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Adverse Pregnancy Outcomes after In Vitro Fertilization: Effect of Number of Embryos Transferred and Plurality at Conception

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Abstract

Objective—To evaluate risks for adverse pregnancy outcomes by number of embryos transferred (ET) and fetal heart beats (FHB) in ART conceived singleton live births.

Design—Longitudinal cohort using cycles reported to the Society for Assisted Reproductive Technology Clinic Outcomes Reporting System between 2004 and 2008 among women who were treated and gave birth in Massachusetts.

Setting—Clinic-based data.

Patients—ART data on 6,073 births between 2004 and 2008 were linked to vital records and hospital data. Likelihood of ET ≥3 vs 1–2, FHB >1 vs 1, and risks of preterm birth (PTB, <37 weeks gestation), low birthweight (LBW, <2,500g), and small-for-gestational age birthweight (SGA, <10th%ile) with FHB >1 were modeled with binary logistic regression using a backward-stepping algorithm, and presented as adjusted odds ratios (AORs) and 95% confidence intervals.

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Interventions—None

Main Outcome Measures—ET≥3, FHB >1, PTB, LBW, and SGA.

Results—Higher ET was significantly more likely with older maternal age, intracytoplasmic sperm injection, assisted hatching, cleavage-stage embryos, and thawed embryos. The likelihood of FHB>1 with ≥3 ET vs 1–2 ET was 2.04 (1.68–2.48). Risks of PTB and LBW with FHB>1 were 1.63 (1.27–2.09) and 1.81 (1.36– 2.39), respectively; the risk of SGA was not significant. Nulliparity was associated with higher risks of PTB (1.34, 1.12–1.59), LBW (1.48, 1.20–1.83), and SGA (2.17, 1.69–2.78).

Conclusions—Number of ETs were strongly associated with FHBs, with twice the risk of FHB>1 with ≥3 ET versus 1–2 ET. Increasing FHBs were associated with significantly greater risks for PTB and LBW outcomes.

Keywords

assisted reproductive technology; embryos transferred; fetal heartbeats; birth outcomes

Introduction

Background

The outcomes of pregnancies conceived through assisted reproductive technology (ART) have been reported to be of lower birthweight and shorter gestation, even when limited to singleton births (1–5). It is unknown whether these decrements are due to parental characteristics or aspects of the ART treatment: this remains a primary challenge to infertility research (6–8). In particular, the effect of number of embryos transferred and plurality at conception versus plurality at birth needs further evaluation (9–12). In addition, an acknowledged drawback of prior ART research in the US has been the self-reported nature of the outcomes data, which is typically reported by the patient herself or by her obstetrical provider. This study seeks to overcome these limitations by linking the Society for Assisted Reproductive Technology Clinic Outcomes Reporting System (SART CORS) data to birth certificate and hospital utilization data.

Objective

This is the third in a series of analyses evaluating the effect of ART diagnoses and treatment parameters on the course and outcome of pregnancy (13, 14). This within-ART set of analyses is part of a larger population-based study of ART in Massachusetts (13–21). The objective of this current analysis is to evaluate the effect of number of embryos transferred (ET) and plurality at the six-week ultrasound (fetal heartbeats, FHB) on the pregnancy and birth outcomes of singleton births, specifically prematurity, low birthweight, and small-for-gestational age birthweight. These associations will be examined overall and by maternal age groups.

Methods and Materials

Study Design and Setting

This longitudinal cohort study included a woman's first singleton live birth of ≥22 weeks' gestation and ≥300g birthweight in Massachusetts between July 1, 2004 through December 31, 2008 that linked to ART cycles in the Society for Assisted Reproductive Technology Clinic Online Reporting System (SART CORS) and the Pregnancy to Early Life (PELL) data system.

