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Embryo donation: national trends and outcomes, 2000 through 2013

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Abstract

BACKGROUND: Limited published data exist detailing outcomes of donor embryo cycles. Patients and clinicians would benefit from information specific to donor embryo cycles to inform fertility treatment options, counselling, and clinical decision-making.

OBJECTIVE: We sought to quantify trends in donor embryo cycles in the United States, to characterize donor embryo recipients, and to report transfer, pregnancy, and birth outcomes of donor embryo transfers.

STUDY DESIGN: This retrospective cohort study of frozen donor embryo transfers uses data from Centers for Disease Control and Prevention National ART Surveillance System to quantify trends in the use of donor embryos and corresponding rates of pregnancy and live birth from 2000 through 2013. For 2007 through 2013, years reflective of current practice, rates of cancellation, pregnancy, miscarriage, live birth, singleton and twin live birth, and delivery of a full-term singleton infant of normal birthweight (< 37 weeks, < 2500 g) are reported.

RESULTS: Among all frozen transfers from 2000 through 2013 (n = 391,662), the annual number of donor embryo transfers increased significantly from 332–1374, however the proportion of donor embryo transfers among all frozen transfers did not change significantly (2.3–2.6%). Both overall pregnancy and live birth rates per frozen donor embryo transfer increased significantly (33.3–49.1% and 26.5–40.8%, respectively) ($P < .01$). Among all initiated donor

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embryo cycles from 2007 through 2013 (n = 7289), the overall cancellation rate prior to transfer was 7.1%. Among all transfers from 2007 through 2013 (n = 6773), 3193 (47.2%) resulted in pregnancy and 2589 (38.2%) resulted in a live birth. Among all pregnancies, 535 (16.9%) resulted in a miscarriage. Among all live births, 1929 (74.5%) delivered a singleton of which 1482 (76.8%) were full term and normal birthweight.

CONCLUSION: The increasing availability of donor embryos, low chance of cancellation, and increasing likelihood of achieving live birth can inform consumers and providers who are considering assisted reproductive technology options. Collection of data surrounding donated embryo formation would allow for additional studies that can elucidate predictors of success among donor embryo transfers.

Keywords

donor; embryo; in vitro fertilization; live birth; outcome; pregnancy; success

Introduction

With the increasing use of assisted reproductive technology (ART), the number of cryopreserved embryos in storage has increased, as residual viable embryos from an in vitro fertilization (IVF) cycle may be frozen for future use. Each embryo maintains attributes reflective of the age of the female at time of the original oocyte retrieval. Embryo donation, a form of third-party reproduction, involves donation without compensation of previously formed embryos to another couple for implantation. The American Society for Reproductive Medicine Ethics Committee suggests that the donation of embryos to a recipient couple to “support family-building efforts of others is an important option for patients considering the disposition of cryopreserved embryos in excess of those needed to meet the patients’ own fertility goals.”¹ Use of donated embryos may be particularly appealing to a couple with both male and female factors contributing to their infertility, to an individual who requires both an oocyte and sperm donor, and to patients who are drawn to the relative affordability of a donor embryo cycle as compared to either an autologous or donor oocyte cycle.

Currently, limited published data exist detailing outcomes of donor embryo cycles. Two prior studies published in 2000 through 2003 surveyed ART clinics to determine the proportion of clinics that performed donor embryo transfers² and the percentage of embryos potentially available to donate to another couple.³ Previously published outcome data from the United States only include data through 2008 and a small number of clinics and embryo donation agencies.^{4–6} The most comprehensive study published in 2012 includes cycles from 2001 through 2008 in several European countries and the United States and reports a live birth rate per transfer ranging from 14–33%; the US contribution (2001 through 2007) included 4595 donor embryo transfers that resulted in 1510 (33%) live births.⁷ To our knowledge, no published national outcomes data reflective of current practice exist for donor embryo transfers performed in the United States since 2007; such information would be helpful in patient counselling.

We aimed to describe national donor embryo trends from 2000 through 2013 and recipient characteristics and donor embryo outcomes from 2007 through 2013 in the United States.

Materials and Methods

The National ART Surveillance System (NASS), a federally mandated reporting system that captured >95% of ART cycles performed in the United States from 2000 through 2013, was used to study trends and outcomes of donated embryo transfers.⁸ Donor embryo cycles are cycles involving “embryos derived from oocytes previously fertilized for another couple’s ART therapy that were subsequently donated.”⁸ We restricted our analysis to frozen cycles as embryos are typically donated after they have been cryopreserved; 6773 of the 6838 or 99% of the reported donor embryo cycles were frozen cycles. NASS contains cycle-level data including patient demographics, medical and obstetric history, infertility diagnoses, detailed parameters of each ART treatment cycle and, if applicable, the resultant pregnancy outcome. Limited data regarding donated embryos’ origins are collected in NASS. No data are collected regarding the genetic patients’ reason for using ART, the outcome of the original ART cycle (whether it resulted in pregnancy or not), or the embryos’ stages (cleavage or blastocyst) at cryopreservation or subsequent transfer. Age of the oocyte source at the time of the donated embryo’s creation was added to NASS in 2007.

