were included in our analysis. Overall, there was a significant female preponderance

Table 2 The Newcastle–Ottawa Scale for assessment of cohort studies

	Selection				Comparability	Outcome			
Studies	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts	Score
Darius 2014[22]	*	*	*	*	*	*	*	*	8
Haseli 2013[23]	*		*	*	*	*	*	*	7
Heaton 2008[24]	*		*	*	*	*	*	*	7
Julka 2014[25]	*	*	*	*	*	*	*	*	8
Kasahara 2021[26]	*	*	*	*	**	*	*	*	9
Lee 2016[27]	*	*	*	*	*	*	*	*	8
Li 2018[28]	*		*	*	*	*	*	*	7
Mohan 2017[29]	*	*	*	*	**	*	*	*	9
Montenovo 2018[30]	*		*	*	*	*	*	*	7
Nikeghbalian 2009[31]	*		*	*	*	*	*	*	7
Oh 2010[32]	*		*	*	*	*	*	*	7
Pan 2020[33]	*		*	*	**	*	*	*	8
Tannuri 2011[34]	*		*	*	*	*	*	*	7
Zhang 2018[35]	*	*	*	*	*	*	*	*	8

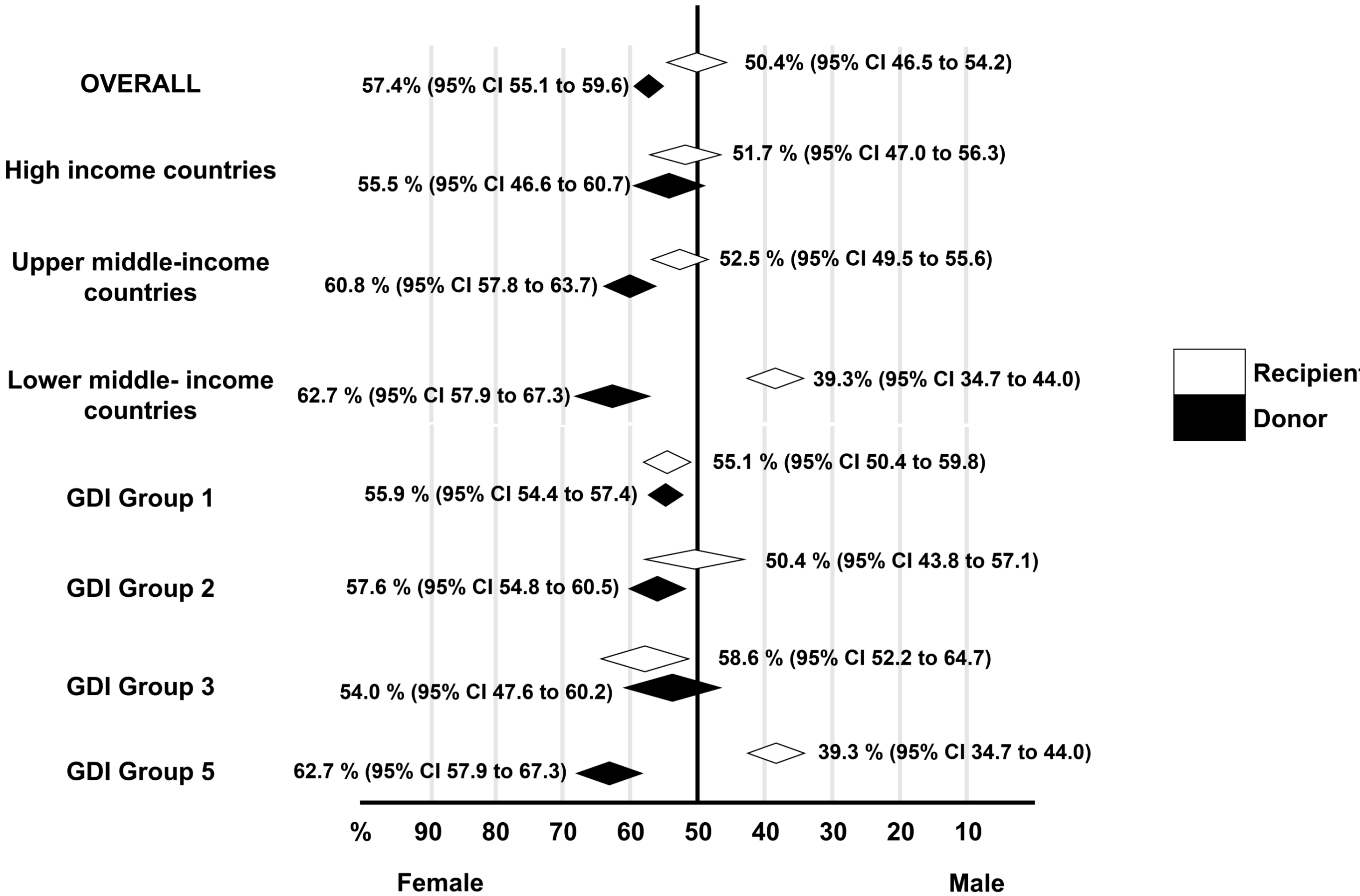

Figure 2 Summary measures and associated 95% CIs.

in paediatric LDLT donors (female proportion 57.6% (95% CI 55.1 to 59.6); I^2=46%) but no significant difference in sex profile among paediatric LDLT recipients (female proportion 50.4 (95% CI 46.5 to 54.2); I^2=84%) (figure 2, online supplemental eTable 1).

Country income level

Recipient

There was no significant difference in recipient sex profiles in both high-income tiers (female proportion 51.7 (95% CI 47.0 to 56.3); I^2=79%) and upper middle-income tiers (female proportion 52.5 (95% CI 49.5 to 55.6); I^2=20%) (figure 2). However, there was significant male preponderance in LMICs (female proportion 39.3 (95% CI 34.7 to 44.0); I^2=0%) (figure 2, online supplemental eTable 2).

Donor

