Meta-analysis

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Pregnancy outcomes in renal transplant recipients: A systematic review and meta-analysis

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Abstract

Background: Kidney transplantation is a superior treatment for end-stage renal disease (ESRD), compared with hemodialysis, offering better quality of life and birth outcomes in women with ESRD and lower fertility rates.

Objectives: To investigate the pregnancy, maternal, fetal, and graft outcomes following kidney transplantation in women with ESRD and evaluate the improvements in quality of life and associated risks.

Design: A systematic review and meta-analysis performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses and the Meta-analysis of Observational Studies in Epidemiology guidelines.

Data Sources and Methods: A thorough search of multiple databases, including PubMed, Embase, Scopus, ATC abstracts, and Cochrane Central Register of Controlled Trials, was conducted to identify studies that analyzed pregnancy outcomes in kidney transplant patients. The search was conducted from the inception of each database to January 2023.

Results: The study reviewed 109 studies that evaluated 7708 pregnancies in 5107 women who had undergone renal transplantation. Of these, 78.48% resulted in live births, 9.68% had induced abortion, and 68.67% had a cesarean section. Miscarriage occurred in 12.54%, preeclampsia in 20.87%, pregnancy-induced hypertension in 24.30%, gestational diabetes in 5.08%, and preterm delivery in 45.30% of cases. Of the 853 recipients, 123 had graft loss after pregnancy and 8.06% suffered acute rejection.

Conclusion: Pregnancy after kidney transplantation is associated with risks for mother and fetus; however, live births are still possible. In addition, there are reduced overall risks of stillbirths, miscarriages, neonatal deaths, and gestational diabetes.

Registration: PROSPERO (CRD42024541659).

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Keywords
pregnancy, renal transplant, live births, neonatal mortality, graft outcomes, preeclampsia

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Introduction

Kidney transplantation, compared with hemodialysis, has significantly improved the quality of life of patients with end-stage renal disease (ESRD).[1] However, women of childbearing age (18–49 years) with ESRD have significantly lower fertility rates than do healthy women; besides, they have an increased risk of adverse pregnancy outcomes, such as preeclampsia, intrauterine growth restriction, preterm birth, and a decline in renal function.[2,3] Therefore, renal transplantation is crucial for improving the prognosis and maternal and fetal outcomes in pregnant women with ESRD; in addition, it increases the rate of fertility in non-pregnant women owing to the rapid restoration of hormonal function.[2] Successful pregnancies have been reported in kidney transplant recipients since 1958, offering hope to those who wish to conceive.[4]

Pregnancies in kidney transplant recipients are considered to have a better prognosis, compared with pregnancies in dialysis patients[1]; however, such pregnancies pose challenges, including adverse maternal and fetal outcomes, such as preeclampsia, gestational diabetes, fetal growth restriction, preterm birth, and a high incidence of cesarean section. Exposure to immunosuppressants increases the chances of congenital disabilities in the unborn child, necessitating rigorous antenatal care and monitoring.[5,6] Kidney transplantation is a common treatment option for women of childbearing age with ESRD; however, the limited availability of high-quality data has made it challenging to guide clinical decision making and support pregnant patients with kidney transplants. The increasing occurrence of such pregnancies in recent decades poses escalating challenges for nephrologists and obstetricians. Moreover, there is a paucity of literature, specifically panoptic meta-analyses, addressing the effects of renal transplantation on pregnancy, thus underscoring the need for further investigation. To address this gap, we aimed to conduct a systematic review and meta-analysis to provide a comprehensive overview of post-kidney transplantation pregnancy outcomes.

Methods

Data sources and search strategy

We conducted a systematic review and meta-analysis following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and Meta-analysis of Observational Studies in Epidemiology guidelines[7,8] to assess pregnancy outcomes in women older than >18 years who underwent kidney transplantation. This review was registered in the International Prospective Register of Systematic Reviews (PROSPERO; registration number CRD42024541659). We conducted a comprehensive search of several databases, such as PubMed, Embase, Scopus, ATC abstracts, and the Cochrane Central Register of Controlled Trials, spanning from inception of the database till January 2023. Our search strategy incorporated relevant Medical Subject Headings terms and pertinent keywords associated with pregnancy outcomes and kidney transplantation. The PubMed search string is provided in Supplemental File 1.

Study selection

All articles identified through the systematic search were exported to EndNote reference library version 20 (Clarivate Analytics, (US), LLC), where duplicates were removed. We included observational studies (prospective cohort, cross-sectional, and retrospective cohort studies), case series, and case reports (with >10 pregnancies) that assessed pregnancy, maternal, and fetal outcomes in women of reproductive age (>18 years of age) who had undergone kidney transplantation. Studies on patients with multiple organ transplants, studies that examined the teratogenic effects of sirolimus or mycophenolate, and non-English publications were excluded. Two investigators (MSM and FJ) independently reviewed the titles and abstracts of the identified studies. If eligibility could not be determined from the abstract, a full-text review was conducted. Any discrepancies were resolved by a third independent investigator (AAR).

Data extraction and quality assessment

Data extraction and quality assessment were performed by three authors (MUS, SR, and AAR) according to established protocols. All three authors verified the accuracy of the data, and any discrepancies were addressed through consultation with a fourth team member (MSM). The location, length, and duration of the study, the number of recipients of kidney transplants, number of pregnancies, mean maternal age, and mean time between kidney transplant and pregnancy were included in the extracted data. In addition, the number of live births, miscarriages, induced abortions, stillbirths, and ectopic pregnancies were included in the pregnancy outcomes. The following data were also included: the number of women with preeclampsia, gestational diabetes mellitus, and cesarean sections; the number

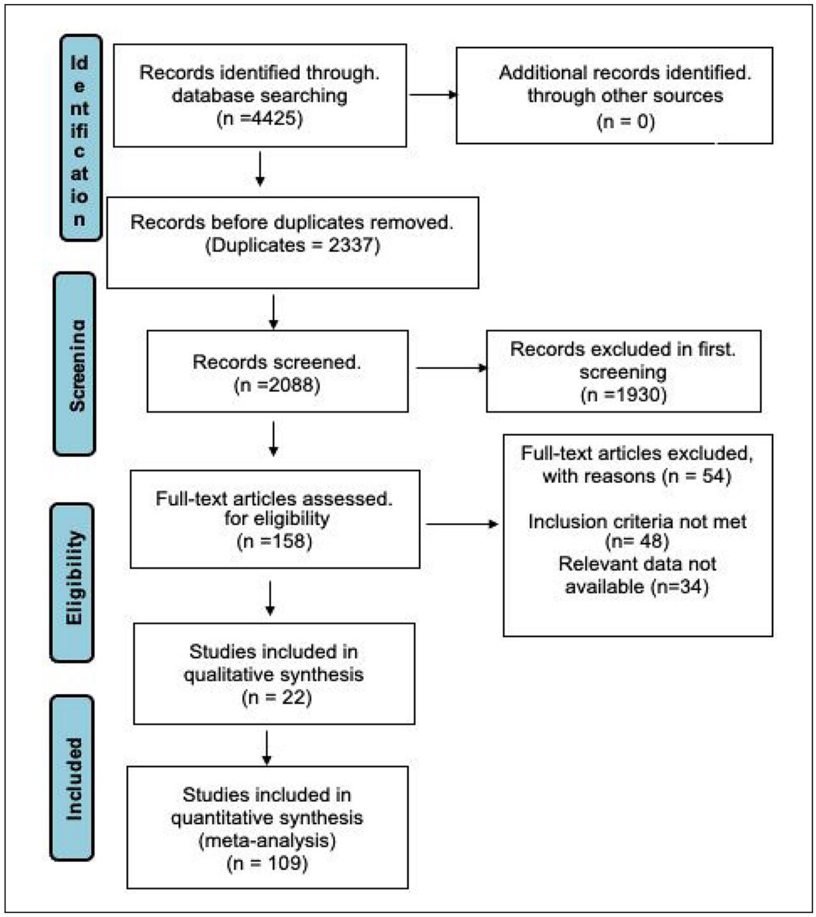

Figure 1. PRISMA flow chart summarizing the systematic review process according to PRISMA guidelines, showing the number of records identified, screened, assessed for eligibility, and included in the systematic review and meta-analysis.
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

of preterm births, mean gestational age, mean gestational weight, and number of neonatal deaths; and the number of graft failures and acute rejection episodes during and after pregnancy. The number of pregnancies was used as the denominator for outcomes, such as live births, miscarriages, induced abortions, stillbirths, ectopic pregnancy, preeclampsia, pregnancy-induced hypertension (PIH), and gestational diabetes mellitus, to guarantee uniformity of the collected data. However, the denominator for preterm delivery, cesarean section, and neonatal mortality was the count of live births. For acute rejection, the denominator was the total number of recipients. A live delivery before 37 weeks of gestation was considered preterm.

Statistical analysis/meta-analysis

The study presented patients' demographic parameters as frequencies and expressed pregnancy incidence as the proportion of women per 1000 live births. Prevalence with 95% confidence intervals (CIs) was used to demonstrate each included study's estimates, and a random-effects model was used to pool the data from individual studies. The Higgins I^2 statistic value was used for heterogeneity evaluation, and a value of >50% was considered significant. For binary outcomes, the Der Simonian and Laird approach was applied; for continuous outcomes, the weighted average methodology was used to compute the pooled estimates and 95% CIs. Furthermore, the study investigated the association between maternal age, the gap between kidney transplants and pregnancy, and pregnancy success. It also offered incidents per 100 observations for continuous outcomes. A location-based subgroup analysis of the pregnancy, maternal, and fetal outcomes was performed. R meta package was used for the analyses. In addition, we conducted a sensitivity analysis using leave-one-out analysis to identify the trials causing significant heterogeneity.

Results

Of the 4425 articles that were retrieved, 2088 full-text articles were reviewed, and 109 were eventually selected for inclusion in the final study,[9–116] as shown in the PRISMA flow diagram (Figure 1). The total number of pregnancies was 7728 in

Table 1. Baseline characteristics of included studies.

Author/study name	Year	Country	Years of data collection	Total number of kidney transplant recipients	Total number of pregnancies
Gosselink et al. (2022)[9]	2022	Netherland	1971–2017	192	288
Devresse et al. (2022)[10]	2022	Belgium	1994–2010	32	57
Schwarz et al. (2022)[11]	2022	Germany	1972–2009	67	92
Dines et al. (2021)[12]	2021	USA	1996–2014	25	52
Puthenveettil et al. (2021)[13]	2021	India	2011–2017	20	20
Mira et al. (2021)[14]	2021	Portugal	1989–2019	34	41
Turgut et al. (2021)[15]	2021	Turkey	2010–2019	20	20
Akcay et al. (2021)[16]	2021	Turkey	2001–2017	18	29
Kovač et al. (2021)[17]	2020	Slovenia	1970–2016	18	22
Dębska-Ślizień et al. (2020)[18]	2020	Poland	1987–2018	26	31
Madazlı et al. (2020)[19]	2020	Turkey	2010–2018	32	32
Ying et al. (2020)[20]	2020	China	2000–2017	11	11
Golocan-Alquiza et al. (2019)[21]	2019	Philippines	2001–2016	32	38
Hortu et al. (2019)[22]	2019	Turkey	1995–2017	51	52
Mariano et al. (2019)[23]	2019	Brazil	1995–2017	22	19
Ozban et al. (2019)[24]	2019	Turkey	2006–2018	5	6
Tebet et al. (2019)[25]	2019	Brazil	2014–2016	43	43
Mohamed Hassan et al. (2018)[26]	2018	Egypt	N/A	44	44
Amine et al. (2017)[27]	2017	Tunisia	1992–2011	12	17
Mohammadi et al. (2017)[28]	2017	Australia	1976–2015	35	56
Itabashi et al. (2017)[29]	2017	Japan	1983–2015	26	34
Kihara et al. (2018)[30]	2018	Japan	1985–2016	7	7
Songin et al. (2014)[31]	2014	Poland	1999–2011	37	43
Piccoli et al. (2017)[1]	2017	Italy	2000–2014	121	121
Yuksel et al. (2017)[32]	2017	Turkey	2009–2016	25	25
Ajaimy et al. (2016)[33]	2016	USA	2009–2014	11	11
Candido et al. (2016)[34]	2016	Portugal	2004–2014	36	53
Cristelli et al. (2016)[35]	2016	Brazil	2004–2014	36	53
El Houssni et al. (2016)[36]	2016	Saudi Arabia	1998–2012	12	21
Lima et al. (2016)[37]	2016	Brazil	2004–2014	36	53
Majak et al. (2016)[38]	2016	Norway	1969–2013	119	119
Mishra et al. (2016)[39]	2016	India	2004–2014	16	16
Orihuela et al. (2016)[40]	2016	Uruguay	1986–2014	32	40
Piccoli et al. (2016)[41]	2016	Italy	1978–2013	N/A	189
Saliem et al. (2016)[42]	2016	Canada	2006–2011	N/A	264
Santos et al. (2016)[43]	2016	Portugal	2010–2014	8	8
Sarween et al. (2016)[44]	2016	UK	2001–2015	387	569
Stoumpos et al. (2016)[45]	2016	UK	1973–2013	89	138
Yoshikawa et al. (2016)[46]	2016	Japan	N/A	49	65
Aktrurk et al. (2015)[47]	2015	Turkey	2004–2014	12	16
Arab et al. (2015)[48]	2015	Canada	2003–2010	N/A	275
Erman et al. (2015)[49]	2015	Turkey	1987–2011	43	43
Yeon et al. (2015)[50]	2015	Korea	1995–2015	84	119
Debska-Slizien et al. (2014)[51]	2014	Poland	1980–2012	17	22
Farr et al. (2014)[52]	2014	Austria	1999–2013	12	12
Hebral et al. (2014)[53]	2014	France	1969–2011	46	61
You et al. (2014)[54]	2014	Korea	1995–2013	29	41
Blume et al. (2013)[55]	2013	Germany	1988–2010	34	53
Guella et al. (2013)[56]	2013	Saudi Arabia	1992–2008	15	33
Rachdi et al. (2013)[57]	2013	Tunisia	2003–2013	12	17
Ribeiro et al. (2013)[58]	2013	Brazil	1995–2007	22	31

(Continued)

Table 1. (Continued)