Data Sources

The Pregnancy to Early Life Longitudinal (PELL) data system—The PELL system, which functions within the Massachusetts Department of Public Health, links records from birth and fetal death certificates, hospital discharges, and program data from child health and development programs. The PELL data system has linked information on more than 99% of all births and fetal deaths in Massachusetts from 1998–2008 to corresponding hospital utilization data (hospital admissions, observational stays, and emergency room visits) for individual women and their children. PELL has linked information on 860,654 deliveries from 1998 through 2008. The Massachusetts Department of Public Health (MDPH) and the Massachusetts Center for Health Information and Analysis are the custodians of the PELL data. PELL is a relational data system composed of individual databases linked together by randomly-generated unique IDs for mother and infant. The PELL data system is housed at MDPH.

The Society for Assisted Reproductive Technology Clinic Online Data Reporting System (SART CORS)—The data source for ART data for this study was the SART CORS, which contains comprehensive data from more than 90% of all clinics performing ART in the US. Data were collected and verified by SART and reported to the Centers for Disease Control and Prevention in compliance with the Fertility Clinic Success Rate and Certification Act of 1992 (Public Law 102–493). SART maintains HIPAA-compliant business associates agreements with reporting clinics. In 2004, following a contract change with CDC, SART gained access to the SART CORS data system for the purposes of conducting research. The national SART CORS database for 2004–08 contains 642,927 ART treatment cycles. The database includes information on demographic factors (age, race/ethnicity); ART factors (infertility diagnoses, oocyte source and state, use of micromanipulation [intracytoplasmic sperm injection, ICSI, and assisted hatching], number of embryos transferred); treatment outcomes (number of fetal heart beats on early ultrasound, early pregnancy loss); and pregnancy outcomes (live born, stillborn, length of gestation, plurality, and genders). The data in the SART CORS are validated annually (22) with some clinics having on-site visits for chart review based on an algorithm for clinic selection. During each visit, data reported by the clinic were compared with information recorded in patients' charts. In 2012, records for 2,045 cycles at 35 clinics were randomly selected for full validation, along with 238 egg/embryo banking cycles (22). The full validation included review of 1,318 cycles for which a pregnancy was reported. Among the non-donor cycles, 331 were multiple-fetus pregnancies. Ten out of 11 data fields selected for

validation were found to have discrepancy rates of ≤5%. The exception was the diagnosis field, which, depending on the diagnosis, had a discrepancy rate between 2.1% and 9.2%.

Massachusetts Outcome Study of Assisted Reproductive Technology (MOSART)—The Massachusetts Outcome Study of Assisted Reproductive Technology (MOSART) project links data from the SART CORS with the PELL data system to evaluate pregnancy and child health outcomes on a population basis. A Memorandum of Understanding was executed between SART and the three entities that participate in the PELL project: Boston University, the Massachusetts Department of Public Health, and the Centers for Disease Control and Prevention. Human subjects approval was obtained from all entities and participating Universities. The study had the approval of the SART Research Committee.

We constructed the MOSART database by linking the SART CORS and PELL data systems for all children born in Massachusetts hospitals to Massachusetts resident women between July 1, 2004 and December 31, 2008. The starting date was chosen based on the availability of SART CORS data (January 1, 2004) to allow us to capture any births associated with ART and the end date reflected the latest available data from both SART and PELL when we began the MOSART study. PELL data from July 1, 2004 and December 31, 2008 included 282,971 women with 334,152 deliveries resulting in 342,035 live births and fetal deaths; these were then linked to 42,649 ART cycles among 18,439 women from SART CORS using a deterministic five phase linkage algorithm methodology (15).

Participants—ART deliveries for women with treatment cycles between January 1, 2004 and December 31, 2008 and that had either a Massachusetts patient zip code or in which the treatment clinic was located in Massachusetts were obtained from SART. The linkage was done by conveying to PELL a file containing patient identifiers but no cycle specific data. Data for 9,092 ART cycles resulting in deliveries were linked to PELL birth or fetal death certificates using mother's first and last name, mother's date of birth, father's name, race of both parents, date of delivery, and number of babies born per delivery; of these, 6,512 were singletons. Of these deliveries, 439 women had two or more deliveries during this time period; these repeat pregnancies were excluded to minimize any correlated variance across these pairs of deliveries. Linked files were later de-identified by use of a linkage ID from which identifiers was removed. Methods for linkage have been described previously (15). The linkage rate was 89.7% overall and 95.0% for deliveries in which both zip code and clinic were located in MA.

