HHS Public Access

Author manuscript

Fertil Steril. Author manuscript; available in PMC 2016 April 01.

Published in final edited form as:

Fertil Steril. 2015 April ; 103(4): 931–938.e2. doi:10.1016/j.fertnstert.2014.12.120.

Association between oocyte number retrieved with live birth rate and birth weight: an analysis of 231,815 cycles of in vitro fertilization

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Abstract

Objective—To determine if number of oocytes correlates with live birth rate and incidence of low birthweight (LBW).

Design—Retrospective cohort.

Setting—N/A.

Patients—Women undergoing fresh embryo transfer utilizing either autologous (n=194,627) or donor (n=37,188) oocytes whose cycles were reported to the Society for Assisted Reproductive Technology 2004–2010.

Main outcome measures—Live birth rate, birthweight, birth weight z-score, LBW.

Interventions—None.

Results—For both autologous and donor oocyte cycles, increasing number of oocytes retrieved paralleled live birth rate and embryos available for cryopreservation in most analyses performed with all models adjusted for age and prior births. For cycles achieving singleton pregnancy using autologous oocytes via transfer of 2 embryos, a higher number of oocytes retrieved was associated with lower mean birth weight, lower birthweight z-score, and greater incidence of LBW. In

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Presented at the 68th annual meeting, American Society for Reproductive Medicine, San Diego, California, October 20–24, 2012.

contrast, for cycles using donor oocytes, there was no association of oocyte number retrieved with measures of birthweight.

Conclusions—A higher number of oocytes retrieved was associated with an increased incidence of LBW in autologous singleton pregnancies resulting from transfer of 2 embryos but not in donor oocyte cycles. Although the effect of high oocyte number on the incidence of LBW in autologous cycles was of modest magnitude, further study is warranted to determine if a subgroup of women may be particularly vulnerable.

Keywords

in vitro fertilization; oocyte number; live birth rate; birth weight; low birth weight; z-score

Introduction

Compared with naturally conceived singletons, singletons conceived using in vitro fertilization (IVF) have a greater risk for low birth weight (LBW) (1–7) even after controlling for maternal age and other factors. A variety of potential contributing factors have been proposed to explain this increase in risk of adverse outcomes (7, 8) including underlying infertility (9), laboratory culture environment (10) and an altered hormonal environment (11–13).

It has been suggested that supraphysiologic hormone levels may increase the risk of adverse pregnancy outcomes by impairing trophoblast invasion and placental function (8). Another potentially related possibility is that high circulating levels of the products from the corpus luteum may lead to a hyperdynamic maternal circulation and an abnormal cardiovascular adaptation to pregnancy (12), thus predisposing to adverse pregnancy outcomes such as LBW. A third hypothesis is that effects of ovarian stimulation on pregnancy outcome may be due to influences on the oocyte and thus ultimately the embryo itself. Indeed, these hypotheses are not mutually exclusive. To test whether the presence of a high number of oocytes retrieved increases the risk for LBW, we analyzed data from a large cohort of patients undergoing IVF.

With fresh embryo transfers using autologous oocytes, there are multiple corpora lutea present and supraphysiologic levels of estradiol and progesterone, as well as other corpora luteal factors like relaxin. In contrast, fresh embryo transfers in donor oocyte cycles are typically performed when the endometrium has been prepared with more physiologic levels of estradiol and progesterone. In this study, we are evaluating birth weight as a function of number of oocytes retrieved for both autologous and donor oocyte cycles to explore whether any differences in birth weight are due to the effects of high oocyte number retrieved on the oocyte and resulting embryo or to effects on the maternal hormonal milieu in early pregnancy.

The risk of ovarian stimulation needs to be considered in relation to the benefit of number of oocytes retrieved and chance of live birth. Previous studies have shown that live birth rates increase as a function of increasing number of oocytes retrieved (14–17). Therefore, in this

study we also report the live birth rate per fresh embryo transfer and percentage of cycles with cryopreservation as a function of oocyte number.