Trends in the absolute number of frozen donor embryo transfers, percentage of frozen donor embryo transfers among all ART frozen transfers, average recipient age, and overall pregnancy and live birth rates per frozen donor embryo transfer are reported from 2000 through 2013. We calculated the trend in the average age of the donor embryo oocyte source, equivalent to oocyte age at time of retrieval, from 2007 through 2013 (the years for which oocyte age was available); however, these results should be interpreted with caution as 65.3% of the donor cycles performed during this period were missing oocyte age information. Linear regression was used to explore trends in the number of cycles and average ages and binomial regression with an identity link was used to explore trends in the proportion of cycles from 2000 through 2013. We tested for quadratic and linear trends, and used generalized estimating equations to adjust for clustering by clinic.

We then investigated characteristics and outcomes of donor embryo transfers performed during 2007 through 2013. We used more recent years since the age of the oocyte donor source was collected in NASS during this period and the results would be more relevant to current practice and patient counselling. We reported the number and percentage of clinics in each geographic region of the United States performing donor embryo transfers. Next, we detailed recipient and cycle characteristics of donor embryo transfer cycles. Finally, we explored outcomes, reporting the number and percentage of frozen donor embryo transfers resulting in intrauterine pregnancy and live birth (the birth of at least 1 live born infant at 20 weeks); the number and percentage of pregnancies after frozen donor embryo transfer resulting in miscarriage (complete loss of the pregnancy at <20 weeks); and the number and percentage of live births after frozen donor embryo transfer resulting in singletons, twins, and full-term and normal birthweight (>37 weeks and >2500 g). Among those cycles for which oocyte donor age was available (n = 2347), we calculated pregnancy and live birth rate per transfer and miscarriage rate per cycles among cycles for which the oocyte donor was <35, 35–37, and ≥38 years at time of oocyte retrieval.

This study was approved by the Institutional Review Board of the Centers for Disease Control and Prevention. All statistical tests were 2-sided and statistical significance was determined using an alpha level of 0.05. All analyses were conducted using software (SAS, v. 9.3; SAS Institute Inc, Cary, NC).

Results

From 2000 through 2013, 10,883 frozen donor embryo transfers were performed in the United States. The number of transfers increased significantly from 332 in 2000 to 1374 in 2013 (Figure, A). However, among all frozen embryo transfers ($n = 391,662$), the proportion of donor embryo transfers did not change significantly (2.3–2.6%). The overall pregnancy rate per frozen donor embryo transfer increased significantly from 33.3–49.1%, and the overall live birth rate increased significantly from 26.5–40.8% (Figure, B). The mean recipient age remained stable at 39 years ($P = .66$). From 2007 through 2013, the average age of the oocyte source at time of retrieval ranged from 29.8–34.7 years; however, the percentage of missing data for this variable during this period was 65.3%.

In 2007, 170 (39.5%) of the existing 430 clinics performed at least 1 donor embryo transfer. In 2013, 201 (43.0%) of the existing 467 clinics performed at least 1 donor embryo transfer.

Most clinics performed between 1–10 donor embryo transfers per year (88.2% in 2007 and 83.6% in 2013). The percentage of clinics within each region of the United States that performed at least 1 donor embryo transfer over the 2007 through 2013 study period were as follows: Northeast (53.3%), South (60.2%), Midwest (61.5%), and West (63.4%).

Of all the donor embryo transfers performed from 2007 through 2013 ($n = 6773$), for cycles where age was reported, the majority of embryos originated from women who were age <35 years at the time of oocyte retrieval (Table 1). The majority of recipients were age 38 years, however women in all age groups underwent transfers using donor embryos. The majority of recipients were non-Hispanic white, held an infertility diagnosis of diminished ovarian reserve and/or male factor infertility, had previously failed at least 1 IVF cycle, had undergone at least 2 prior cycles, and had never been pregnant. Two donor embryos were most frequently transferred; in 4.1% of cycles >3 embryos were transferred.

Among all initiated donor embryo cycles from 2007 through 2013 ($n = 7289$), 431 (5.9%) were cancelled prior to donor embryo thaw, and 85 (1.2%) were canceled after embryos were thawed but before transfer. The overall donor embryo cycle cancellation rate was 7.1%.