Variables—Independent variables included parental ages, race/ethnicity, and education; parity; infertility diagnoses, plurality at the six-week ultrasound (FHB as 1 and >1); oocyte and semen sources; the use of ICSI and assisted hatching; embryo state (fresh or thawed), embryo stage (for fresh, autologous cycles only, day 2–3 and day 5–6), and number of embryos transferred (ET of 1–2 and ≥3). Dependent variables included ET≥3, FHB>1, and prematurity, low birth weight, and small-for-gestational age birthweight.

Parental Factors—Parental ages at delivery were obtained from the birth certificates in PELL. Parental age was evaluated as both continuous and categorical variables (<35, 35–40,

and >40). Because maternal age is critically important in the decision-making process of ART treatments, we conducted analyses of the likelihood of ET ≥3 vs 1–2 overall and by maternal age categories. Parental race/ethnicity was also obtained from the birth certificate, and categorized as white and non-white. ART treatment parameters were obtained from the SART CORS database, including parity (0 and ≥1), diagnoses (male factor, endometriosis, ovulation disorders, tubal factors, uterine factors, other factors, and unexplained); oocyte and semen sources (autologous or donor); use of ICSI and assisted hatching (no or yes), number of embryos transferred (1, 2, 3, ≥4, and 1–2 vs ≥3), number of fetal heartbeats at the six-week ultrasound (1 and >1), embryo state (fresh or thawed), and embryo stage (for fresh, autologous cycles, day 2–3 and day 5–6). Plurality at the six-week ultrasound was obtained from the SART CORS database.

Length of Gestation and Prematurity—Length of gestation was calculated by using the SART CORS outcome date minus date of transfer and adding 17 days and the cycle day of transfer, effectively the outcome date minus the date of conception (or fertilization) plus 14 days. Deliveries prior to 37 completed weeks gestation were classified as premature and those which were 37 weeks or greater were classified as term.

Low Birthweight and Small-for-Gestational Age Birthweight—Birthweight was obtained from the birth certificate. Birthweights at each gestational age are normally distributed, and a z-score (or standard deviation score) is the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population (19). Birthweight z-scores were calculated to evaluate adequacy of weight-for-age using population-based standards, as recommended by Land (24) and modeled as continuous and categorical variables. We generated gender-, race/ethnicity-, and gestation-specific birthweight means and standard deviations using Massachusetts data for all live births from 1998–2008. Infants with z-scores of ≤1.28 (below the 10^{th} percentile for gestation) were classified as small-for-gestational age (SGA). Birthweights which were less than 2,500 grams were classified as low birthweight (LBW).

Statistical Methods

We compared maternal and paternal demographic characteristics, parental reproductive and ART treatment parameters, and pregnancy and birth outcomes by the two ET groups (1–2 and ≥3) and the two FHB groups (1 and >1) using Student's t test for continuous variables and χ^2 for categorical variables. Logistic regression modeling was performed, using a backward-stepping algorithm, eliminating variables until those remaining were all significant at $p<0.05$ for 1) the likelihood of ET≥3 vs 1–2 overall and by maternal age groups; 2) the likelihood of FHB>1 vs 1 overall and by maternal age groups; and 3) the risks of adverse pregnancy outcomes (preterm birth, low birthweight, and small-for-gestational age). Results were considered significant with p values <0.05 for univariate analyses, and when the 95% confidence intervals did not include 1. All analyses were performed using the Statistical Package for the Social Sciences, version 19.0 (IBM SPSS, Inc., Chicago, IL, USA, 2010).

Results

Participants

The 6,073 ART cycles which resulted in singleton live births were categorized into two ET groups (1–2 and ≥3) and two FHB groups (1 and >1).