Materials and Methods

Study population

The study population included fresh IVF cycles using autologous or donor oocytes which were reported to the Society for Assisted Reproductive Technology Clinical Outcomes Reporting System (SART CORS) from 2004–2010. SART CORS contains data from more than 90% of all clinics providing IVF in the United States. Data are collected and verified by SART, then reported to the Centers for Disease Control and Prevention (CDC) in compliance with the Fertility Clinic Success Rate and Certification Act of 1992 (Public Law 102–493). Cycles were excluded if they were used for research, embryo banking or used a gestational carrier.

Women were only included if they had no prior IVF treatment reported in the SART CORS. Data for autologous cycles were obtained from the first cycle for each woman. Data for donor cycles were obtained from the first donor cycle if fresh. Only cycles with one or two embryos transferred were included.

The study was approved by the Institutional Review Boards at Stanford University, Michigan State University, University of Michigan, and approved by the SART Research Committee.

Definitions used in description of birth weight

Analysis of birth weight was restricted to singleton pregnancies. Reference birth weights at each gestational age are normally distributed. A birth weight z-score (or standard deviation score) is the deviation of the birth weight of an individual from the median value of the reference population, divided by the standard deviation for the reference population (18). Birthweight z-scores were calculated to evaluate the adequacy of weight for age using gender-specific population-based standards, as recommended by Land (19). Infants with z-scores of ≤ -1.28 (below the 10^{th} percentile for gestation) were classified as small-for-gestational age (SGA). Cycles with z-scores from −4 to +4 were included.

Low birth weight (LBW) was defined as birthweight < 2500 grams. Because cleaved embryo transfer (day 2–3) was associated with a lower live birth rate compared with day 5–6 transfer among autologous cycles in our dataset, data were analyzed separately for day 2–3 transfers and day 5–6 transfers.

Statistical analysis

Maternal demographic factors, reproductive history, and ART-specific parameters were compared between day of transfer (day 2–3 versus day 5–6) groups for autologous and donor oocyte cycles using Student's t tests for continuous variables and χ^2 for categorical variables. Tests for trend across categories of number of oocytes retrieved in live birth rates, length of gestation, birthweight, birthweight z-score, and percent LBW and SGA were analyzed either by logistic regression or a general linear model, as appropriate, where a

linear term (1–5) was assigned to the five categories of the number of oocytes retrieved. All models were adjusted for maternal age and number of prior births. Data were analyzed by SAS software, version 9.2 (SAS Institute), and Excel (Microsoft).

Results

The study population using autologous oocytes included 194,627 cycles and 55,878 singleton live births and the study population using donor oocytes included 37,188 cycles and 12,862 singleton live births (Supplemental Table 1 includes all IVF cycles used to calculate live birth rate whereas Supplemental Table 2 is restricted to the population who achieved singleton live birth via transfer of 1 or 2 embryos). Women using donor oocytes were older and more likely to have the diagnoses of diminished ovarian reserve or other factor; women using their own oocytes were more likely to have the diagnosis of male factor and a higher percentage of nearly all diagnoses, as well as a lower number of oocytes retrieved. The day 2–3 group had fewer oocytes retrieved than the day 5–6 group. Retrieval of over 15 oocytes occurred in 22.4% of autologous cycles with day 2–3 transfer and 50.3 % of autologous cycles with day 5–6 transfer.

Table 1 presents the live birth rates by number of oocytes retrieved, oocyte source, number of embryos transferred and supernumerary embryos cryopreserved. We focused our conclusion about statistical significance on the analysis that was adjusted for female age. With one embryo transferred, the live birth rate paralleled the number of oocytes retrieved, but only significantly with donor cycles and day 2–3 transfers. With two embryos transferred, a similar pattern was seen, with significance for both autologous and donor cycles, and day 2–3 and day 5–6 transfers. The percentage of cycles with supernumerary embryos cryopreserved increased with higher number of oocytes retrieved for both autologous and donor oocyte cycles.

Table 2 shows the singleton birth outcomes with one embryo transferred and Table 3 presents singleton birth outcomes when two embryos were transferred. With one embryo transferred, there were no substantial differences by oocyte source, day of transfer, or number of oocytes retrieved, with the exception of borderline significance (p values of 0.02–0.07) for autologous cycles with day 5–6 transfer. Birth outcomes with two embryos transferred (Table 3) differed significantly only in autologous cycles (both day 2–3 and day 5–6 transfers), with subtle decrements in length of gestation and birthweight and a rise in LBW with greater numbers of oocytes retrieved.