Author/study name	Year	Country	Years of data collection	Total number of kidney transplant recipients	Total number of pregnancies
Rocha et al. (2013)[59]	2013	Portugal	1983–2009	24	24
Wyld et al. (2013)[60]	2013	Australia	1971–2010	447	692
Kennedy et al. (2012)[61]	2012	Ireland	—	18	29
Neyatani et al. (2012)[62]	2012	Japan	1975–2011	22	34
Van Buren et al. (2012)[63]	2012	Netherlands	1971–2010	30	42
Celik et al. (2011)[64]	2011	Turkey	1998–2008	24	31
Gerlei et al. (2011)[65]	2011	Hungary	1974–2010	23	25
Lopez et al. (2011)[66]	2011	Spain	1986–2010	20	24
Xu et al. (2011)[67]	2011	China	1989–2008	25	38
Gorgulu et al. (2010)[68]	2010	Turkey	1983–2008	19	22
Areia et al. (2009)[69]	2009	Portugal	1989–2007	28	34
Gill et al. (2009)[70]	2009	USA	1990–2003	483	530
Levidiotis et al. (2009)[71]	2009	Australia	1966–2005	381	577
Rizvi et al. (2009)[72]	2009	Pakistan	1985–2008	N/A	72
Sharma et al. (2009)[73]	2009	Oman	1988–2006	42	82
Al Duraihimh et al. (2008)[74]	2008	Middle East	1996–2006	140	234
Alfi et al. (2008)[75]	2008	Saudi Arabia	1989–2005	12	20
Cruz Lemini et al. (2007)[76]	2007	Mexico	1990–2005	60	75
Oliveira et al. (2007)[77]	2007	Brazil	2001–2005	52	52
Sibanda et al. (2007)[78]	2007	UK	1994–2001	176	193
Yassaee et al. (2007)[79]	2007	Iran	1996–2001	74	95
Kurata et al. (2006)[80]	2006	Japan	1984–2003	42	53
Rahamimov et al. (2006)[81]	2006	Israel	1983–1998	39	69
Galdo et al. (2005)[82]	2005	Chile	1982–2002	30	37
Garcia-Donaire et al. (2005)[83]	2005	Spain	1997–2004	16	19
Ghanem et al. (2005)[84]	2005	Egypt	1989–2004	41	67
Pour-Reza-Gholi et al. (2005)[85]	2005	Iran	1984–2004	60	74
Yildirim et al. (2005)[85]	2005	Turkey	1998–2005	17	20
Keitel et al. (2004)[87]	2004	Brazil	1977–2001	41	44
Pezeshki et al. (2004)[88]	2004	Iran	1991–1998	18	20
Hooi et al. (2003)[89]	2003	Malaysia	1984–2001	46	72
Queipo et al. (2003)[90]	2003	Spain	1980–2000	29	40
Thompson et al. (2003)[91]	2003	UK	1976–2001	24	48
Sgro et al. (2002)[92]	2002	Canada	1988–1998	26	44
Tan et al. (2002)[93]	2002	Singapore	1986–2000	25	42
Park et al. (2001)[94]	2001	South Korea	N/A–2000	36	47
Kuvacic et al. (2000)[95]	2000	Croatia	1986–1996	15	23
Little et al. (2000)[96]	2000	Ireland	1985–1998	19	29
Moon et al. (2000)[97]	2000	Korea	N/A–1998	36	48
Ventura et al. (2000)[98]	2000	Portugal	1983–1999	15	15
Arsan et al. (1997)[99]	1997	France	N/A	20	33
Rahbar et al. (1997)[100]	1997	Iran	1985–1993	13	14
Rieu et al. (1997)[101]	1997	France	1970–1995	22	33
Al Hassani et al. (1995)[102]	1995	Oman	1985–1993	25	44
Sabagh et al. (1995)[103]	1995	Saudi Arabia	1984–1994	33	52
Saber et al. (1995)[104]	1995	Brazil	1968–1992	19	25
Wong et al. (1995)[105]	1995	New Zealand	1972–1992	9	16
Hadi et al. (1986)[106]	1986	South Korea	1969–1992	11	17
Talaat et al. (1994)[107]	1994	Sweden	1977–1992	19	25
Pahl et al. (1993)[108]	1993	USA	1969–1990	21	32

(Continued)

Table 1. (Continued)

Author/study name	Year	Country	Years of data collection	Total number of kidney transplant recipients	Total number of pregnancies
Muirhead et al. (1992)[109]	1992	UK	1977–1988	22	22
Brown et al. (1991)[110]	1991	Ireland	1965–1989	14	27
Sturgiss et al. (1991)[111]	1991	UK	1967–1987	17	22
O'Connell et al. (1989)[112]	1989	Australia	1974–1986	11	18
Ha et al. (1994)[113]	1994	Korea	1970–1982	11	13
Marushak et al. (1986)[114]	1986	Denmark	1972–1983	20	24
O'Donnell et al. (1985)[115]	1985	South Africa	1971–1984	21	38
Waltzer et al. (1980)[116]	1980	USA	N/A	12	15

N/A: not applicable.

Table 2. Maternal demographics, pregnancy outcomes, obstetric complications and delivery outcomes among kidney transplant recipients.

Demographic/Outcome	Statistics/Results	95% confidence interval
Number of papers	109	
Number of pregnancies	7728	
Number of recipients	5107	
Mean maternal age (years)[a]	30.31 ± 3.21	
Mean interval from transplant to pregnancy	5.6 ± 1.95 years	
Pregnancy outcomes		
Live birth	78.48%	75.48–81.49
Induced abortion	9.68%	7.67–11.69
Miscarriages	12.54%	10.61–14.47
Still birth	3.06%	2.35–3.77
Cesarean section	68.67%	63.95–73.39
Ectopic pregnancies	0.94%	0.12–1.77
Maternal outcomes		
Preeclampsia	20.87%	18.25–23.48
Pregnancy-induced hypertension	24.30%	18.40–30.20
Gestational diabetes	5.08%	3.61–6.55
Fetal outcomes		
Preterm delivery	45.30%	41.26–49.34
Neonatal mortality	1.50%	0.87–2.13
Mean gestation time (weeks)[a]	34.35 ± 2.36	
Mean birth weight (g)[a]	2387.79 ± 241.67	
Graft outcomes		
Acute rejection	8.06%	5.61–10.51
Mean creatinine before pregnancy (mg/dL)	1.16 ± 0.16	
Mean creatinine after pregnancy(mg/dL)	1.36 ± 0.18	
Graft loss post-pregnancy (out of 19 Studies, 853 recipients)	123 cases (14.42%)	

[a]Reported in mean ± standard deviation. Remaining outcomes reported in rates in percentage.

5107 transplant recipients. The mean maternal age was 30.3 ± 3.21 years, and the mean interval from transplant to pregnancy was 5.6 ± 1.95 years. Baseline characteristics of the included studies are presented in Table 1. Maternal demographics and pregnancy, maternal, and fetal outcomes are presented in Table 2. Forty-one studies conducted in Asia, 5 in Africa, 39 in Europe, 9 in South America, 10 in North America, and 5 in Oceania were included (Table 3).

Table 3. Number of studies according to region.

Asia	41 studies
Africa	5 studies
Europe	39 studies
South America	9 studies
North America	10 studies
Oceania	5 Studies

Pregnancy outcomes

The total number of events reported was 5974, of which live births comprised 78.48% ($n=4505$; 95% CI, 75.48–81.49), which was higher than the percentage in the United States (US) general population (56.6%)[117] and was favorable across all geographic locations. The percentage of induced abortions was 9.68% ($n=567$; 95% CI, 7.67–11.69) and that of miscarriages was 12.54% ($n=688$; 95% CI, 10.61–14.47), both of which were lower than those in the US general population (24.8% and 19.8%, respectively).[118] The rate of stillbirths was 3.06% ($n=189$; 95% CI, 2.35–3.77), which was lower than that in the US general population (5.74%).[119] Ectopic pregnancies were reported in 0.94% ($n=25$; 95% CI, 0.12–1.77) of transplant recipients, which was lower than that in the US general population (1.4%).[120] The rate of ectopic pregnancy in the present study differed from the result of a previous meta-analysis, which found an ectopic pregnancy rate higher than that in the US general population (2.4% vs 1.4%).[120] Globally, the live birth rate was highest in Europe (84.50%); however, it was generally favorable across all geographic regions: Africa (80.69%), Asia (74.41%), North America (70.57%), South America (76.90%), and Oceania (76.35%) (Figure 2). The induced abortion rate was highest in South America (17.02%), followed by Asia (11.91%), Oceania (10.28%), North America (8.07%), Europe (7.03%), and Africa (6.39%) (Figure 3). The overall miscarriage rate was low, with the lowest incidence in Oceania (8.64%), followed by Asia (12.02%), Europe (12.24%), Africa (12.71%), North America (14.59%), and South America (17.07%) (Figure 4). The overall stillbirth rate was linear worldwide, with the highest rate in Asia (3.7%) and the lowest in North America (1.48%) (Figure 5). The overall incidence of ectopic pregnancy was low, with the highest rate in North America (2.64%) (Figure 6).

Maternal outcomes

The maternal outcomes included in our study were preeclampsia, cesarean section, gestational diabetes, and PIH. Of these, the most frequently reported outcome was a cesarean section, at 68.67% ($n=2043$; 95% CI, 63.95–73.39), which was twice as high as that in the US general population (32.1%).[121] This was followed, in descending order, by PIH (24.30%) ($n=491$; 95% CI, 18.40–30.20), preeclampsia (20.87%) ($n=864$; 95% CI, 18.25–23.48), and gestational diabetes (5.08%) ($n=224$; 95% CI, 3.61–6.55). Although the rate of preeclampsia in the US population was six times lower than that in our study (3.8%),[122] the rate of gestational diabetes in the US population was higher than that in our study (7.8% vs. 5.08%).[123] Globally, the overall cesarean section rate was high, with the highest rate reported in South America (89.4%), followed by Africa (70.6%); the lowest rate was reported in North America (61.4%) (Figure 7). There was an overall increase in the rate of preeclampsia, with the highest rate reported in Oceania (27.3%), followed by North America (25.6%), Asia (22.0%), Europe (19.17%), South America (18.27%), and Africa (16.21%) (Figure 8). Gestational diabetes rates were significantly promising worldwide, with the lowest incidence reported in Oceania (0.65%) and the highest in Europe (7.09%) (Figure 9). Lastly, the rate of PIH was highest in South America (51.3%) and lowest in Africa (15.5%) (Figure 10).

Fetal outcomes

The fetal outcomes considered in our study included preterm delivery, neonatal mortality, mean gestational age, and mean birth weight. Preterm birth is defined as babies born alive before 37 weeks of gestation.[124] Neonatal mortality is defined as the number of deaths during the first 28 days of life per 1000 live births each year or in another period.[125] The overall rate of preterm birth was 45.3% ($n=1620$; 95% CI, 41.26–49.34), compared with 10.8% in the US general population[117]; neonatal mortality was 1.89% ($n=60$; 95% CI, 1.07–2.71), compared with 3.4% in the US general population.[126] The rate of preterm births was highest in South America (59.8%) and lowest in Asia (39.3%) (Figure 11). Neonatal mortality was highest in Africa (31%), followed by Asia (2.69%), showing a significantly lower rate; no neonatal mortalities were reported in North America (0.00%) (Figure 12). The average birth weight of the infants was 2387.7 g (US mean birth weight, 3389 g), and their mean gestational age was 34.3 weeks (US mean gestational age, 38.7 weeks)[127,128] (Table 2).

Graft outcomes

Regarding 911 kidney transplant recipients, the total acute rejection rate during pregnancy was 8.06% ($n=92$; 95% CI, 5.61–10.51). This rate is comparable to the average rejection rate in transplant recipients in the US general population (7.1%).[129] The following are the rates in each region: Asia, 12.14%; South America, 9.6%; Oceania, 9.09%; North America, 6.67%; Europe, 5.54%; and Africa, 4.76%. Asia had the highest acute renal allograft rejection rates (Figure 13). Although there was a significant variation in graft failure during the follow-up period (1–14 years), there were 123 cases of graft loss (14.42%)

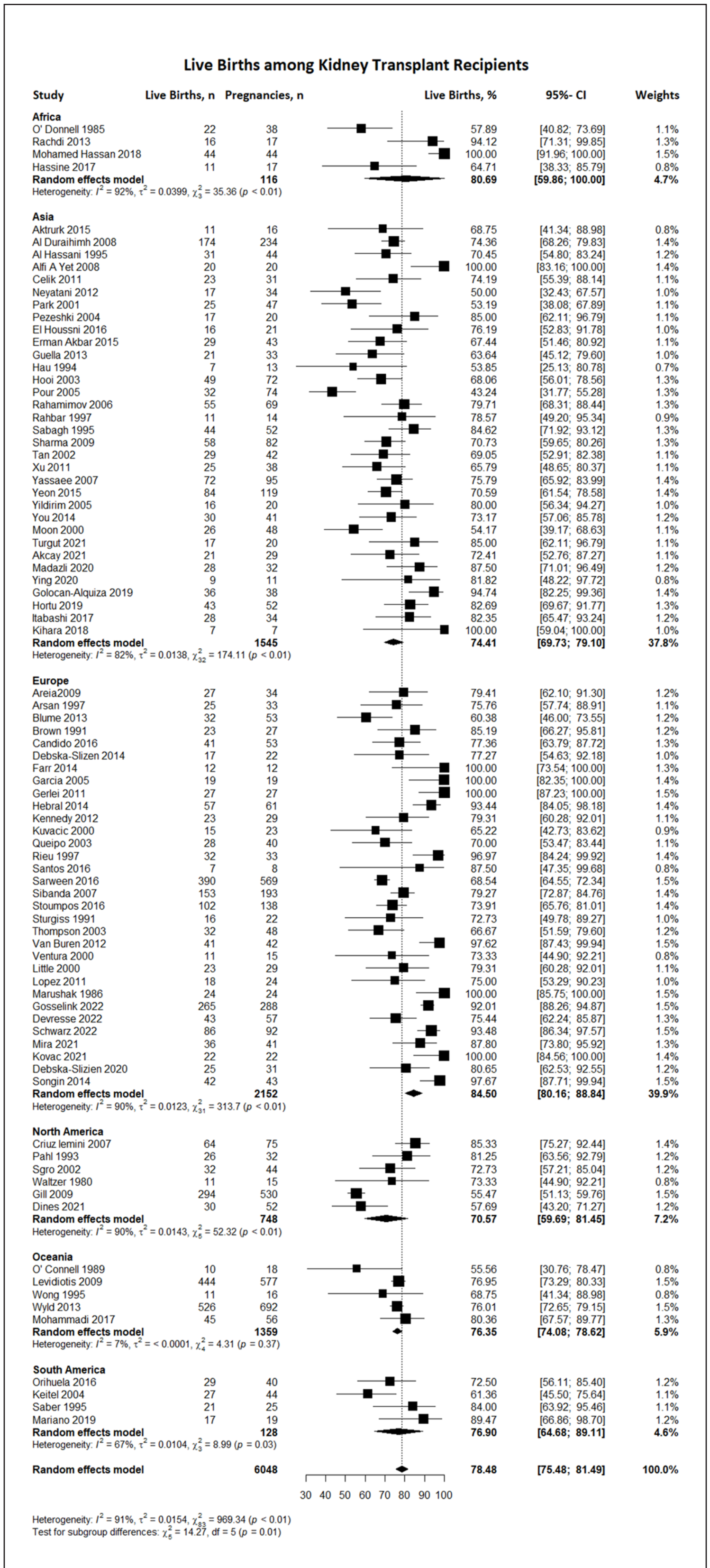

Figure 2. Forest plot illustrating the incidence of live births among kidney transplant recipients, both globally and within distinct geographical regions.