Descriptive and Outcome Data

The descriptive statistics of the 6,073 singleton live births are shown in Table 1. Women with fewer ET were significantly younger; more likely to be nulliparous; have the diagnoses of male factor or ovulation disorders; and to have blastocyst-stage embryos to transfer. Women with more ET had higher parity; were more likely to have the diagnoses of tubal factor, other factors, or unexplained; to have intracytoplasmic sperm injection or assisted hatching performed; and to have cleavage-stage embryos to transfer. Birth outcomes did not differ significantly by ET groups. Higher FHB was significantly associated with older maternal and paternal ages, the use of assisted hatching, shorter length of gestation and more prematurity, lower birthweight and more LBW, and lower mean birthweight z-score.

The likelihood of ET ≥3 vs 1–2 overall and by maternal age categories is shown in Table 2. Overall, the likelihood of ET≥3 increased with maternal age, the diagnoses of tubal factor and other factors, the use of ICSI and assisted hatching, thawed embryos, and cleavage-stage embryos; and decreased with the diagnoses of male factor and ovulation disorders, and the use of donor oocytes. Within each of the maternal age categories, the use of assisted hatching and cleavage-stage embryos were associated with an increased likelihood of ET ≥3 vs 1–2. Among women younger than age 35, the likelihood of ET ≥3 vs 1– 2 increased with the diagnosis of other factor, the use of ICSI, and thawed embryos; and decreased with the diagnosis of male factor. Among women ages 35–40 years of age, the likelihood of ET ≥3 vs 1–2 increased with the diagnosis of tubal factor and the use of ICSI; and decreased with the diagnosis of male factor or ovulation disorders. Among women older than 40 years of age, the likelihood of ET ≥3 vs 1–2 decreased with the use of donor oocytes.

The likelihood of FHB>1 by ET overall and by maternal age categories are shown in Table 3. ET ≥3 was associated with an increased likelihood of FHB>1 overall and among women ages 40 and younger. The use of donor oocytes and assisted hatching in the overall model were also associated with FHB>1; assisted hatching was also significant for women younger than age 35 years. No factors were significant in the model of women over age 40 years.

The risks for adverse pregnancy outcomes by FHB are shown in Table 4. Nulliparity was associated with significantly higher risks for all three adverse outcomes. The risk of preterm birth decreased with the diagnosis of male factor, and increased with the use of donor oocytes, thawed embryos, and FHB>1. The risk of low birthweight decreased with the diagnoses of male factor and endometriosis, and increased with FHB>1. The risk for small-for-gestational age birthweight decreased with the use of thawed embryos.

Discussion

This analysis found that 1) the use of assisted hatching and cleavage-stage embryos was associated with a significantly greater likelihood of transferring ≥3 embryos compared to 1–2 embryos; 2) the number of embryos transferred was significantly associated with plurality at six-week's gestation (higher FHB), 3) which in turn was associated with greater risks for prematurity and low birthweight. In this analysis, factors associated with transferring a higher number of embryos reflected suboptimal maternal conditions (older age and the use of autologous oocytes), less favorable oocyte or embryo quality, less favorable prognosis, or unsuccessful prior cycles (the use of micromanipulation, embryos which were thawed or cleavage-stage), in accord with current national guidelines [25].

The goal of contemporary ART is a singleton pregnancy resulting in a healthy singleton infant born at full-term [26–28]. In 1998, the Society for Assisted Reproductive Technology issued the first clinical guidelines on the number of embryos to transfer with the goal of reducing the number of multiple births from ART. These guidelines have been revised downward in 1999, 2004, 2006, 2008, 2009, and most recently in 2013 [25, 29–34]. The results have been a national reduction in the number of embryos transferred, as well as a steep decline in the higher-order multiple rate (triplets, quadruplets, and higher) due to IVF [35–37]. Data from the SART CORS for 2004–12 shows that single embryo transfer and double embryo transfer have increased from 7% to 23%, and 33% to 50%, respectively, while the transfer of three or more embryos has decreased from 60% to 27%. During this time period, the proportion of singleton births from IVF increased from 68% to 74%, while twin and higher-order births decreased from 30% to 25%, and 2.4% to 0.8%, respectively. During the study period (2004 to 2008) in Massachusetts, the proportion of 1–2 ET increased significantly (from 59.0% to 77.8%, $p<0.0001$), whereas the proportion of FHB =1 increased only slightly (from 89.8% to 93.2%, $p=0.26$), most likely reflecting an improvement in techniques over this five-year period.