There was a trend for a lower rate of pre-term delivery with cleaved embryo transfer compared with blastocyst transfer. For autologous cycles, the rate of pre-term delivery for cleaved versus blastocyst transfer was 15.1% vs 17.5% (p=0.007) with transfer of one embryo and 15.5% vs 20.6% ($p < 0.0001$) with transfer of 2 embryos. Although there was also a trend to lower pre-term delivery rate with cleaved versus blastocyst embryo transfer for donor oocyte cycles (17.6% vs 19.2%, p=0.60 with transfer of one embryo; 19.8 vs 21.2%, p=0.075 with transfer of 2 embryos), the difference did not reach statistical significance possibly due to the fact that there were fewer donor oocyte pregnancies available for analysis. These observations regarding rate of pre-term delivery are included to

point out the importance of considering stage of embryo development when analyzing outcomes from in vitro fertilization.

Discussion

These results demonstrate the subtle but significant detrimental effect of increasing number of oocytes retrieved on length of gestation, birthweight, and birthweight-for-gestation. There was no effect of high oocyte number on birth weight in pregnancies conceived using oocyte donation, suggesting that the potential adverse effect of the altered hormonal milieu associated with ovarian stimulation manifests in the endometrium or perhaps the maternal circulation rather than in the oocyte. There could also be an effect of a high number of oocytes retrieved directly on the embryo due to transfer within a non-physiologic environment at a time of critical developmental events.

Few studies have investigated the association between birth weight and the number of oocytes retrieved in fresh stimulated cycles (6, 20, 21). Our observation regarding the effect of oocyte number retrieved on birth weight differs from these prior studies which reported no differences possibly due to differences in patient populations or more cycles with a high number of oocytes retrieved in our dataset. A German study (21) found no effect of oocyte number retrieved on birth weight in their population of women ages 25–35 years. Their study included a smaller number of cycles with high oocyte number (5155 with ≥16 oocytes retrieved). A study using data generated in Sweden which found no influence of oocyte number retrieved on birth weight included only 919 cycles with retrieval of ≥15 eggs (6). The range of oocytes retrieved was not stated in an Australian study (20), but the total number of fresh IVF cycles in the study was limited to 4406 with data collected from cycles performed by a single service from 1978–2005.

Our findings regarding the effect of oocyte number on birth weight in autologous cycles with transfer of 2 embryos are consistent in principle with studies which compared IVF in a modified natural cycle with IVF associated with ovarian stimulation. A report from the Japanese ART registry found a two-fold increase in the risk of LBW in fresh autologous cycles with ovarian stimulation compared with those performed in the context of a natural cycle (22). Pelinck and coworkers (23) reported a higher birth weight among singletons conceived with modified natural cycle IVF versus standard ovarian stimulation with retrieval of a mean of 10 oocytes. However, they found no effect on pregnancy duration or increase in LBW or SGA in stimulated versus natural cycles, possibly due to the lower mean number of oocytes retrieved in their population or smaller sample size (n=190). Furthermore, a follow-up report of 451 singleton births from the same group (24), including women who underwent IVF with and without ovarian stimulation as well as women who spontaneously conceived, confirmed a trend towards lower birthweight after ovarian stimulation. However, the authors concluded that lower birthweight associated with conventional IVF was largely attributable to patient factors, and that larger studies are warranted.

We found that high oocyte number did not compromise birth weight in donor oocyte cycles, suggesting that the effect is mediated via the maternal hormonal mileu. Furthermore, the

difference in the rate of pre-term delivery with cleaved compared with blastocyst transfer was statistically significant only for autologous cycles. It is possible that this lower rate of pre-term delivery was seen only for autologous cycles because of a difference in the hormonal mileu around conception and implantation or because of the lower number of donor oocyte pregnancies available for analysis. The circulating maternal concentrations of estradiol and progesterone in frozen embryo transfers and oocyte donation cycles are similar and more physiologic compared to fresh autologous cycles. We chose not to examine frozen embryo cycles in this paper, as our primary objective was to determine if the number of oocytes retrieved affected birth weight in the fresh cycle, Other investigators have found that compared with cycles with fresh embryo transfer, cycles of frozen embryo transfer are associated with higher birth weight (5, 11, 25, 26) and have proposed that this difference may be due to the maternal hormonal mileu in early pregnancy. This line of thinking is similar to our hypothesis that the elevated levels of estradiol and progesterone in highly stimulated autologous cycles may have a negative effect on birthweight.