There was no significant difference in donor sex profiles in HICs (female proportion 55.5% (95% CI 46.6 to 60.7) I^2=17%). Significantly more female donors were observed in both UMICs (female proportion 60.8 (95% CI 57.8 to 63.7); I^2=0%) and LMIC (female proportion 62.7 (95% CI 57.9 to 67.3); I^2=0%).

GDI groups

Recipient

Female preponderance was observed in recipients from countries in GDI group 1 (female proportion 55.1 (95% CI 50.4 to 59.8); I^2=79%) and group 3 (female proportion 58.6 (95% CI 52.2 to 64.7); I^2=0%). Conversely, male recipient preponderance was seen in GDI group 5 (female proportion 39.3 (95% CI 34.7 to 44.0); I^2=0%). No difference in gender was observed in GDI group 2 (female proportion 50.4 (95% CI 43.8 to 57.1); I^2=78%). There were no studies from countries classified as GDI group 4. All GDI group 5 countries were lower middle income countries (figure 2, online supplemental eTable 3).

Donor

A significantly higher proportion of female donors was seen in all except one of the GDI groups represented in the study, as follows: in GDI group 1 (female proportion 55.9 (95% CI 54.4 to 57.4); I^2=11%), in GDI group 2 (female proportion 57.6 (95% CI 54.8 to 60.5); I^2=53%) and in GDI group 5 (female proportion 62.7 (95% CI 57.9 to 67.3); I^2=0%). There was no difference seen in GDI group 3.

DISCUSSION

Our meta-analysis shows that there are gender imbalances in recipient–donor profile in paediatric LDLT, in which there is overall female donor preponderance, a pattern seen across income tiers and levels of gender disparity. Male recipient preponderance was seen in LMICs, all of which were also GDI group 5, while female recipient preponderance was seen in GDI groups 1 and 3.