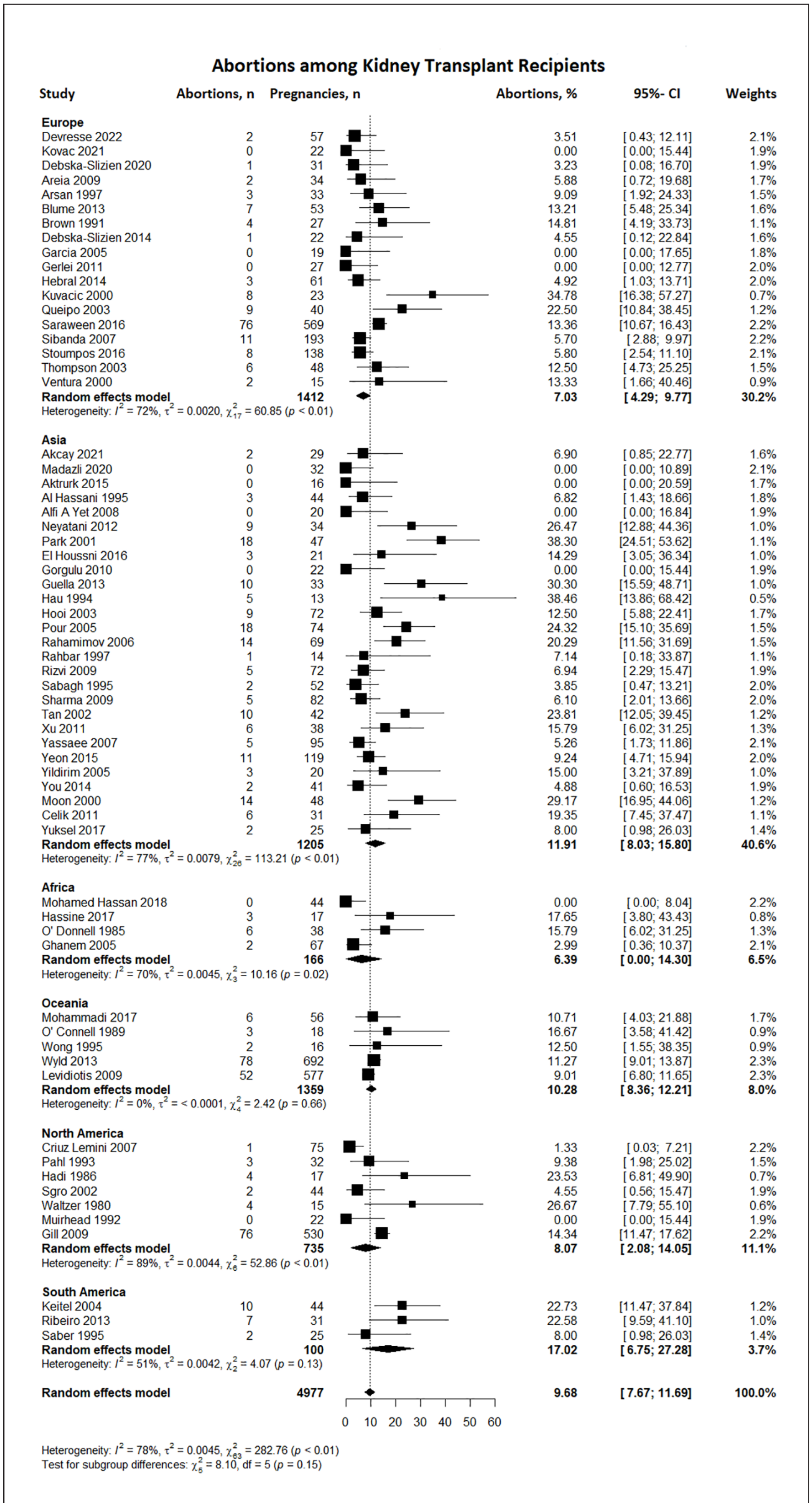

Figure 3. Forest plot illustrating the occurrence of induced abortions among kidney transplant recipients overall and in various geographical regions.

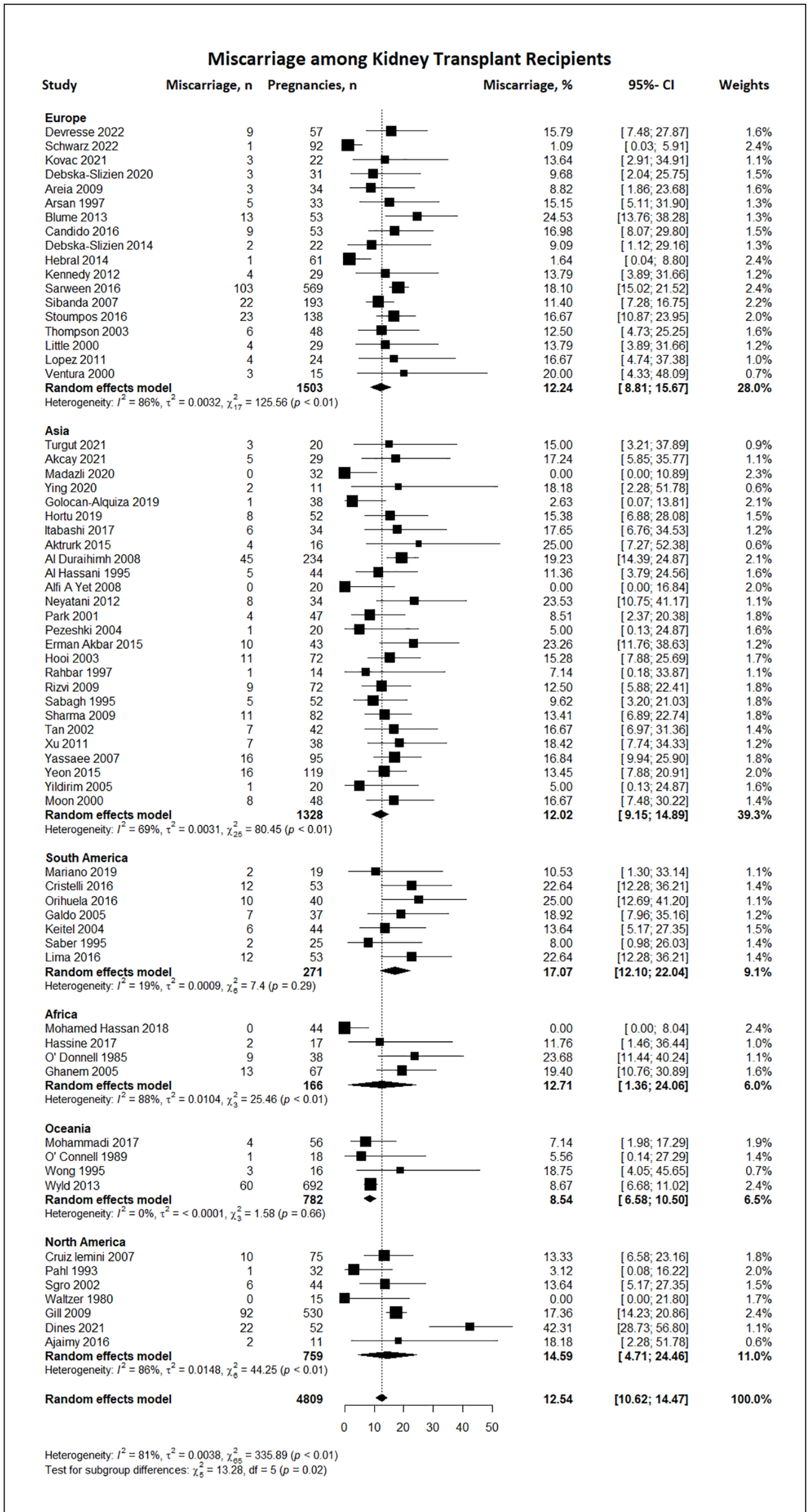

Figure 4. Forest plot illustrating the incidence of miscarriages among kidney transplant recipients overall and in diverse geographical regions.

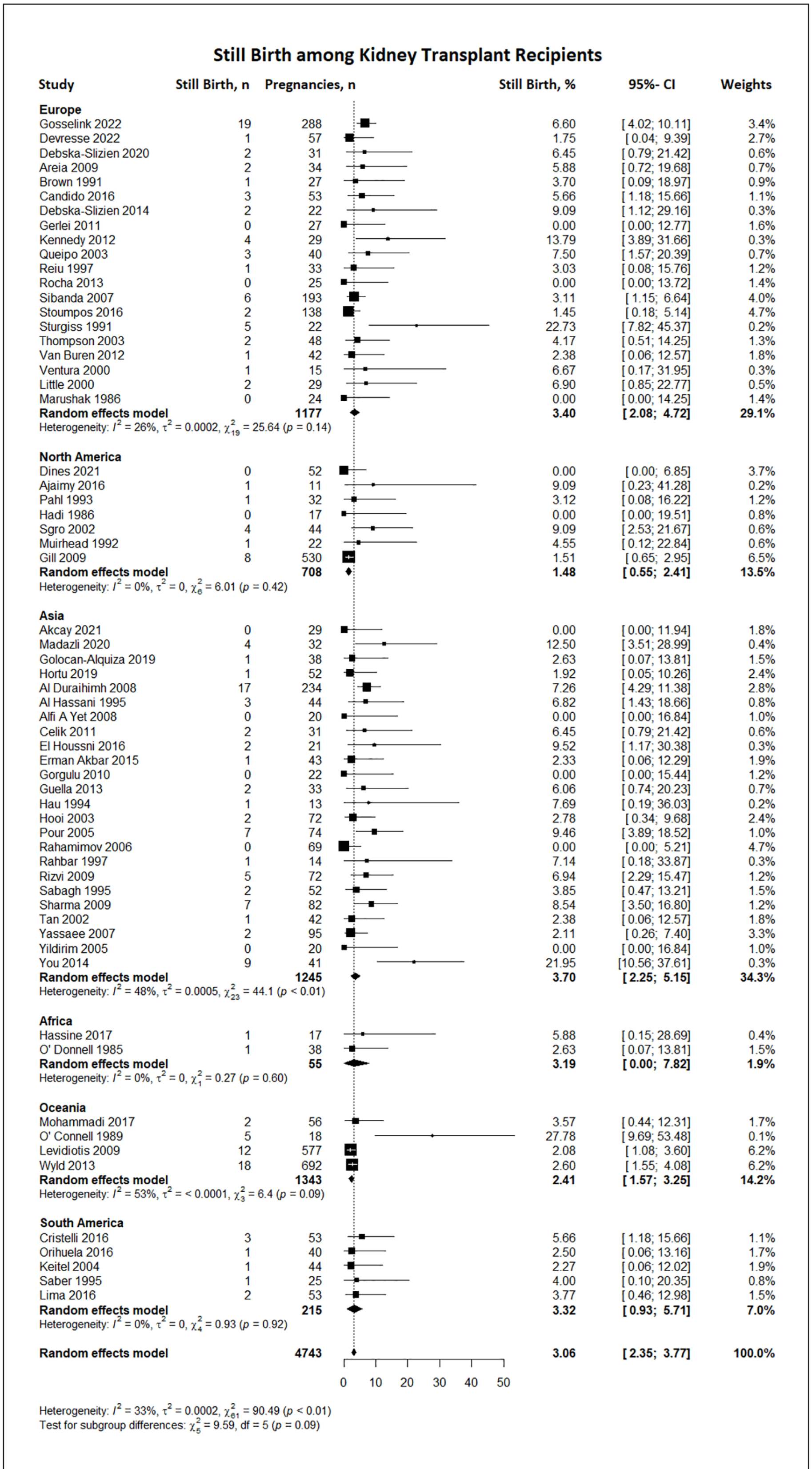

Figure 5. Forest plot depicting the occurrence of stillbirths among kidney transplant recipients overall and across various geographical regions.

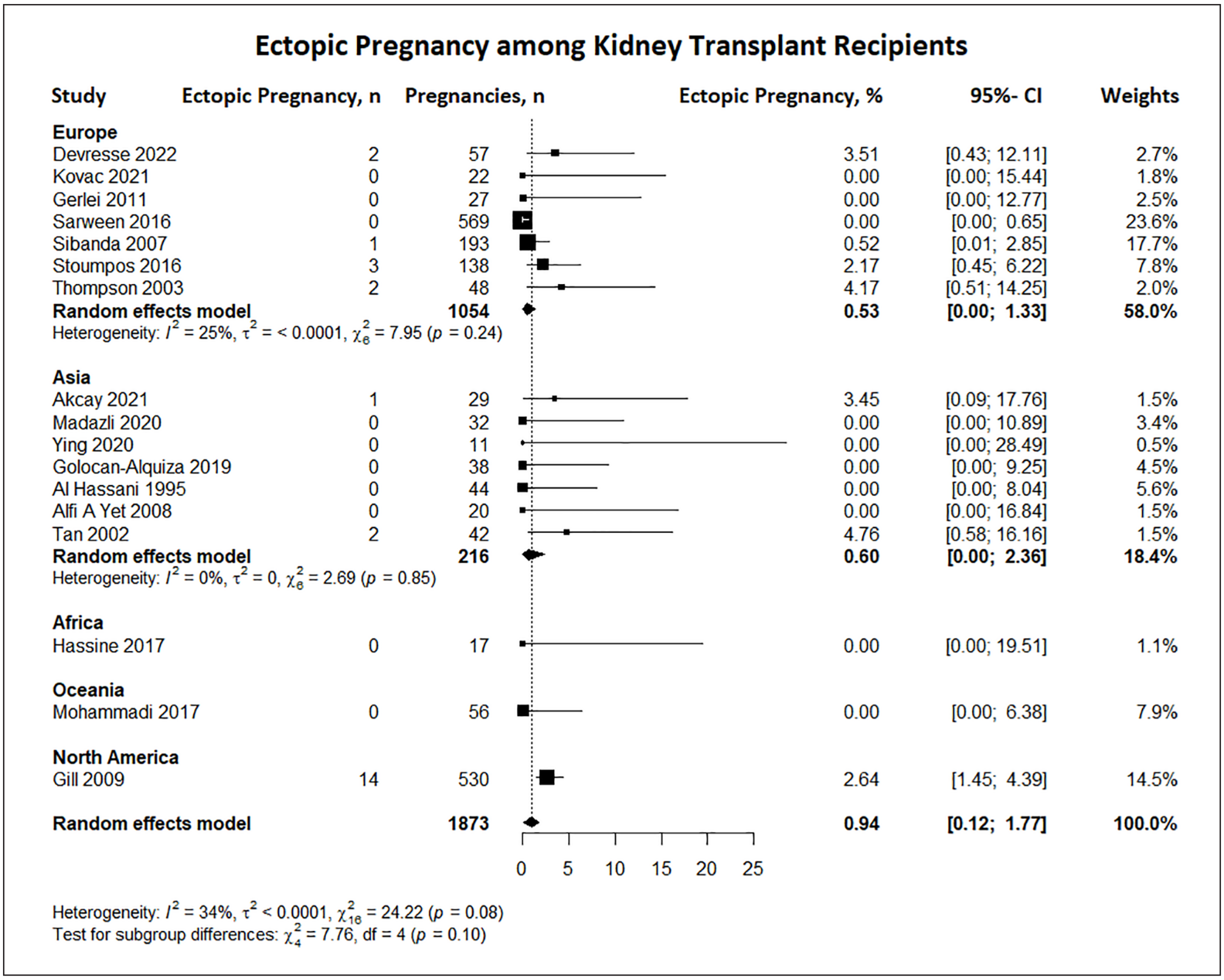

Figure 6. Forest plot illustrating the outcomes of ectopic pregnancies among kidney transplant recipients both overall and across different geographical regions.

among 853 recipients in 19 studies in which 2-year post-pregnancy graft loss was reported. Mean creatinine before pregnancy (mg/dL) and mean creatinine after pregnancy (mg/dL) were 1.16 ± 0.16 and 1.36 ± 0.18, respectively.