Among all donor embryo cycles for which a transfer was performed ($n = 6773$ transfers) from 2007 through 2013, 3193 (47.2%) resulted in pregnancy and 2589 (38.2%) resulted in a live birth (Table 2). Among all transfers resulting in pregnancy ($n = 3166$), 535 (16.9%) resulted in a miscarriage. Among all pregnancies resulting in live birth ($n = 2589$), 1929 (74.5%) delivered a singleton, of which 1482 (76.8%) were full term and normal birthweight. Among all live births, 613 (23.7%) were twin births, and 47 (1.8%) were triplet or higher-order births.

Among those cycles (n = 2347) for which oocyte donor age was available, pregnancy, live birth, and miscarriage rates were as follows: age <35 years (53.1% pregnancy rate per transfer, 44.0% live birth rate per transfer, and 14.6% miscarriage rate per pregnancy), age 35–37 years (44.8% pregnancy rate per transfer, 35.1% live birth rate per transfer, and 20.3% miscarriage rate per pregnancy), and age ≥ 38 years (43.6% pregnancy rate per transfer, 34.4% live birth rate per transfer, and 20.3% miscarriage rate per pregnancy).

Comment

From 2000 through 2013, the annual number of donor embryo transfers and the likelihood of achieving pregnancy and live birth after a donor embryo transfer increased significantly, but the overall percentage among all frozen cycles did not change. No significant patterns were noted in the geographic distribution of clinics performing donor embryo transfers in the United States. For donor embryo cycles initiated from 2007 through 2013, the cancellation rate was low and, among successful pregnancies resulting in a live birth, the majority of women delivered a singleton of normal birthweight at term.

The miscarriage rate in embryo donation cycles was similar to national averages among frozen embryo transfers.⁹ The pregnancy rate and live birth rate in our study are comparable, although slightly higher, than previously reported. Prior reported live birth rates per transfer were as low as 17%,^{4–6} with more recent studies reporting live birth rates of 35% and 33% as compared to our 38% per donor embryo transfer.^{6,7} The increase likely reflects improvements in controlled ovarian stimulation, embryo culture, and embryo cryopreservation (transition from slow freezing to vitrification) that are also reflected in the steadily increasing pregnancy rates among autologous ART cycles.⁸ Admittedly, we cannot determine which of these factors is most responsible for the improvement. Nonetheless, donor embryo transfers, then, are a viable option for infertile individuals or couples that may wish to avoid either the financial or physical toll of an autologous or donor oocyte IVF cycle, with the caveat that neither individual will be genetically related to the fetus. The cost of an embryo donation cycle is roughly one third of that of an autologous cycle and one fourth of that of a donor oocyte cycle since the embryos are already formed and the donating couple is not compensated.¹⁰ The success rates in donor embryo cycles are lower than donor oocyte cycles, which are often used to overcome female age-related fertility factors; among all (fresh/noncryopreserved and frozen/cryopreserved) donor egg transfers (n = 113,809) from 2007 through 2013, the overall chance of pregnancy and live birth per transfer were 57.2% and 47.8%, respectively.¹¹ The lower chance of pregnancy with donor embryo as compared to donor egg may reflect the fact that the donor embryos' original parents likely used the best-quality embryos and donated remaining embryos that may be of lesser quality. Additionally, oocyte donors are typically purposely chosen because of their young age; donated embryos may originate from the oocytes of older women on average.

Limitations of the study include the lack of data about the cycle from which the donated embryos originated; the genetic parents' reason for infertility, embryo stage at transfer, number of supernumerary embryos initially cryopreserved, use of preimplantation genetic screening, and outcome of the initial treatment, which would have allowed for analysis of predictors of success among donor embryo transfers. Additionally, the amount of missing

data for age of oocyte source at time of initial retrieval made a comparative analysis between donor embryo transfers and another group less feasible, as the primary predictor of success is known to be oocyte age. The study is also limited by factors intrinsic to using a large surveillance system in that collected variables are dependent on the accuracy of individual clinic entry. Additionally, cycles are not linked; if an individual couple donated embryos to multiple couples, each transfer would contribute separately to the results.

The study is strengthened by its comprehensiveness and generalizability. The study incorporates the most recent available data and reflects current ART practice, important attributes in the rapidly changing field of reproductive medicine. Additionally, because the study includes all reporting clinics in the United States, the results are relevant to women across the country that are considering using donor embryos.

The increasing availability of donor embryos, low chance of cancellation, and increasing likelihood of achieving pregnancy and live birth with a low miscarriage rate suggest that transfer of donated embryos is a viable option. Our findings can be used by clinicians when discussing the likelihood of pregnancy and live birth with their patients who are deciding whether or not to pursue donor embryo transfer. Collection of data surrounding donated embryo formation would allow for additional studies that can elucidate predictors of success among donor embryo transfers.