In their study on the impact of socioeconomic position on women's health, O'Neil *et al*[8] stated that poverty and gender inequality are more likely to affect women in terms of healthcare access especially in early life. In the sphere of solid organ transplantation, many have observed gender disparities, with an abundance of data in kidney transplantation. Garg *et al*[9] showed that female patients of all ages who have end-stage renal failure are less likely to be considered as transplant candidates compared with their male counterparts. According to Bloembergen *et al*,[10] men are more likely to receive a renal transplant while women are more likely to donate their kidneys. Moreover, a multinational study revealed that it takes longer for a woman to be considered a kidney transplant candidate on initiation of renal replacement therapy.[11]

In a review in 2010, Hermann *et al*[12] reported on gender-specific differences in LDLT. Their study included both adult and paediatric patients and showed a male preponderance among recipients, with a more skewed ratio in Asia favouring male recipients compared with the USA and Europe. In addition, a 1.5:1 ratio was observed when they compared female donors to male donors. In our study, we did not compare gender ratios across geographical regions but chose to focus instead on income levels and gender disparity between countries.

We have some postulations regarding the female preponderance of donors seen in some of the countries in our study. It is possible that a higher incidence of comorbidities in the male population reduces their eligibility for consideration as living organ donors. It is also conceivable that human leucocyte antigen (HLA) type overlap for certain conditions renders female donors immunologically more suitable, although HLA typing is not routinely used in liver transplantation. Another potential cause is hypothesised by Thiel *et al*,[13] in that the caregiving role of women in a patriarchal society nudges them to volunteer as donors in preference to male relatives who are breadwinners for their families. This hypothesis may also explain the significantly higher proportion of male recipients in LMICs where male children may be viewed as sources of future income. Nevertheless, this may not explain the pattern of female donor preponderance in countries with high gender parity, suggesting that other factors are at play.

We acknowledge several limitations in our study. An important consideration is the sex differences inherently found in common causes of end-stage liver disease in children. For example, female children are more likely to suffer from biliary atresia, autoimmune hepatitis and primary biliary cholangitis, while diseases such as primary sclerosing cholangitis and viral hepatitis have a male predominance.[14–16] There are also different disease profiles seen across geographical regions. For example, biliary atresia, which is more common in females, and is the lead indication for paediatric liver transplantation, is up to 10 times more frequent in East and Southeast Asia than in Europe and the USA.[17] This higher incidence of hepatobiliary disease in females may explain the female recipient preponderance seen in GDI groups 1 and 3.

Another notable limitation in our study is the under-reporting of sex in publications that resulted in the exclusion of a large number of papers (74). Many have alluded to this phenomenon as the gendered nature of academic publishing, thus recommending the initiation and implementation of The Sex and Gender Equity in Research guidelines.[12 18] Leslie *et al*[19] stated that only two-fifths of publications in the field of anaesthesia report gender of participants; the male gender is emphasised while none mention transgender or differences of sex development. This gender bias in academic publishing is also seen in authorship and publication, where gender is more likely to be reported if the paper has a female first and last author, while sex-related articles are associated with lower journal impact factor.[20]

We could not find any studies reporting outcomes from LICs, and this likely reflects the resource intensive nature of solid organ transplantation in general, with LICs preferentially allocating precious healthcare resources to more pressing disease conditions with wider public health impact. All the studies included were retrospective studies and might not be representative of the wider national population case profile. Some studies were from the same country, and this might have led to additional weightage towards factors such as income tier, although there was no overlap in patient data. The use of GDI grouping might have led to overgeneralisation as there exist regional variations in healthcare resources, disease profile and socioeconomic status within the same country. Finally, transplant tourism, which is likely to be grossly underestimated and is known to take place to some degree in at least four of the countries in our review, further confounds accurate data analysis.[21]

Notwithstanding these limitations, our study is the first systematic review and meta-analysis of gender distribution in donors and recipients in paediatric LDLT. Our results highlight the need for further studies regarding detailed epidemiological data on underlying diseases in paediatric LDLT that could clarify the link between liver pathology and donor–recipient gender profiles. Importantly, there must be further research on the role of both explicit and unconscious cultural and societal pressures driving gender-related discrepancies in donors and recipients.

CONCLUSION

There are gender differences in recipient–donor profile in paediatric LDLT that are not well explained. The reasons for overall female donor preponderance and male recipient preponderance in LMICs must be scrutinised.