Sensitivity analysis

Sensitivity analyses were performed using the leave-one-out method for some outcomes with high heterogeneity to evaluate the studies responsible for heterogeneity, enhance the accuracy of our research findings, and provide more reliable results. The live birth rate after sensitivity analysis was 74.6%, compared with the mean of 56.6% in the US.[117] The miscarriage rate was 13.6%, compared to 19.8% in the US general population.[118] The rate of induced abortions was 7.1%, compared with 24.8% in the US general population.[118] The rates of preeclampsia and gestational diabetes were 20.36% and 3.7%, respectively, compared with 3.8%[122] and 7.8%,[123] respectively, in the US general population. After sensitivity analysis, the rate of PIH was lower than that in the US general population (24.3% vs. 13.7%), whereas the cesarean section rate was higher (74.5%) than the rate in the US (32.1%).[122] Ultimately, the preterm birth rate was 45.3% in the sensitivity analysis. The preterm birth rate in the US general population was 10.8% (Supplemental Figures 1–8).[116]

Interval between renal transplant and pregnancy

The study analyzed pregnancy-related outcomes, based on the interval between renal transplantation and the time of conception, which was categorized into three groups: <2, 2–3, and >3 years. The <2-year interval analysis was based on four studies comprising 141 pregnancies; the 2–3-year interval analysis was based on 11 studies that included 400 pregnancies; and the >3-year interval analysis was based on 66 studies, encompassing a total of 4748 pregnancies.

In cases where the interval between pregnancies was <2 years, the live birth rate was 81.96%, whereas the rates

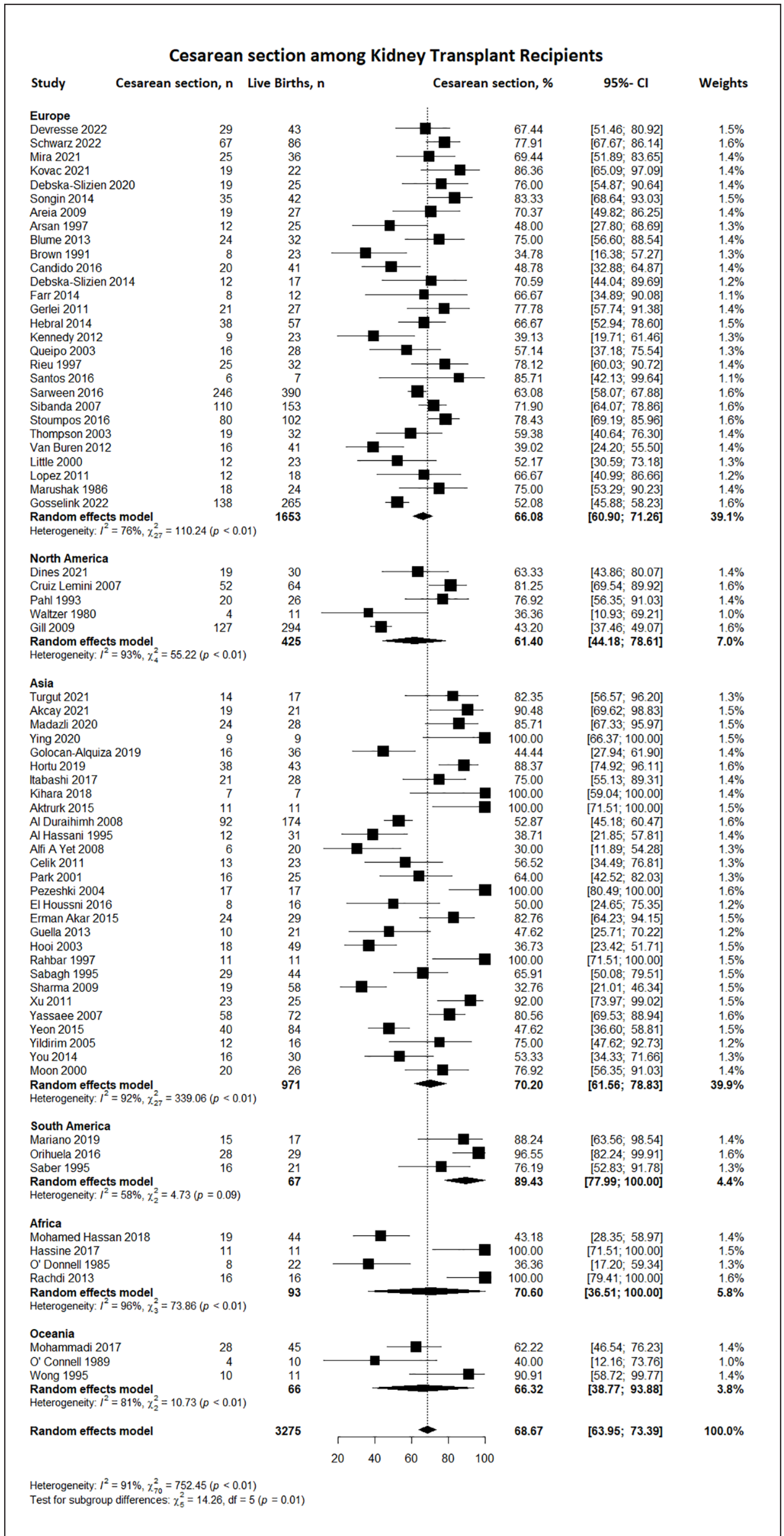

Figure 7. Forest plot displaying the outcomes of cesarean sections among kidney transplant recipients overall, as well as across different geographical regions.

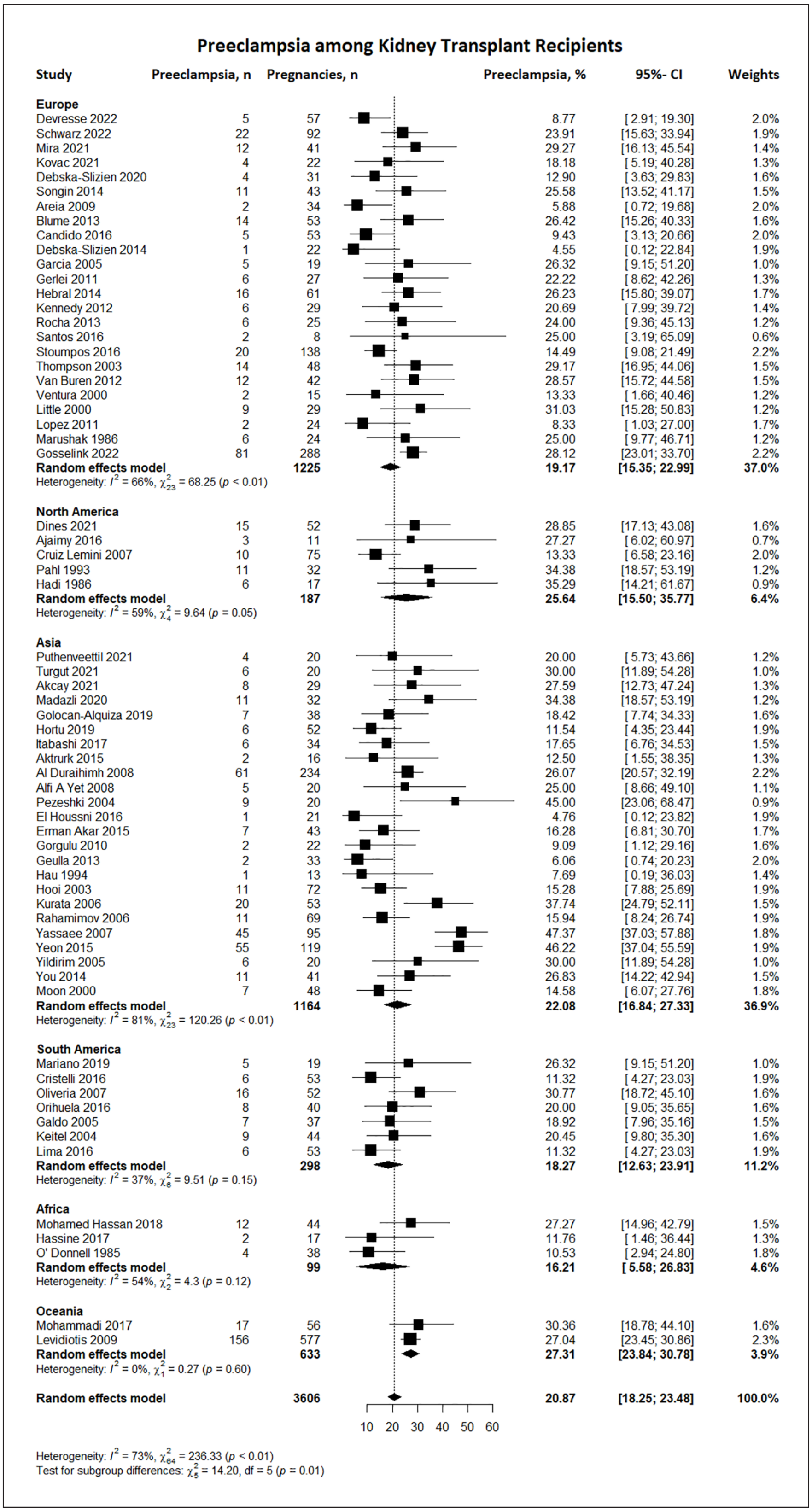

Figure 8. Forest plot depicting the occurrence of preeclampsia among kidney transplant recipients overall and in various geographical regions.

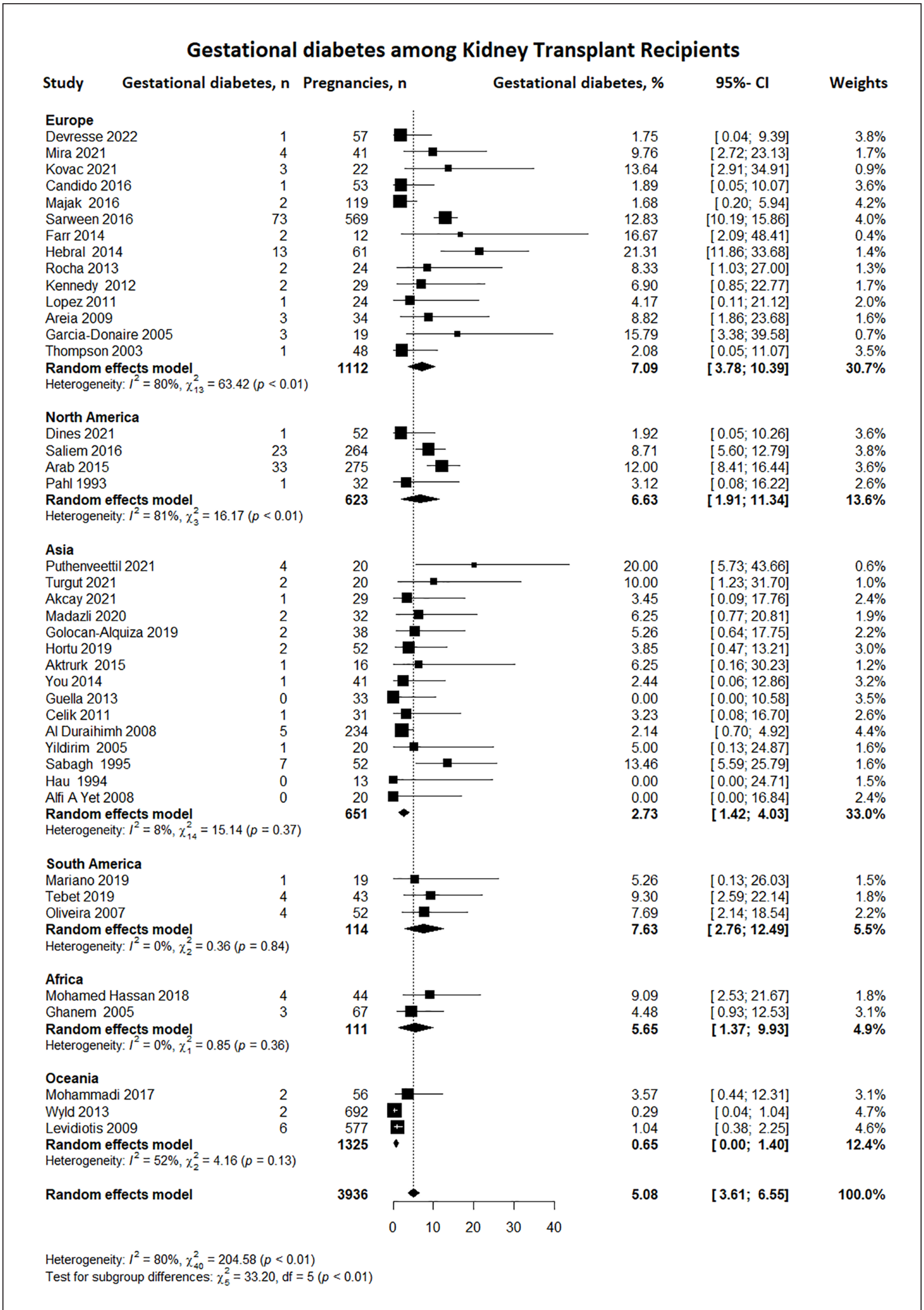

Figure 9. Forest plot illustrating the incidence of gestational diabetes among kidney transplant recipients overall and across diverse geographical regions.