The effect of fetal loss confirms results from prior reports in both singletons (11) and twins (12) of a progressively increased adverse effect of higher plurality at six-weeks' gestation than at birth. Other studies have demonstrated that when the fetal loss occurs later in gestation, the surviving child is at greater risk for severe neurodevelopmental consequences, including cerebral palsy (38–40). It has been suggested that the higher rates of cerebral palsy among children born from assisted conception might be an outcome of transferring more than a single embryo, occurring in a greater frequency with the early intrauterine death of an unrecognized twin (40).

Strengths and Limitations

The MOSART study, which includes linking ART cycles to the vital records and hospital utilization data, represents the first time these datasets have been linked using direct identifiers from both datasets. ART national surveillance summaries are limited to birth outcomes reported by the patient herself or her obstetric provider (41–43). Prior studies (41, 42) have relied on linkages between ART cycles and vital records using only maternal and infant dates of birth, or probabilistic algorithms (43). Although there is a high degree of comparability between the SART CORS and vital records (44), our study design assures

more accurate linkage between ART treatment cycles, vital records, and the hospital discharge birth data, and a more complete picture of perinatal outcomes.

Although this study has several unique advantages over prior ART research, it is also subject to a number of limitations. This study uses retrospective data from several centralized datasets and although this is advantageous to achieve large numbers, we had the disadvantage that data entered into the SART CORS system is not as rigorously controlled as data collected for a prospective research study. Likewise, the primary purpose of vital records is civil registration, with public health research and surveillance being secondary uses. One of the limitations of comparing our results to the published literature is that the latter is often based on data spanning decades, during which time both ART procedures and ART outcomes have improved. Another limitation of this analysis is that it only includes women in Massachusetts. There may be significant demographic and outcome differences in patients in other regions of the country and with other healthcare systems, potentially limiting the generalizability of our findings. In addition, we were not able to account for possible clinic-specific effects.

Conclusions

In summary, this analysis demonstrates that 1) factors associated with transferring a higher number of embryos reflected suboptimal maternal conditions (older age and the use of autologous oocytes), less favorable oocyte or embryo quality, less favorable prognosis, or unsuccessful prior cycles (the use of micromanipulation, embryos which were thawed or cleavage-stage); 2) the number of embryos transferred was significantly associated with plurality at six-week's gestation (higher FHB), and 3) higher FHB was associated with greater risks for prematurity and low birthweight.

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Table 1

Paternal Demographic and Reproductive Characteristics, and ART Treatment Parameters