Contributors ZYW and SAN had full access to all of the data in the study and take responsibility for the integrity of the data and accuracy of the data analysis. Study concept and design (ZYW and SAN); acquisition of the data (ZYW and ZRL); analysis and interpretation of the data (ZYW, ZRL, YC and MD); drafting of the manuscript (SAN, ZYW and ZRL); critical revision of the manuscript for important intellectual content (SAN, YC and MD); study supervision (SAN). SAN accepts 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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Patient consent for publication Not applicable.

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eTable 1: Summary of donor and recipient female proportion and sample size

Study	Country	Recipient		Donor	
		N (total)	Female Proportion (%) (95% CI)	N (total)	Female Proportion (%) (95% CI)
Darius 2014[8]	Belgium	203	46.8 (39.8 to 53.9)	203	53.7 (46.6 to 60.7)
Haseli 2013[9]	Iran	191	38.2 (31.3 to 45.5)	176	65.3 (57.8 to 72.3)
Heaton 2008[10]	United Kingdom	50	34.0 (21.2 to 48.8)	50	46.0 (31.8 to 60.7)
Julka 2014[11]	Taiwan	87	46.0 (35.2 to 57.0)	87	56.3 (45.3 to 66.9)
Kasahara 2021[12]	Japan	3271	56.8 (55.1 to 58.5)	3271	55.3 (53.6 to 57.0)
Lee 2016[13]	Korea	136	60.3 (51.6 to 68.6)	136	48.5 (39.9 to 57.3)
Li 2018[14]	China	252	48.8 (42.5 to 55.2)	252	58.3 (52.0 to 64.5)
Mohan 2017[15]	India	200	40.0 (33.2 to 47.2)	198	61.1 (53.9 to 67.9)
Montenovo 2018[16]	United States	800	51.0 (47.5 to 54.5)	800	57.5 (54.0 to 61.0)
Nikeghbalian 2009[17]	Iran	50	40.0 (26.4 to 54.8)	50	60.0 (45.2 to 73.6)
Oh 2010[18]	Korea	113	56.6 (47.0 to 65.9)	116	60.4 (50.8 to 69.3)
Pan 2020[19]	China	544	52.8 (48.5 to 57.0)	544	61.2 (57.0 to 65.3)

Tannuri 2011[20]	Brazil	121	59.5 (50.2 to 68.3)	121	60.3 (51.0 to 69.1)
Zhang 2018[21]	China	134	64.2 (55.4 to 72.3)	134	52.2 (43.4 to 61.0)
Total		6152	50.4 (46.5 to 54.2)	6138	57.4 (55.1 to 59.6)
I^2 (p-value for heterogeneity)		84%, p<0.0001; random effects model		46%, p=0.0322; random effects model	

eTable 2: Summary of subgroup analysis according to country income

Income	Study	Recipient		Donor	
		N (total)	Female Proportion (%) (95% CI)	N (total)	Female Proportion (%) (95% CI)
High-income countries	Darius 2014[8]	203	46.8 (39.8 to 53.9)	203	53.7 (46.6 to 60.7)
	Heaton 2008[10]	50	34.0 (21.2 to 48.8)	50	46.0 (31.8 to 60.7)
	Julka 2014[11]	87	46.0 (35.2 to 57.0)	87	56.3 (45.3 to 67.0)
	Kasahara 2021[12]	3271	56.8 (55.1 to 58.5)	3271	55.3 (53.6 to 57.0)
	Lee 2016[13]	136	60.3 (51.6 to 68.6)	136	48.5 (39.9 to 57.3)
	Montenovo 2018[16]	800	51.0 (47.5 to 54.5)	800	57.5 (54.0 to 61.0)
	Oh 2010[18]	113	56.6 (47.0 to 65.9)	116	60.4 (50.8 to 69.3)
	Total	4660	51.7 (47.0 to 56.3)	4663	55.5 (46.6 to 60.7)
	I^2 (p-value for heterogeneity)	79%, P = 0.0001; random effects model		17%, P = 0.3028; fixed effects model	
Upper middle income countries	Li 2018[14]	252	48.8 (42.5 to 55.2)	252	58.3 (52.0 to 64.5)
	Pan 2020[19]	544	52.8 (48.5 to 57.0)	544	61.2 (57.0 to 65.3)
	Tannuri 2011[20]	121	59.5 (50.2 to 68.3)	121	60.3 (51.0 to 69.1)
	Zhang 2018[21]	134	52.2 (43.4 to 60.9)	134	64.2 (55.4 to 72.3)
	Total	1051	52.5 (49.5 to 55.6)	1051	60.8 (57.8 to 63.7)
	I^2 (p-value for heterogeneity)	20%, P = 0.2871; fixed effects model		0%, P = 0.7234; fixed effects model	
Lower middle	Haseli 2013[9]	191	38.2 (31.3 to 45.5)	176	65.3 (57.8 to 72.3)
	Mohan 2017[15]	200	40.0 (33.2 to 47.2)	198	61.1 (53.9 to 67.9)