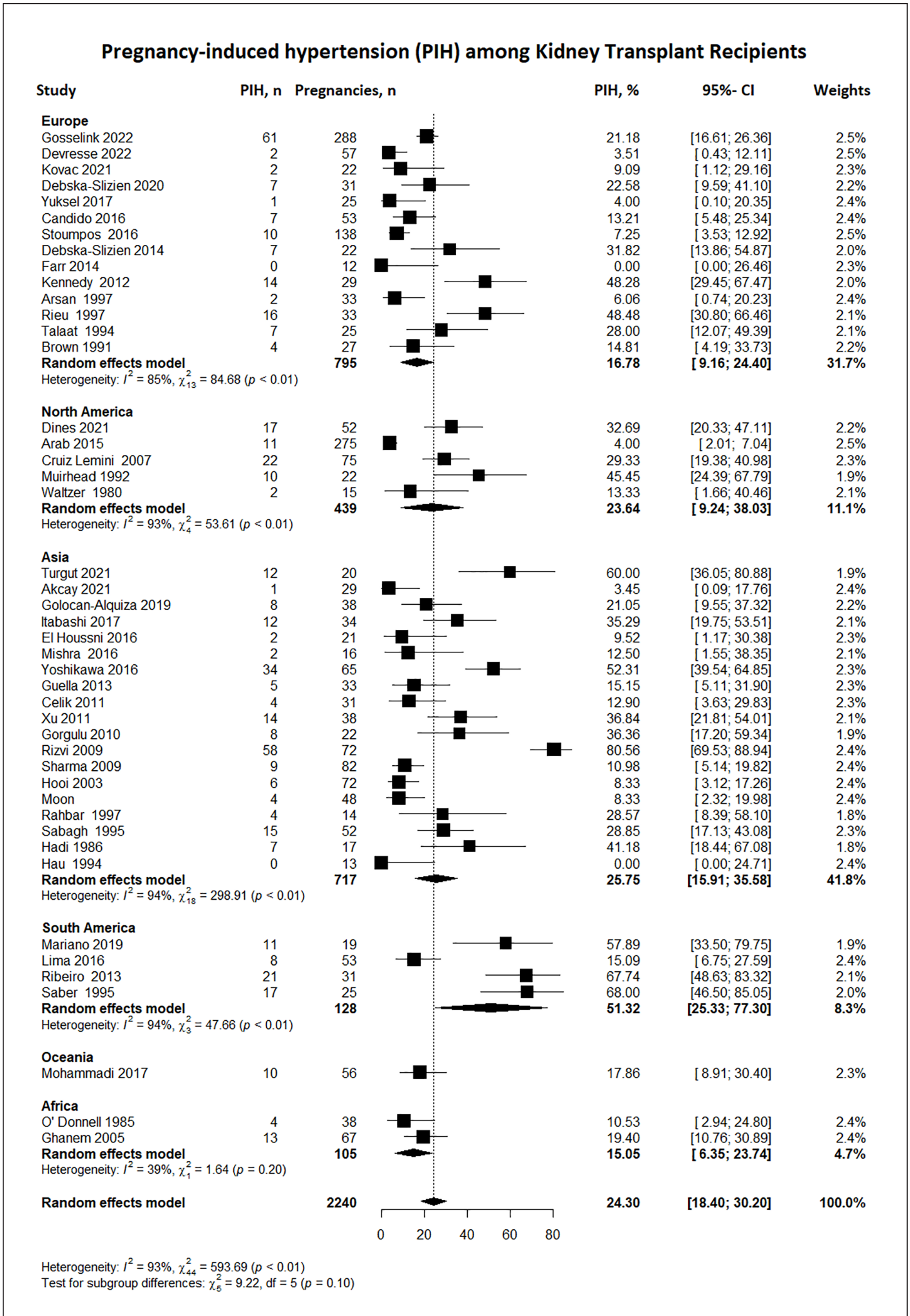

Figure 10. Forest plot demonstrating the occurrence of pregnancy-induced hypertension among kidney transplant recipients overall and in various geographical regions.

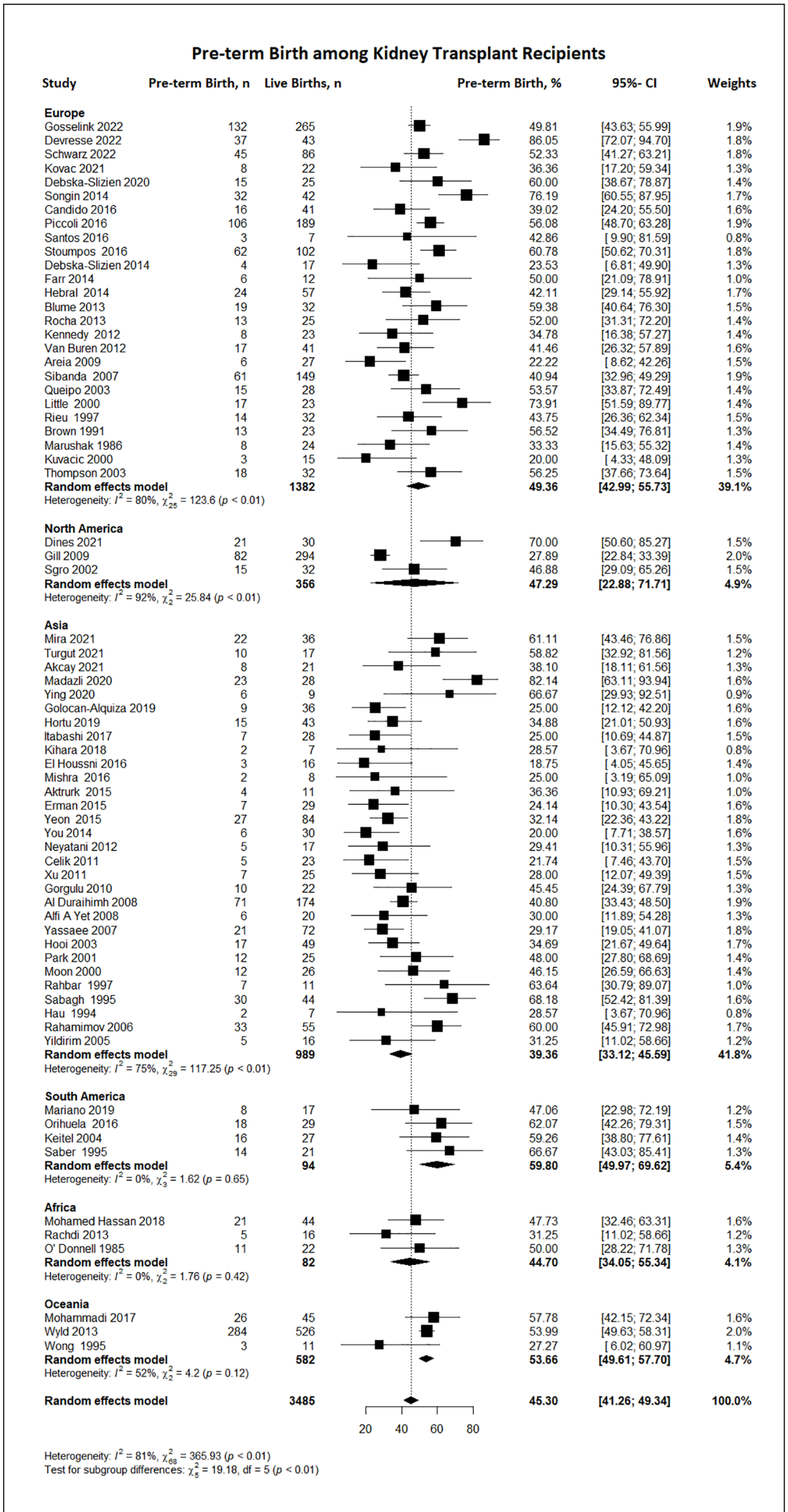

Figure 11. Forest plot illustrating the occurrence of preterm births among kidney transplant recipients overall and across various geographical regions.

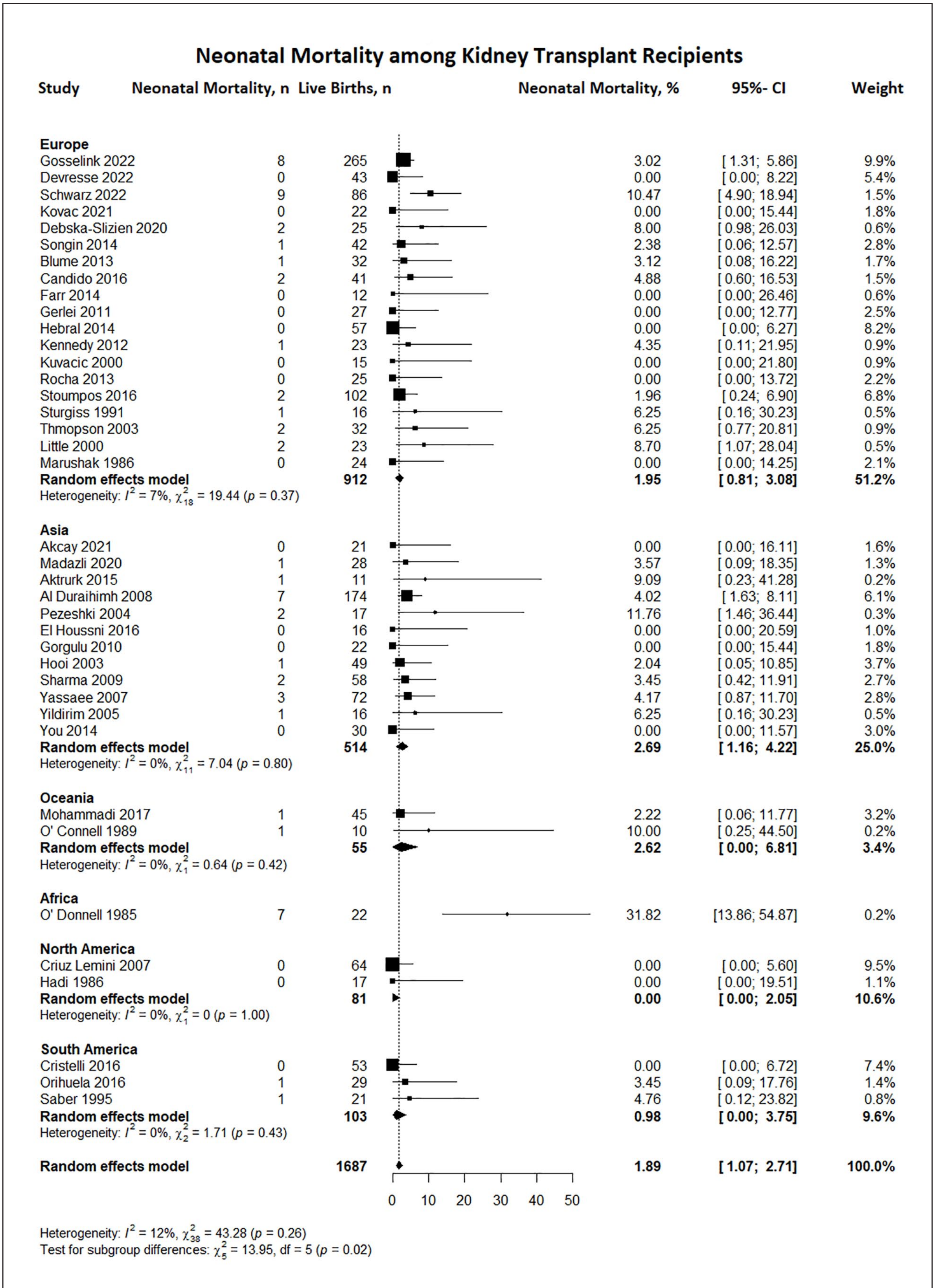

Figure 12. Forest plot illustrating the occurrence of neonatal mortality among kidney transplant recipients overall and across diverse geographical regions.

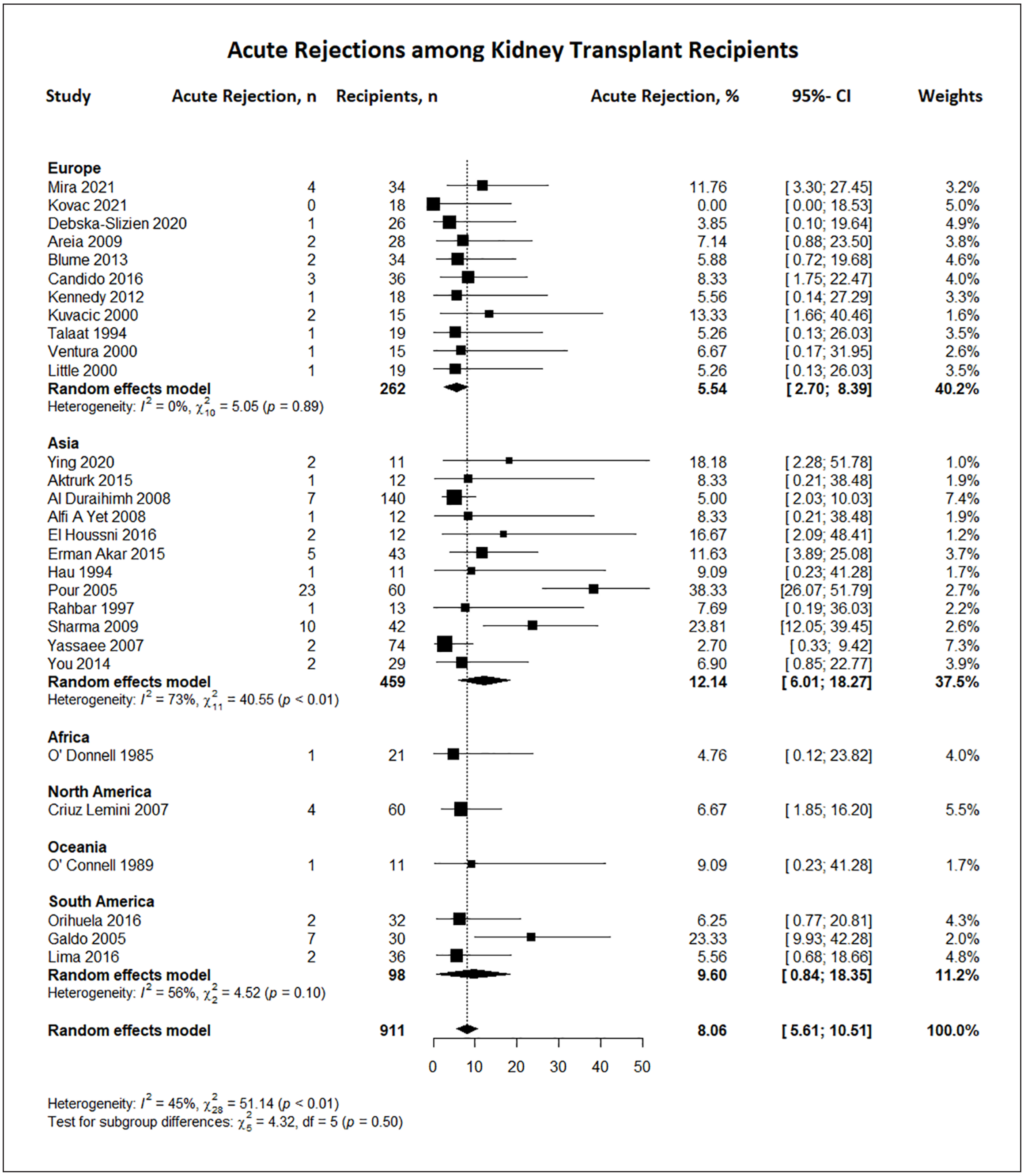

Figure 13. Forest plot displaying the rates of acute rejection among kidney transplant recipients overall and across various geographical regions.

of induced abortion, spontaneous abortion, stillbirth, and neonatal death were 3.59%, 12.72%, 8.04%, and 2.44%, respectively. The maternal outcomes in these cases included a cesarean section rate of 54.6%, a preeclampsia rate of 18.6%, and a PIH rate of 15.9%. Fetal outcomes revealed a preterm delivery rate of 45.2%, a mean gestational age of 37.11 weeks, and an average birth weight of 2868.5 g. The acute rejection and graft loss rates were 11.95% and 16.67%, respectively.