		All	Embryos Transferred (ETs)			Fetal Heartbeats (FHBs)		
			1–2	≥3		1	>1	
	N, pregnancies	**6,073**	**4,402**	**1,671**	**P Value**	**5,574**	**499**	**P Value**
Mother's Age	Mean years, SD	35.4 ± 4.5	35.0 ± 4.5	38.1 ± 3.7	<0.0001	35.7 ± 4.5	36.7 ± 4.6	<0.0001
	% <35	39.4	47.9	17.1		40.1	31.3	
	35–40	45.5	41.5	56.1		45.2	49.5	
	>40	15.1	10.7	26.8		14.7	19.2	
Father's Age	Mean years, SD	37.8± 5.8	37.1 ± 5.6	39.7 ± 5.8	<0.0001	37.7 ± 5.7	38.8 ± 6.1	<0.0001
	% <35	29.2	34.1	16.3		29.4	27.0	
	35–40	43.8	43.7	44.1		44.2	39.6	
	>40	26.9	22.2	39.6		26.4	33.4	
Parental Race/Ethnicity	Mother	85.6	85.0	87.3	0.03	85.8	84.2	0.32
White (%)	Father	85.8	85.6	86.4	0.46	86.0	83.0	0.06
Parity (%)	0	66.5	68.1	62.4		66.6	65.5	
	≥1	33.5	31.9	37.6	<0.0001	33.4	34.5	0.62
Infertility Diagnoses (%)	Male factor	32.7	33.8	29.7	0.002	32.5	34.3	0.43
	Endometriosis	8.7	8.6	8.9	0.68	8.6	9.8	0.36
	Ovulation disorders	13.1	14.7	8.7	<0.0001	13.2	11.4	0.30
	Dim. Ovarian Reserve	9.1	9.3	8.4	0.25	8.9	10.6	0.22
	Tubal factors	14.1	13.4	15.7	0.02	14.0	14.2	0.89
	Uterine factors	2.9	3.0	2.9	0.97	3.0	2.4	0.58
	Other factors	17.1	16.4	18.9	0.02	17.1	17.0	0.98
	Unexplained	21.8	20.6	25.0	<0.0001	22.0	20.0	0.34
Autologous	Oocyte	90.6	88.5	96.2	<0.0001	90.8	89.0	0.20
Gametes (%)	Semen	84.9	85.1	84.4	0.002	85.0	83.1	0.20
Micromanipulation (%)	Intracytoplasmic Sperm Injection	38.5	37.4	41.4	0.005	38.4	39.7	0.60
	Assisted Hatching	28.7	22.1	46.2	<0.0001	28.0	37.1	<0.0001
Embryo State (%)	Fresh	87.7	87.2	88.8	0.10	87.7	87.6	0.94

		All	Embryos Transferred (ETs)			Fetal Heartbeats (FHBs)		
			1–2	≥3		1	>1	
	N, pregnancies	6,073	4,402	1,671	P Value	5,574	499	P Value
Day of Transfer (%)	2–3	70.6	65.9	82.7	<0.0001	70.5	70.9	0.26
	4	0.4	0.3	0.6		0.4	0.8	
	5–6	9.6	12.0	3.4		9.8	7.6	
	Fresh, not specified	7.1	9.0	2.2		7.0	8.2	
Embryos Transferred	(mean, SD)	2.3 ± 1.0	1.8 ± 0.4	3.5 ± 0.9	<0.0001	2.2 ± 0.9	2.7 ± 1.1	<0.0001
	Range	1–10	1–2	3–10		1–10	1–10	
	(%) 1	14.8	20.4	--	---	16.0	57.3*	<0.0001
	2	57.7	79.6	--		57.8		
	3	19.1	--	69.5		18.4	27.1	
	≥4	8.4	--	30.5		7.7	15.6	
Length of Gestation	Mean Weeks, SD	38.3 ± 2.2	38.3 ± 2.2	38.4 ± 2.1	0.22	38.4 ± 2.2	38.0 ± 2.5	<0.0001
	(%) Preterm (<37 weeks)	11.7	11.9	11.3	0.59	11.2	17.0	<0.0001
Birthweight	Mean grams, SD	3,306 ± 614	3,298 ± 618	3,325 ± 602	0.14	3,317 ± 608	3,179 ± 666	<0.0001
	(%) Low Birthweight (<2,500 g)	8.1	8.1	8.2	0.88	7.7	12.8	<0.0001
Birthweight Z-score	Mean, SD	0.10 ± 1.0	0.10 ± 1.0	0.12 ± 1.0	0.48	0.11 ± 1.0	−0.02 ± 1.0	0.005
	(%) ≤1.28 (10^{th} %ile)	7.1	7.0	9.1	0.08	7.1	7.2	0.91