income countries	Nikeghbalian 2009[17]	50	40.0 (26.4 to 54.8)	50	60.0 (45.2 to 73.6)
	Total	441	39.3 (34.7 to 44.0)	424	62.7 (57.9 to 67.3)
	I^2 (p-value for heterogeneity)	0%, P = 0.9286; fixed effects model		0%, P = 0.6347; fixed effects model	

eTable 3: Summary of subgroup analysis according to Gender Disparity Index (GDI) grouping

Income	Study	Recipient		Donor	
		N (total)	Female Proportion (%) (95% CI)	N (total)	Female Proportion (%) (95% CI)
GDI Group 1	Kasahara 2021[12]	3271	56.8 (55.1 to 58.5)	3271	55.3 (53.6 to 57.0)
	Montenovo 2018[16]	800	51.0 (47.5 to 54.5)	800	57.5 (54.0 to 61.0)
	Tannuri 2011[20]	121	59.5 (50.2 to 68.3)	121	60.3 (51.0 to 69.1)
	Total	4192	55.1 (50.4 to 59.8)	4192	55.9 (54.4 to 57.4)
	I^2 (p-value for heterogeneity)	79%, P = 0.0090; random effects model		11%, P = 0.3257; fixed effects model	
GDI Group 2	Darius 2014[8]	203	46.8 (39.8 to 53.9)	203	53.7 (46.6 to 60.7)
	Heaton 2008[10]	50	34.0 (21.2 to 48.8)	50	46.0 (31.8 to 60.7)
	Li 2018[14]	252	48.8 (42.5 to 55.2)	252	58.3 (52.0 to 64.5)
	Pan 2020[19]	544	52.8 (48.5 to 57.0)	544	61.2 (57.0 to 65.3)
	Zhang 2018[21]	134	52.2 (43.4 to 60.9)	134	64.2 (55.4 to 72.3)
	Total	1183	50.4 (43.8 to 57.1)	1183	57.6 (54.8 to 60.5)
	I^2 (p-value for heterogeneity)	78%, P = 0.0013; random effects model		53%, P = 0.0736; fixed effects model	
GDI Group 3	Lee 2016[13]	136	60.3 (51.6 to 68.6)	136	48.5 (39.9 to 57.3)
	Oh 2010[18]	113	56.6 (47.0 to 65.9)	116	60.4 (50.8 to 69.3)
	Total	249	58.6 (52.2 to 64.7)	252	54.0 (47.6 to 60.2)

	I^2 (p-value for heterogeneity)	0%, P = 0.5601; fixed effects model		72%, P = 0.0610; fixed effects model	
GDI Group 5	Haseli 2013[9]	191	38.2 (31.3 to 45.5)	176	65.3 (57.8 to 72.3)
	Mohan 2017[15]	200	40.0 (33.2 to 47.2)	198	61.1 (53.9 to 67.9)
	Nikeghbalian 2009[17]	50	40.0 (26.4 to 54.8)	50	60.0 (45.2 to 73.6)
	Total	441	39.3 (34.7 to 44.0)	424	62.7 (57.9 to 67.3)
	I^2 (p-value for heterogeneity)	0%, P = 0.9286; fixed effects model		0%, P = 0.6347; fixed effects model	