In cases where the interval between pregnancies was 2–3 years, the live birth rate was 73.13%, whereas the rates of induced abortion, spontaneous abortion, stillbirth, and neonatal death were 14%, 12.61%, 3.31%, and 2.80%, respectively. Maternal outcomes in these cases included a cesarean section rate of 74.02%, preeclampsia rate of 25.95%, PIH rate of 28.79%, and gestational diabetes rate of 8.76%. Fetal outcomes revealed a preterm delivery rate of 47.70%, a mean gestational age of 33.7 weeks, and an

Table 4. Pregnancy-related outcomes stratified by study mean interval between transplant and pregnancy.

Mean interval between transplant and pregnancy	<2 years	2–3 years	>3 years
Number of papers	4	11	66
Number of pregnancies	131	400	4748
Mean maternal age (years)	28.45	28.04	29.15
Pregnancies outcomes			
Live birth	81.96%	73.13%	81.89%
Induced abortion	3.59%	14%	10.72%
Spontaneous abortion	12.72%	12.61%	12.67%
Still birth	8.04%	3.31%	2.65%
Neonatal deaths	2.44%	2.80%	1.65%
Maternal outcomes			
Cesarean section	54.63%	74.02%	70.76%
Preeclampsia	18.60%	25.95%	21.81%
Pregnancy-induced hypertension	15.97%	28.79%	21.69%
Gestational diabetes	N/A	8.76%	5.25%
Fetal outcomes			
Preterm delivery	45.25%	47.70%	44.86%
Mean gestational age (weeks)	37.11	33.7	35.32
Birth weight (g)	2868.5	2463.74	2470.77
Graft outcomes			
Acute rejection	11.95%	19.58%	4.21%
Graft loss	16.67%	N/A	14.49%

N/A: not applicable.

average birth weight of 2463.74 g. Regarding graft outcomes, the acute rejection rate was 19.58%.

In cases where the interval between pregnancies was >3 years, the live birth rate was 81.89%, whereas the rates of induced abortion, spontaneous abortion, stillbirth, and neonatal death were 10.72%, 12.67%, 2.65%, and 1.65%, respectively. Maternal outcomes in these cases included a cesarean section rate of 70.76%, preeclampsia rate of 21.81%, PIH rate of 21.69%, and gestational diabetes rate of 5.25%. Fetal outcomes revealed a preterm delivery rate of 45.30%, a mean gestational age of 35.32 weeks, and an average birth weight of 2470.77 g. Regarding graft outcomes, the acute rejection rate was 4.21%, whereas the graft loss rate was 14.49% (Table 4; Supplemental Figures 9–20).

Maternal age at conception

Pregnancy-related outcomes were stratified into four groups based on the mean maternal age: <25, 25–29, 30–34, and >35 years. The analysis for the <25-years age group was based on 10 studies with 299 pregnancies. For the 25–29-year age group, we analyzed 38 studies with 2588 pregnancies. The analysis of the 30–34-year age group was based on 36 studies with 2939 pregnancies. For the >35-years age group, we included only one study with 11 pregnancies.

The live birth rate was 75.04% among individuals aged <25 years. The rates of induced abortions, spontaneous abortions, and stillbirths were 14.89%, 14.88%, and 2.15%, respectively. Maternal outcomes included a cesarean section rate of 74.07%, preeclampsia rate of 12.29%, PIH rate of 20.95%, and gestational diabetes rate of 2.12%. Fetal outcomes revealed a preterm delivery rate of 56.87%, a mean gestational age of 33.7 weeks, and an average birth weight of 2483.4 g. Graft outcomes showed an acute rejection rate of 6.67% and a graft loss rate of 0.00%.

For individuals aged 25–29 years, the live birth rate was 79.23%. The rates of induced abortions, spontaneous abortions, stillbirths, and neonatal deaths were 12.67%, 14.73%, 3.34%, and 2.68%, respectively. Maternal outcomes included a cesarean section rate of 72.79%, preeclampsia rate of 23.57%, PIH rate of 23.80%, and gestational diabetes rate of 6.32%. Fetal outcomes revealed a preterm delivery rate of 47.57%, a mean gestational age of 35.36 weeks, and an average birth weight of 2481.50 g. Graft outcomes showed an acute rejection rate of 7.97% and a graft loss rate of 9.49%.

For individuals aged 30–34 years, the live birth rate was 80.79%. The rates of induced abortion, spontaneous abortion, stillbirth, and neonatal death were 8.93%, 12.93%, 2.84%, and 1.53%, respectively. Maternal outcomes included a cesarean section rate of 68.93%, preeclampsia rate of 22.68%, PIH rate of 24.62%, and gestational

Table 5. Pregnancy-related outcomes stratified by study mean maternal age.

Mean maternal age (years)	<25	25–29	30–34	>35
Number of papers	10	38	36	1
Number of pregnancies	299	2588	2939	11
Mean maternal age (years)	23.13	28.09	31.5	36
Pregnancy outcomes				
Live birth	75.04%	79.23%	80.79%	100%
Induced abortion	14.89%	12.67%	8.93%	N/A
Spontaneous abortion	14.88%	14.73%	12.93%	18.18%
Still birth	2.15%	3.34%	2.84%	9.09%
Neonatal deaths	0.00%	2.68%	1.53%	N/A
Maternal outcomes				
Cesarean section	74.07%	72.79%	68.93%	N/A
Preeclampsia	12.29%	23.57%	22.68%	27.27%
Pregnancy-induced hypertension	20.95%	23.80%	24.62%	N/A
Gestational diabetes	2.12%	6.32%	4.32%	N/A
Fetal outcomes				
Preterm delivery	56.87%	47.57%	42.18%	N/A
Mean gestation time (weeks)	33.7	35.36	35.25	N/A
Birth weight (g)	2483.4	2481.50	2462.9	N/A
Graft outcomes				
Acute rejection	6.67%	7.97%	5.20%	N/A
Graft loss	0.00%	9.49%	13.26%	27.27%

N/A: not applicable.

diabetes rate of 4.32%. Fetal outcomes revealed a mean preterm delivery rate of 42.18%, a mean gestational age of 35.25 weeks, and an average birth weight of 2462.9 g. The graft outcomes showed an acute rejection rate of 5.20% and a graft loss rate of 13.26%.

For individuals aged >35 years, the live birth rate was reported to be 100%. However, the rates of spontaneous abortion, stillbirth, and preeclampsia were reported to be 18.18%, 9.09%, and 27.27%, respectively. As for graft outcomes, the graft loss rate was 27.27% (Table 5; Supplemental Figures 21–32).

Discussion

The findings of our meta-analysis suggest that, although most pregnancies in women who have undergone kidney transplantation resulted in live births, there were significant incidences of maternal and fetal adverse events. The most common adverse outcomes were cesarean section, preterm delivery, PIH, and pre-eclampsia. Other significant adverse outcomes included gestational diabetes, neonatal mortality, stillbirth, miscarriage, and induced abortion. Compared with the rates in the US general population, this study reported higher rates of live births, stillbirths, preeclampsia, and cesarean sections but lower rates of ectopic pregnancies, gestational diabetes, mean gestational age, birth weight, and graft rejection.

Our study reported a higher live birth rate compared with that in the US general population.[117] The 2018 Annual Report of the Transplant Pregnancy Registry International reported a 75% live birth rate in renal transplant recipients.[130] However, a single-center study reported a lower live birth rate, of only 33.3%, among 182 renal transplant recipients.[131] The high live birth rate in our study may be attributed to reporting and selection bias and the exclusion of pregnancies with confirmed intrauterine fetal abnormalities and/or transplant recipients managed with teratogenic immunosuppressants, such as mycophenolate and sirolimus. Our study's live birth rate agrees with the live birth rates of 72.9% and 73.5% reported in previous meta-analyses by Shah et al. and Deshpande et al., respectively.[120,132]

Although our study reports encouraging live birth rates, preterm delivery-induced abortions and miscarriages are common. The preterm birth rate in our study was approximately three-fold higher than that in the US general population,[117] and similar rates (50%–64%) have been reported by the UK, US, and European transplant registries.[133] The higher preterm delivery rate may be due to greater risk factors in renal transplant recipients, such as premature rupture of membranes, urinary tract infections, and acute graft rejection.[134] However, the literature suggests that iatrogenic preterm deliveries should be reserved for patients with suspected fetal renal compromise and preeclampsia.[135]

The higher rates of induced abortion and miscarriages in the US than those in our study may be due to the use of mycophenolate, which is associated with a higher risk of miscarriage and fetal malformation.[136] Thus, it is essential to advise transplant recipients to discontinue mycophenolate for at least 6 weeks before conception.[137] Consequently, the lower rates of abortions and miscarriages in our study may be due to the selection of women who were qualified to continue with their pregnancies. Neonatal mortality and stillbirth rates in our study were comparatively lower than the rates in the US[119,126]; however, excessive preventive measures in terms of pre-pregnancy counseling and antenatal care are still required. Similar neonatal mortality rates have been described in a retrospective cohort study with data pooled from the Australia and New Zealand Dialysis and Transplant Registry and perinatal datasets, advocating the need for antenatal care and preconception counseling for pregnancies in renal transplant recipients.[138]

Our study highlights the significantly increased risk of complications for mothers who have undergone kidney transplantation, with preeclampsia affecting almost a quarter of women and being approximately six times more common than that in the US population.[122] Preeclampsia can lead to several maternal and fetal complications and poses a significant challenge for clinicians in terms of diagnosis and management.[132] Our research outcomes correspond with those reported by Coscia et al., who observed notably elevated incidence rates of preeclampsia (31%) and hypertension (54%) in female transplant recipients.[135] Furthermore, in another study of 15 female transplant recipients, the rate of hypertension was 46.6%.[139] The high rate of hypertension in pregnant transplant recipients could be associated with the use of calcineurin inhibitors and corticosteroids, donor kidney type, and modifiable maternal factors, such as smoking, alcohol consumption, and obesity.[140]

The incidence of gestational diabetes in transplant recipients was lower in our study than in the US general population[123]; however, close monitoring is important because of the potential risks for the mother and newborn. Moreover, factors such as immunosuppressive drugs, like tacrolimus, pre-existing conditions such as obesity, family history of diabetes, and advanced maternal age can increase this risk.[141] Women who have received a transplant require guidance on managing pre-existing conditions before becoming pregnant to optimize their health before conception.[142]

Regarding the regional disparities in acute renal allograft rejection rates, observed variations, Asia had the highest rejection rates followed by South America, Oceania, North America, Europe, and Africa. Medical management, including pre-transplant evaluation and preparation, surgical techniques, post-operative care, immunosuppressive therapy protocols, and monitoring strategies, are more accessible in developed countries than in developing countries. Moreover, regions with higher rejection rates face challenges related to access to advanced medical technology, medications, or healthcare professionals specialized in transplant care. In contrast, regions with lower rejection rates, like Europe and North America, have extensive resources in transplant centers. Furthermore, variations in donor characteristics, such as donor age, Human Leukocyte Antigens matching, and organ preservation techniques affect transplant outcomes and rejection rates. Regions with limited access to suitable donors or where donor quality may be compromised could experience higher rejection rates, compared with regions with more favorable donor profiles.[143]

The mode of delivery for renal transplant recipients remains controversial. In our study, the rate of cesarean sections in renal transplant recipients was at least twice as high as that in the US general population,[122] and several studies have reported similar findings.[144,145] The reasons for this include non-medical factors, such as fear of infection and graft injury, newborn welfare, and low optimism for a trial of labor. However, trials of labor and normal delivery did not increase the risk of renal and cardiovascular complications, allograft injury, or sepsis, as suggested by Yin et al.[146] Therefore, cesarean delivery should only be reserved for obstetric reasons, and hospital and delivery unit policies should be revised to lower the rate of cesarean delivery after organ transplantation. Preconception and prenatal care within a patient's transplant center may improve interdisciplinary management and communication during vaginal delivery.[146]

The optimal time interval between transplantation and pregnancy remains debatable. Previously, it was suggested that pregnancy should be delayed for at least 2 years post-transplantation; however, these guidelines have been replaced by the American Society of Transplantation guidelines, which suggest that a transplant recipient can conceive as early as 1-year post-transplantation.[133] Our study showed fewer adverse outcomes and rates with intervals of <2 years, whereas more outcomes and higher rates were found with a 2–3-year interval between transplantation and pregnancy. These outcomes include induced abortion, neonatal death, cesarean delivery, preeclampsia, PIH, gestational diabetes, and acute graft rejection. The mean gestational age and live birth rates were lowest in the 2–3-year interval and highest in the <2 year interval. This is consistent with a meta-analysis by Shah et al. that reported the lowest rates of fetal and maternal complications within 2 years of transplantation, whereas the outcomes were reported to be the highest during the 2–3-year interval.[120] Another study reported that 97% of transplant recipients had successful pregnancies 1 year after transplantation, with 73% having live births.[71] This finding reinforces the importance of following the current guidelines regarding the optimal time interval between transplantation and pregnancy, as well as including preconception counseling, family planning, and contraception as crucial components of the transplant counseling process.[132]

Our study provides valuable information on pregnancy outcomes in renal transplant recipients from a diverse region-specific population over several decades. This information can assist in updating the guidelines and management of pregnancy in transplant recipients that are specific to a particular region. However, this study has limitations, including potential bias in participant selection and data reporting owing to voluntary participation. This study excluded patients treated with mycophenolate and sirolimus, which may have affected the overall favorable results of the meta-analysis. Therefore, future research should further investigate this parameter. In addition, there were inconsistencies in the diagnostic criteria for complications such as PIH, preeclampsia, and gestational diabetes, as well as potential confounding factors, such as baseline variations in medical care and socioeconomic differences between countries and regions. The absence of comprehensive data on post-pregnancy reproductive planning among transplant recipients limits the depth of our analysis. This underscores the need to address this crucial aspect of care, considering the associated risks.