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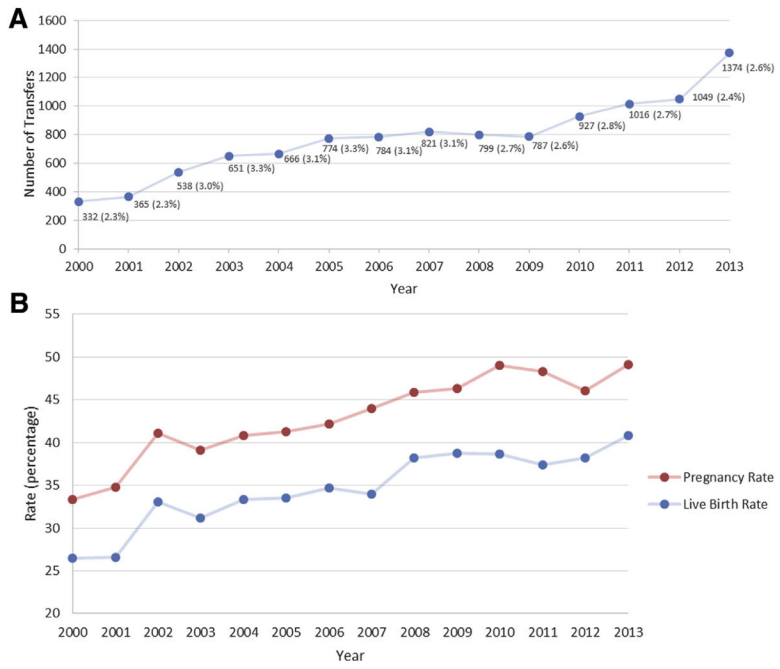


FIGURE. Frozen embryo transfers and overall pregnancy and live birth rates, 2000–2013
A, Number of frozen donor embryo transfers and percentage of all frozen embryo transfers performed. $P < 0.01$
B, Overall pregnancy and live birth rates per frozen donor embryo transfer. United States, 2000 through 2013. $P < 0.01$ for both pregnancy and live birth rates.

TABLE 1

Recipient characteristics of frozen donor embryo transfers, 2007 through 2013

	Donor embryo	
	n	%
Total	6773	100.0
Age of woman providing oocyte at retrieval, y		
<35	1598	23.6
35–37	319	4.7
38–40	188	2.8
41–42	80	1.2
43	162	2.4
Missing ^a	4426	65.3
Recipient age, y		
<35	1538	22.7
35–37	905	13.4
38–40	1133	16.7
41–42	986	14.6
43	2211	32.6
Recipient race/ethnicity		
Non-Hispanic white	4271	63.1
Non-Hispanic black	169	2.5
Hispanic	222	3.3
Other	182	2.7
Missing ^a	1929	28.5
Recipient infertility diagnosis ^b		
Diminished ovarian reserve	3483	51.4
Male factor	2171	32.1
Endometriosis	653	9.6
Ovulatory dysfunction	592	8.7
Tubal factor	549	8.1
Uterine factor	321	4.7
Unexplained	450	6.6
Recipient cycle history		
First IVF, no previous birth	1771	26.2
First IVF, 1 previous birth	526	7.8
1 Previous IVF, no previous birth	2867	42.3
1 Previous IVF, 1 previous birth	1556	23.0
Recipient no. of prior ART cycles		
0	2318	34.2

	Donor embryo	
	n	%
1	1541	22.8
2	2889	42.7
Recipient no. of prior pregnancies		
0	2706	40.0
1	1706	25.2
2	2337	34.5
Recipient no. of prior spontaneous abortions		
0	4298	63.5
1	1370	20.2
2	1055	15.6
Recipient no. of prior preterm births		
0	6410	94.6
1	254	3.8
2	31	0.5
Recipient no. of prior full-term births		
0	4821	71.2
1	1266	18.7
2	636	9.4
Recipient no. of embryos transferred		
1	976	14.4
2	3926	58.0
3	1595	23.6
>3	276	4.1

ART, assisted reproductive technology; *IVF*, in vitro fertilization.

^aIncluded for all characteristics with >5% missing values, for remainder of characteristics <1% missing;

^bDiagnoses are not mutually exclusive; sum is >100% as cycle may be associated with >1 diagnosis.

TABLE 2

Outcomes of frozen donor embryo transfers, pregnancies, and live births, 2007 through 2013

	n	%
Among transfers	6773	
Intrauterine pregnancy	3193	47.2
Live birth (\geq 20 wk)	2589	38.2
Among pregnancies	3166	
Miscarriage (<20 wk)	535	16.9
Among live births	2589	
Singleton	1929	74.5
Twin	613	23.7
Singleton, \geq 2500 g, \geq 37 wk	1482	57.2

All variables <2.5% missing data.

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