* cells combined due to need to suppress small cell numbers

Table 2

Likelihood of Embryos Transferred ≥3 versus 1–2 by Maternal Age Categories*

		All		<35 years		35–40 years		>40 years	
	N, pregnancies	**6,073**		**2,392**		**2,764**		**917**	
Variable	**Categories**	**AOR**	**95% CI**	**AOR**	**95% CI**	**AOR**	**95% CI**	**AOR**	**95% CI**
Mother's Age	<35	1.00	Reference						
(years)	35–40	3.84	3.30, 4.47						
	>40	15.50	12.21, 19.67						
Diagnoses	Male factor	0.65	0.55, 0.77	0.53	0.38, 0.73	0.65	0.52, 0.80		
	Ovulation disorders	0.76	0.62, 0.94			0.67	0.50, 0.89		
	Tubal factor	1.23	1.02, 1.47			1.30	1.04, 1.63		
	Other factor	1.22	1.02, 1.45	1.82	1.31, 2.54				
Oocyte Source	Autologous	1.00	Reference					1.00	Reference
	Donor	0.15	0.09, 0.25					0.34	0.18, 0.65
ICSI	No	1.00	Reference	1.00	Reference	1.00	Reference		
	Yes	1.45	1.23, 1.71	2.00	1.43, 2.81	1.40	1.13, 1.73		
Assisted Hatching	No	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference
	Yes	1.79	1.56, 2.07	1.87	1.40, 2.49	1.67	1.39, 2.00	1.63	1.10, 2.42
Embryo State	Fresh	1.00	Reference	1.00	Reference	1.00	Reference		
	Thawed	4.17	2.90, 5.99	17.63	6.75, 46.05	3.01	1.91, 4.75		
Day of Transfer	5–6	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference
	2–3	4.34	3.21, 5.88	7.03	2.84, 17.37	4.34	2.96, 6.34	4.72	2.77, 8.04

*Models adjusted for all factors in the table

Table 3

Likelihood of Fetal Heartbeats >1 versus 1 by Embryos Transferred and Maternal Age Categories*

		All		<35 years		35–40 years	
	N, pregnancies	6,073		2,392		2,764	
Variable	Categories	AOR	95% CI	AOR	95% CI	AOR	95% CI
Oocyte Source	Autologous	1.00	Reference				
	Donor	1.49	1.10, 2.01				
Assisted Hatching	No	1.00	Reference	1.00	Reference		
	Yes	1.31	1.07, 1.59	1.49	1.03, 2.15		
Embryos Transferred	1–2	1.00	Reference	1.00	Reference	1.00	Reference
	≥3	2.04	1.68, 2.48	1.66	1.08, 2.55	2.39	1.84, 3.11

*Models adjusted for all factors in the table

Table 4

Risks of Adverse Pregnancy Outcomes*

		Preterm (PT)			Low Birthweight (LBW)			Small-for-Gestation (SGA)		
	All	11.7%			8.1%			7.1%		
Variable	Categories	% PT	AOR	95% CI	% LBW	AOR	95% CI	% SGA	AOR	95% CI
Parity	≥1	10.0%	1.00	Reference	6.4%	1.00	Reference	4.0%	1.00	Reference
	0	12.6%	1.34	1.12, 1.59	9.0%	1.48	1.20, 1.83	8.7%	2.17	1.69, 2.78
Diagnoses	Male factor	12.7%	0.76	0.64, 0.91	8.7%	0.74	0.61, 0.91			
	Endometriosis				7.0%	0.47	0.30, 0.72			
Oocyte Source	Autologous	11.1%	1.00	Reference						
	Donor	17.5%	1.53	1.21, 1.94						
Embryo State	Fresh	11.3%	1.00	Reference				7.8%	1.00	Reference
	Thawed	14.4%	1.30	1.03, 1.63				2.3%	0.31	0.19, 0.51
Fetal Heartbeats	One	11.2%	1.00	Reference	7.7%	1.00	Reference			
	> One	17.0%	1.63	1.27, 2.09	12.8%	1.81	1.36, 2.39			

*Models adjusted for all factors in the table