Conclusion

Pregnancy after kidney transplantation poses significant risks to maternal and fetal health, including preeclampsia, hypertension, cesarean delivery, stillbirth, preterm birth, and low birth weight. Our meta-analysis revealed variations in outcomes across geographic regions, with differences in the rates of ectopic pregnancy, live births, induced abortions, miscarriages, and stillbirths. Notably, we observed a decrease in ectopic pregnancies over time. Trials of labor and normal delivery do not escalate maternal or graft-related complications and advocate judicious cesarean delivery. Regarding the interval between transplantation and pregnancy, we found that, although the outcomes in those pregnant 2–3 years post-transplantation were worse, outcomes in those pregnant >3 years post-transplantation were the best when compared with the outcomes in the other groups. Improvements in antenatal care have mitigated risks, such as preeclampsia and maternal mortality, with decreased rates of miscarriage attributed to better immunosuppressive regimens and prenatal care. Despite advancements, the risk of congenital abnormalities remains elevated owing to immunosuppressive medications. Although progress has been made, pregnant kidney transplant recipients still require specialized care. Our findings underscore the importance of ongoing research and technological advancements to further enhance outcomes in this high-risk population.

Author's Note

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Declarations

Ethical considerations

Not applicable, as the study is based exclusively on published literature/medical records.

Consent to participate

Not applicable.

Consent for publication

Not applicable.

Author contribution(s)

Muhammad Saqlain Mustafa: Writing – review & editing; Formal analysis; Data curation; Software; Conceptualization.
Amber Noorani: Conceptualization; Writing – original draft; Writing – review & editing; Project administration.
Aniqa Abdul Rasool: Data curation; Validation; Writing – original draft; Conceptualization.
Fatema Ali Asgar Tashrifwala: Writing – original draft; Writing – review & editing; Project administration.
Shubha Jayaram: Methodology; Writing – original draft.
Sandesh Raja: Data curation; Writing – original draft.
Fatima Jawed: Data curation; Writing – original draft.
Muhammad Usama Siddiq: Data curation; Writing – original draft.
Sowmya Govindanahalli Shivappa: Methodology; Writing – original draft.
Ishaque Hameed: Supervision; Writing – review & editing; Conceptualization.
Sriharsha Dadana: Supervision; Writing – review & editing.

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Competing interests

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Data availability statement

All data underlying the results are available as part of the article and no additional source data are required.

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Supplemental material

Supplemental material for this article is available online.

References

1. Piccoli GB, Cabiddu G, Attini R, et al. Outcomes of pregnancies after kidney transplantation: lessons learned from CKD. A comparison of transplanted, non-transplanted chronic kidney disease patients and low-risk pregnancies: a multicenter nationwide analysis. *Transplantation* 2017; 101: 2536–2544.
2. Chittka D and Hutchinson JA. Pregnancy after renal transplantation. *Transplantation* 2017; 101: 675–678.
3. Webster P, Lightstone L, McKay DB, et al. Pregnancy in chronic kidney disease and kidney transplantation. *Kidney Int* 2017; 91: 1047–1056.
4. Shah S and Verma P. Overview of pregnancy in renal transplant patients. *Int J Nephrol* 2016; 2016: 4539342.
5. You JY, Kim MK, Choi SJ, et al. Predictive factors for adverse pregnancy outcomes after renal transplantation. *Clin Transplant* 2014; 28: 699–706.
6. Bramham K, Nelson-Piercy C, Gao H, et al. Pregnancy in renal transplant recipients: a UK national cohort study. *Clin J Am Soc Nephrol* 2013; 8: 290–298.
7. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Int J Surg* 2021; 88: 105906.
8. Brooke BS, Schwartz TA and Pawlik TM. MOOSE reporting guidelines for meta-analyses of observational studies. *JAMA Surg* 2021; 156: 787–788.
9. Gosselink ME, van Buren MC, Kooiman J, et al. A nationwide Dutch cohort study shows relatively good pregnancy outcomes after kidney transplantation and finds risk factors for adverse outcomes. *Kidney Int* 2022; 102: 866–875.
10. Devresse A, Jassogne C, Hubinont C, et al. Maternal risks, and pregnancy outcomes after kidney transplantation: a single center experience. *Am J Transplant* 2017; 17: 253.
11. Schwarz A, Schmitt R, Einecke G, et al. Graft function and pregnancy outcomes after kidney transplantation. *BMC Nephrol* 2022; 23: 27.
12. Dines VA, Garovic VD, Parashuram S, et al. Pregnancy, contraception, and menopause in advanced chronic kidney disease and kidney transplant. *Women's Health Rep (New Rochelle)* 2021; 2: 488–496.
13. Puthenveettil N, Mohan A, Rahman S, et al. Pregnancy outcomes in renal transplant recipients. *Indian J Anaesth* 2021; 65: 695–699.
14. Mira FS, Oliveira J, Sousa F, et al. Kidney graft function before pregnancy as a predictor of graft, maternal and fetal outcomes in pregnant renal transplant recipients. *J Perinat Med* 2022; 50: 185–191.
15. Turgut E, İnan G, Günaydın DB, et al. Antenatal follow-up, anesthesia management and perinatal outcomes in pregnancy with renal transplant. *Turk J Obstet Gynecol* 2021; 18: 109.
16. Akcay OF, Yeter HH, Karcaaltincaba D, et al. Obstetric and long-term graft outcomes in pregnant kidney transplant recipients: a single-center experience. *Clin Transplant* 2021; 35: e14349.
17. Kovač D, Kovač L, Mertelj T, et al. Pregnancy after kidney transplantation. *Transplant Proc* 2021; 53: 1080–1084.
18. Dębska-Ślizień A, Gałgowska J, Bułło-Piontecka B, et al. Pregnancy after kidney transplantation with maternal and pediatric outcomes: a single-center experience. *Transplant Proc* 2020; 52: 2430–2435.
19. Madazlı R, Kaymak D, Alpay V, et al. Evaluation of obstetric outcomes and prognostic significance of graft function in kidney transplant recipient pregnancies. *Hypertens Pregnancy* 2020; 39: 89–94.
20. Ying J, Li L, Zhai Y, et al. Pregnancy outcomes after renal transplantation: a retrospective case series. *Women's Health Rep (New Rochelle)* 2020; 1: 55–59.
21. Golocan-Alquiza IF, Cabanayan-Casasola CB, Faustino KM, et al. Patient and graft outcomes among Filipino post-kidney transplant pregnancies. *Transplant Proc* 2019; 51: 2718–2723.
22. Hortu I, Arı SA, Akdemir A, et al. Perinatal outcomes of renal transplant pregnancies: a 22-year experience at a single tertiary referral center. *J Matern Fetal Neonatal Med* 2020; 33: 3028–2034.
23. Mariano S, Guida JP, Sousa MV, et al. Pregnancy among women with kidney transplantation: a 20-years single-center registry. *Rev Bras Ginecol Obstet* 2019; 41: 419–424.
24. Özban M, Özban AS, Birsen O, et al. Pregnancy after renal transplantation. *Bratisl Lek Listy* 2019; 120: 368–371.
25. Tebet JL, Kirsztajn GM, Facca TA, et al. Pregnancy in renal transplant patients: renal function markers and maternal–fetal outcomes. *Pregnancy Hypertens* 2019; 15: 108–113.
26. Hassan SM, Fahmy R, Omran EF, et al. Outcome of pregnancy after renal transplantation. *Int J Womens Health* 2018; 10: 65-68.
27. Amine BHH, Haythem S, Kais H, et al. Pregnancy after renal transplantation: a retrospective study at the military hospital of Tunis from 1992 to 2011. *Pan Afr Med J* 2017; 28: 137.
28. Mohammadi FA, Borg M, Gulyani A, et al. Pregnancy outcomes and impact of pregnancy on graft function in women after kidney transplantation. *Clin Transplant* 2017; 31: e13089.
29. Itabashi Y, Ohashi Y, Muramatsu M, et al. Association between the fertile period and live birth post-kidney transplantation: a retrospective single-center cohort study. *Transplant Proc* 2017; 49: 1068–1072.
30. Kihara Y, Konno O, Yokoyama T, et al. An examination of pregnancy cases after kidney transplantation: single-center experience. *Transplant Proc* 2018; 50: 2531–2534.
31. Songin T, Pietrzak B, Brawura-Biskupski-Samaha R, et al. Pregnancy after kidney and liver transplantation: its outcome and effect on the graft, mother, and neonate. *Ann Transplant* 2014; 19: 660–666.
32. Yuksel Y, Tekin S, Yuksel D, et al. Pregnancy and delivery in the sequel of kidney transplantation: a single-center study of 8 years' experience. *Transplant Proc* 2017; 49: 546–550.
33. Ajaimy M, Lubetzky M, Jones T, et al. Pregnancy in sensitized kidney transplant recipients: a single-center experience. *Clin Transplant* 2016; 30: 791–795.
34. Candido C, Cristelli MP, Fernandes AR, et al. Pregnancy after kidney transplantation: high rates of maternal complications. *J Bras Nefrol* 2016; 38: 421–426.
35. Cristelli M, Candido CD, Fernandes AR, et al. 109 Pregnancy among kidney transplanted women: feasibility

of pregnancy and effects on the mother and renal graft. *Pregnancy Hypertens* 2016; 6: 232.
36. El Houssni S, Sabri S, Benamar L, et al. Pregnancy after renal transplantation: effects on mother, child, and renal graft function. *Saudi J Kidney Dis Transpl* 2016; 27: 227–232.
37. Lima A, Cristelli M, Teixeira C, et al. Pregnancy in the renal transplant recipient: pregnancy viability and effects on graft function. *Am J Transplant* 2016; 16: 783–784.
38. Majak GB, Sandven I, Lorentzen B, et al. Pregnancy outcomes following maternal kidney transplantation: a national cohort study. *Acta Obstet Gynecol Scand* 2016; 95: 1153–1161.
39. Mishra VV, Nanda S, Mistry K, et al. Pregnancy outcome in renal transplant recipients: Indian scenario. *Indian J Transplant* 2016; 10: 57–60.
40. Orihuela S, Nin M, San Roman S, et al. Successful pregnancies in kidney transplant recipients: experience of the National Kidney Transplant Program from Uruguay. *Transplant Proc* 2016; 48: 643–645.
41. Piccoli GB, Cabiddu G, Attini R, et al. Pregnancy outcomes after kidney graft in Italy: are the changes over time the result of different therapies or of different policies? A nationwide survey (1978–2013). *Nephrol Dial Transplant* 2016; 31: 1957–1965.
42. Saliem S, Patenaude V and Abenhaim HA. Pregnancy outcomes among renal transplant recipients and patients with end-stage renal disease on dialysis. *J Perinat Med* 2016; 44: 321–327.
43. Santos S, Malheiro J, Campos A, et al. Pregnancy in renal transplant recipients: obstetric outcomes and risk of allosensitization. *Medicine* 2016; 95.
44. Sarween N, Hughes S, Evison F, et al. Pregnancy outcomes in renal transplant recipients in England over 15 years. *Nephrol Dial Transplant* 2016; 31: i6.
45. Stoumpos S, McNeill SH, Gorrie M, et al. Obstetric and long-term kidney outcomes in renal transplant recipients: a 40-yr single-center study. *Clin Transplant* 2016; 30: 673–681.
46. Yoshikawa Y, Uchida J, Akazawa C, et al. Analyses of relationship between obstetric complications and preterm delivery in Japanese recipients received kidney transplant. *Transplantation* 2016; 100: S884–S885.
47. Akturk S, Celebi ZK, Erdogmus S, et al. Pregnancy after kidney transplantation: outcomes, tacrolimus doses, and trough levels. *Transplant Proc* 2015; 47: 1442–1444.
48. Arab K, Oddy L, Patenaude V, et al. Obstetrical and neonatal outcomes in renal transplant recipients. *J Matern Fetal Neonatal Med* 2015; 28: 162–167.
49. ErmanAkar M, Ozekinci M, Sanhal C, et al. A retrospective analysis of pregnancy outcomes after kidney transplantation in a single center. *Gynecol Obstet Invest* 2015; 79: 13–18.
50. Yeon HK, Shim JY, Won HS, et al. Risk factors for developing the preeclamptic disorder in the pregnancy after kidney transplantation. *J Perinat Med* 2015; 43: 1293.
51. Debska-Slizien A, Galgowska J, Chamienia A, et al. Pregnancy after kidney transplantation: a single-center experience and review of the literature. *Transplant Proc* 2014; 46: 2668–2672.
52. Farr A, Bader Y, Husslein PW, et al. Ultra-high-risk pregnancies in women after renal transplantation. *Eur J Obstet Gynecol Reprod Biol* 2014; 180:72–76.
53. Hebral AL, Cointault O, Connan L, et al. Pregnancy after kidney transplantation: outcome and anti-human leucocyte antigen alloimmunization risk. *Nephrol Dial Transplant* 2014; 29: 1786–1793.
54. You JY, Kim MK, Choi SJ, et al. Predictive factors for adverse pregnancy outcomes after renal transplantation. *Clin Transplant* 2014; 28: 699–706.
55. Blume C, Sensoy A, Gross MM, et al. A comparison of the outcome of pregnancies after liver and kidney transplantation. *Transplantation* 2013; 95: 222–227.
56. Guella A and Mohamed E. Pregnancy in Saudi kidney transplant recipients: a local experience. *Transplant Int* 2013; 26: 287.
57. Rachdi M, Amine BH, Mohamed B, et al. Pregnancy after renal transplantation and neonatal outcome. *J Perinat Med* 2013; 41.
58. Ribeiro R, Grecco R, Ribeiro T, et al. Analysis of obstetrical and neonatal outcomes in pregnant women post renal transplantation. *J Perinat Med* 2013; 41.
59. Rocha A, Cardoso A, Malheiro J, et al. Pregnancy after kidney transplantation: graft, mother, and newborn complications. *Transplant Proc* 2013; 45: 1088–1091.
60. Wyld ML, Clayton PA, Jesudason S, et al. Pregnancy outcomes for kidney transplant recipients. *Am J Transplant* 2013; 13: 3173–3182
61. Kennedy C, Hussein W, Spencer S, et al. Reproductive health in Irish female renal transplant recipients. *Ir J Med Sci* 2012; 181: 59–63.
62. Neyatani N, Yamaguchi N, Takagi H, et al. Clinical study on fertility in women received renal transplantation. *Int J Gynecol Obstet* 2012; 119: S435–S436.
63. Van Buren MC, Van De Wetering J, Roodnat JI, et al. Pregnancy after kidney transplantation: "Will mothers see their children grow up?" *Transplantation* 2012; 94: 141.
64. Celik G, Toz H, Ertilav M, et al. Biochemical parameters, renal function, and outcome of pregnancy in kidney transplant recipient. *Transplant Proc* 2011; 43: 2579–2583.
65. Gerlei Z, Wettstein D, Rigo J, et al. Childbirth after organ transplantation in Hungary. *Transplant Proc* 2011; 43: 1223–1224.
66. Lopez V, Martinez D, Vinolo C, et al. Pregnancy in kidney transplant recipients: effects on mother and newborn. *Transplant Proc* 2011; 43: 2177–2178.
67. Xu LG, Han S, Liu Y, et al. Timing, conditions, and complications of post-operative conception and pregnancy in female renal transplant recipients. *Cell Biochem Biophys* 2011; 61: 421–426.
68. Gorgulu N, Yelken B, Caliskan Y, et al. Does pregnancy increase graft loss in female renal allograft recipients? *Clin Exp Nephrol* 2010; 14: 244–247.
69. Areia A, Galvao A, Pais MS, et al. Outcome of pregnancy in renal allograft recipients. *Arch Gynecol Obstet* 2009; 279: 273–277.
70. Gill JS, Zalunardo N, Rose C, et al. The pregnancy rate and live birth rate in kidney transplant recipients. *Am J Transplant* 2009; 9: 1541–1549.

71. Levidiotis V, Chang S and McDonald S. Pregnancy and maternal outcomes among kidney transplant recipients. *J Am Soc Nephrol* 2009; 20: 2433–2440.
72. Rizvi SAH, Kumari K, Naqvi R, et al. An update on pregnancy outcome in renal transplant recipients. *Am J Transplant* 2009; 9: 518–519.
73. Sharma U and Minocha S. O617 Pregnancy after renal transplant – Oman perspective. *Int J Gynecol Obstet* 2009; 107: S269.
74. Al Duraihimh H, Ghamdi G, Moussa D, et al. Outcome of 234 pregnancies in 140 renal transplant recipients from five middle eastern countries. *Transplantation* 2008; 85: 840–843.
75. Alfi AY, Al-essawy MA, Al-lakany M, et al. Successful pregnancies post renal transplantation. *Saudi J Kidney Dis Transpl* 2008; 19: 746–750.
76. Cruz Lemini MC, Ibargüengoitia Ochoa F and Villanueva González MA. Perinatal outcome following renal transplantation. *Int J Gynaecol Obstet* 2007; 96: 76–79
77. Oliveira LG, Sass N, Sato JL, et al. Pregnancy after renal transplantation – a five-yr single-center experience. *Clin Transplant* 2007; 21: 301–304.
78. Sibanda N, Briggs JD, Davison JM, et al. Pregnancy after organ transplantation: a report from the UK transplant pregnancy registry. *Transplantation* 2007; 83: 1301–1307.
79. Yassaee F and Moshiri F. Pregnancy outcome in kidney transplant patients. *Urol J* 2007; 4: 14–17.
80. Kurata A, Matsuda Y, Tanabe K, et al. Risk factors of preterm delivery at less than 35 weeks in patients with renal transplant. *Eur J Obstet Gynecol Reprod Biol* 2006; 128: 64–68.
81. Rahamimov R, Ben-Haroush A, Wittenberg C, et al. Pregnancy in renal transplant recipients: long-term effect on patient and graft survival. A single-center experience. *Transplantation* 2006; 81: 660–664.
82. Galdo T, Gonzalez F, Espinoza M, et al. Impact of pregnancy on the function of transplanted kidneys. *Transplant Proc* 2005; 37: 1577–1579.
83. Garcia-Donaire JA, Acevedo M, Gutierrez MJ, et al. Tacrolimus as basic immunosuppression in pregnancy after renal transplantation. A single-center experience. *Transplant Proc* 2005; 37: 3754–3755.
84. Ghanem ME, El-Baghdadi LA, Badawy AM, et al. Pregnancy outcome after renal allograft transplantation: 15 years experience. *Eur J Obstet Gynecol Reprod Biol* 2005; 121: 178–181.
85. Pour-Reza-Gholi F, Nafar M, Farrokhi F, et al. Pregnancy in kidney transplant recipients. *Transplant Proc* 2005; 37: 3090–3092.
86. Yildirim Y and Uslu A. Pregnancy in patients with previous successful renal transplantation. *Int J Gynaecol Obstet* 2005; 90: 198–202.
87. Keitel E, Bruno RM, Duarte M, et al. Pregnancy outcome after renal transplantation. *Transplant Proc* 2004; 36: 870–871.
88. Pezeshki M, Taherian AA, Gharavy M, et al. Menstrual characteristics and pregnancy in women after renal transplantation. *Int J Gynaecol Obstet* 2004; 85: 119–25.
89. Hooi LS, Rozina G, Shaariah MY, et al. Pregnancy in patients with renal transplants in Malaysia. *Med J Malaysia* 2003; 58: 27–36.
90. Queipo-Zaragoza JA, Vera-Donoso CD, Soldevila A, et al. Impact of pregnancy on kidney transplant. *Transplant Proc* 2003; 35: 866–867.
91. Thompson BC, Kingdon EJ, Tuck SM, et al. Pregnancy in renal transplant recipients: the Royal Free Hospital experience. *QJM* 2003; 96: 837–844.
92. Sgro MD, Barozzino T, Mirghani HM, et al. Pregnancy outcome post renal transplantation. *Teratology* 2002; 65: 5–9.
93. Tan PK, Tan AS, Tan HK, et al. Pregnancy after renal transplantation: experience in Singapore General Hospital. *Ann Acad Med Singapore* 2002; 31: 285–289.
94. Park Y, Cho J, Kim Y, et al. 360 Pregnancy outcome in renal transplant recipients: the experience of a single center in Korea. *Am J Obstet Gynecol* 2001; 185: S180.
95. Kuvacic I, Sprem M, Skrablin S, et al. Pregnancy outcome in renal transplant recipients. *Int J Gynaecol Obstet* 2000; 70: 313–317.
96. Little MA, Abraham KA, Kavanagh J, et al. Pregnancy in Irish renal transplant recipients in the cyclosporine era. *Ir J Med Sci* 2000; 169: 19–21.
97. Moon JI, Park SG, Cheon KO, et al. Pregnancy in renal transplant patients. *Transplant Proc* 2000; 32: 1869–1870.
98. Ventura A, Martins L, Dias L, et al. Pregnancy in renal transplant recipients. *Transplant Proc* 2000; 32: 2611–2612.
99. Arsan A, Guest G, Gagnadoux MF, et al. Pregnancy in renal transplantation: a pediatric unit report. *Transplant Proc* 1997; 29: 2479.
100. Rahbar K and Forghani F. Pregnancy in renal transplant recipients: an Iranian experience with a report of triplet pregnancy. *Transplant Proc* 1997; 29: 2775.
101. Rieu P, Neyrat N, Hiesse C, et al. Thirty-three pregnancies in a population of 1725 renal transplant patients. *Transplant Proc* 1997; 29: 2459–2460.
102. al Hassani MK, Sharma U, Mohsin N, et al. Pregnancy in renal transplantation recipients: outcome and complications in 44 pregnancies. *Transplant Proc* 1995; 27: 2585.
103. Sabagh TO, Eltorkey MM, El Awad MA, et al. Outcome of pregnancy in renal transplant recipients taking cyclosporin a. *J Obstet Gynaecol* 1995; 15: 226–229.
104. Saber LT, Duarte G, Costa JA, et al. Pregnancy and kidney transplantation: experience in a developing country. *Am J Kidney Dis* 1995; 25: 465–470.
105. Wong KM, Bailey RR, Lynn KL, et al. Pregnancy in renal transplant recipients: the Christchurch experience. *N Z Med J* 1995; 108: 190–192.
106. Hadi HA, Stafford CR, Williamson JR, et al. Pregnancy outcome in renal transplant recipients: experience at the Medical College of Georgia and review of the literature. *South Med J* 1986; 79: 959–964.
107. Talaat KM, Tyden G, Bjorkman U, et al. Thirty successful pregnancies in organ transplant recipients: a single-center experience. *Transplant Proc* 1994; 26: 1773.
108. Pahl MV, Vaziri ND, Kaufman DJ, et al. Childbirth after renal transplantation. *Transplant Proc* 1993; 25: 2727–2731.
109. Muirhead N, Sabharwal AR, Rieder MJ, et al. The outcome of pregnancy following renal transplantation – the experience of a single center. *Transplantation* 1992; 54: 429–432.
110. Brown JH, Maxwell AP and McGeown MG. Outcome of pregnancy following renal transplantation. *Ir J Med Sci* 1991; 160: 255–256.

111. Sturgiss SN and Davison JM. Perinatal outcome in renal allograft recipients: prognostic significance of hypertension and renal function before and during pregnancy. *Obstet Gynecol* 1991; 78: 573–577.
112. O'Connell PJ, Caterson RJ, Stewart JH, et al. Problems associated with pregnancy in renal allograft recipients. *Int J Artif Organs* 1989; 12: 147–152.
113. Ha J, Kim SJ and Kim ST. Pregnancy following renal transplantation. *Transplant Proc* 1994; 26: 2117–2118.
114. Marushak A, Weber T, Bock J, et al. Pregnancy following kidney transplantation. *Acta Obstet Gynecol Scand* 1986; 65: 557–559.
115. O'Donnell D, Sevitz H and Seggie JL. Pregnancy after renal transplantation. *Aust NZ J Med* 1985; 15: 320–325.
116. Waltzer WC, Coulam CB, Zincke H, et al. Pregnancy in renal transplantation. *Transplant Proc* 1980; 12: 221–226.
117. Hamilton BE, Martin JA, Osterman MJK. Births: Provisional data for 2021. Vital Statistics Rapid Release; no 20. Hyattsville, MD: National Center for Health Statistics. May 2022
118. Kortsmit K, Nguyen AT, Mandel MG, et al. Abortion surveillance – United States, 2020. *MMWR Surveill Summ*, 2022; 71: 1–27.
119. Gregory ECW, Valenzuela CP, Hoyert DL. Fetal mortality: United States, 2020. National Vital Statistics Reports; vol 71 no 4. Hyattsville, MD: National Center for Health Statistics. 2022.
120. Shah S, Venkatesan RL, Gupta A, et al. Pregnancy outcomes in women with kidney transplant: metaanalysis and systematic review. *BMC Nephrol* 2019; 20: 24.
121. Osterman MJK. Changes in primary and repeat cesarean delivery: United States, 2016–2021. Vital Statistics Rapid Release; no 21. Hyattsville, MD: National Center for Health Statistics. July 2022.
122. Ananth CV, Keyes KM and Wapner RJ. Pre-eclampsia rates in the United States, 1980–2010: age-period-cohort analysis. *BMJ* 2013; 347.
123. Gregory ECW, Ely DM. Trends and characteristics in gestational diabetes: United States, 2016–2020. National Vital Statistics Reports; vol 71 no 3. Hyattsville, MD: National Center for Health Statistics. 2022.
124. World Health Organization. Preterm birth, www.who.int/news-room/fact-sheets/detail/preterm-birth (2023, accessed 9 June 2023).
125. Pathirana J, Muñoz FM, Abbing-Karahagopian V, et al. Neonatal death: case definition & guidelines for data collection, analysis, and presentation of immunization safety data. *Vaccine* 2016; 34: 6027–6037.
126. Centers for Disease Control and Prevention. Products – vital statistics rapid release – infant mortality, www.cdc.gov/nchs/nvss/vsrr/infant-mortality.htm (2023, accessed 9 June 2023).
127. Declercq E, Wolterink A, Rowe R, et al. The natural pattern of birth timing and gestational age in the U.S. compared to England, and the Netherlands. *PLoS One* 2023; 18: e0278856.
128. Donahue SM, Kleinman KP, Gillman MW, et al. Trends in birth weight and gestational length among singleton term births in the United States: 1990–2005. *Obstet Gynecol* 2010; 115: 357–364.
129. Health Resources and Services Administration. OPTN/SRTR 2019 Annual Data Report: Kidney, https://srtr.transplant.hrsa.gov/annual_reports/2019/Kidney.aspx (accessed 9 June 2023).
130. Moritz MJ, Constantinescu S, Coscia LA, et al. *Transplant Pregnancy Registry International 2017 Annual Report*. Philadelphia: Gift of Life Institute, 2018.
131. Fontana I, Santori G, Fazio F, et al. The pregnancy rate and live birth rate after kidney transplantation: a single-center experience. *Transplant Proc* 2012; 44: 1910–1911.
132. Deshpande NA, James NT, Kucirka LM, et al. Pregnancy outcomes in kidney transplant recipients: a systematic review and meta-analysis: pregnancy outcomes in kidney transplant recipients. *Am J Transplant* 2011; 11: 2388–2404.
133. McKay DB and Josephson MA. Pregnancy after kidney transplantation. *Clin J Am Soc Nephrol* 2008; 3: S117–S125.
134. del Mar Colon M and Hibbard JU. Obstetric considerations in the management of pregnancy in kidney transplant recipients. *Adv Chronic Kidney Dis* 2007; 14: 168–177.
135. Coscia, L. A., Constantinescu, S., Moritz, M. J., Frank, A. M., Ramirez, C. B., Maley, W. R., Doria, C., McGrory, C. H., & Armenti, V. T. (2010). *Clinical transplants* (Chapter 7).
136. Klein CL and Josephson MA. Post-transplant pregnancy and contraception. *Clin J Am Soc Nephrol* 2022; 17: 114–120.
137. Coscia LA, Armenti DP, King RW, et al. Update on the teratogenicity of maternal mycophenolate mofetil. *J Pediatr Genet* 2015; 4: 42–55
138. Hewawasam E, Davies CE, Li Z, et al. Determinants of perinatal outcomes in dialyzed and transplanted women in Australia. *Kidney Int Rep* 2022; 7: 1318–1331.
139. Sayin B, Akdur A, Dogan B, et al. P8. 112: Pregnancy outcomes in kidney transplant recipients and their newborns. *Transplantation* 2022; 106: S610.
140. Haas M and Mayer G. Cyclosporin A-associated hypertension – pathomechanisms and clinical consequences. *Nephrol Dial Transplant* 1997; 12: 395–398.
141. Armenti VT, Daller JA, Constantinescu S, et al. Report from the National Transplantation Pregnancy Registry: outcomes of pregnancy after transplantation. *Clin Transpl* 2006: 57–70.
142. Cosio FG, Pesavento TE, Kim S, et al. Patient survival after renal transplantation: IV. Impact of post-transplant diabetes. *Kidney Int* 2002; 62: 1440–1446.
143. Gordon EJ, Ladner DP, Caicedo JC, et al. Disparities in kidney transplant outcomes: a review. *Semin Nephrol* 2010; 30: 81–89.
144. Wielgos M, Szpotanska-Sikorska M, Mazanowska N, et al. Pregnancy risk in female kidney and liver recipients: a retrospective comparative study. *J Matern Fetal Neonatal Med* 2012; 25: 1090–1095.
145. Madej A, Mazanowska N, Szpotańska-Sikorska M, et al. Delivery method in patients after liver or kidney transplantation. *Transplant Proc* 2018; 50: 2150–2153.
146. Yin O, Kallapur A, Coscia L, et al. Mode of obstetric delivery in kidney and liver transplant recipients and associated maternal, neonatal, and graft morbidity during 5 decades of clinical practice. *JAMA Netw Open* 2021; 4: e2127378.