Our observations support the hypothesis that the hormonal milieu associated with ovarian stimulation may have detrimental effects by impairing placentation and fetal development through direct effects on the endometrium (11, 27, 28). However, hormonal levels are not available in SART CORS, and thus we were not able to directly test this hypothesis. In conceptions achieved using autologous oocytes and fresh embryo transfer, multiple corpora lutea are present, with resultant high production of sex steroids. Although estradiol levels are not available in SART CORS, it is interesting to note that Imudia and colleagues (29) reported an increased risk for SGA with peak estradiol level at the 90th percentile. However, it is important to note that elevated estradiol or progesterone should be considered markers of the non-physiologic environment and there may not be a cause-effect relationship between elevated sex steroids and any outcome.

In addition to sex steroids, other products of the corpus luteum such as relaxin are elevated when multiple corpora lutea are present (30, 31). Relaxin has direct effects on the endometrium (32, 33) and likely has an important role in the hemodynamic changes that occur during pregnancy (12, 34–36). We hypothesize that excessive production of relaxin and potentially other vasoactive products of the corpus luteum which rise with superovulation such as vascular endothelial growth factor (37) may compromise early placentation and maternal cardiovascular adaptation to pregnancy. Abnormal placentation or compromised maternal cardiovascular adaptation may in turn affect fetal growth (12). However, the hypothesis that any particular product of the corpus luteum could affect birth weight in our population is speculative and further study is warranted to test these hypotheses.

Our study confirmed the general observation that live birth rate increases as a function of egg number (14–17). However, we did not find the decline in live birth with an oocyte number over 20 as previously described (15), even though our dataset contained a larger number of cycles with high oocyte number. In fact, it is interesting to note that even a very high oocyte number (≥26 oocytes) did not appear to be associated with a decrease in live birth rate with autologous cycles, suggesting that either endometrial receptivity was not significantly impaired or that the better cohort of embryos available in high responders

offset any negative effect on endometrial receptivity. Although our study does demonstrate that pregnancy rates are generally higher if there are better quality (blastocyst) or a greater number (2 vs 1) of embryos transferred, our study does not confirm the recent postulate that the chance of achieving a live birth is independent of the number of oocytes retrieved if patients have the same number and quality of embryos transferred (38).

The percentage of cycles with embryos available for cryopreservation was positively correlated with oocyte number. Therefore, by restricting analysis to fresh embryo transfer (necessary to test our primary hypothesis), we have underestimated the value of a higher number of eggs retrieved with respect to total reproductive potential (39), i.e. the cumulative live birth rate from all fresh and frozen transfers associated with one oocyte retrieval. As reported most recently by Fatemi et al (16), the difference in live birth rate between low and high oocyte number retrieved is even greater when the cumulative live birth rate (including fresh and frozen transfers) is compared with the live birth rate with fresh transfer alone.

It is important to note that the magnitude of effect of increasing oocyte number on mean birth weight and incidence of LBW in autologous cycles is small, found to be statistically significant only with transfer of 2 embryos, and could be thought to be of questionable clinical significance. It is difficult to be certain why the adverse effect of ovarian stimulation on birthweight was seen only for autologous transfer of 2 embryos, but the results could be hypothetically due to combined detrimental effects of ovarian stimulation and vanishing twins which could theoretically be more common with a higher number of oocytes retrieved. It is plausible to conclude that many and perhaps even most women will not experience adverse pregnancy outcomes such as LBW that are attributable to the ovarian stimulation. However, we believe that although the increased risk of LBW with high oocyte number in autologous cycles is small, this risk should not be dismissed, as lower birth weight is associated with greater long-term adverse health consequences (40–42). In addition, the risk of other complications, such as ovarian hyperstimulation syndrome (17), also increases with high oocyte number, particularly if fresh embryo transfer is performed. Finally, although the magnitude of risk of ovarian stimulation is not great for the entire population, it may be important for particular subgroups of women. Further studies are warranted including data not available in SART CORS to identify subpopulations who may be at most risk for LBW in autologous fresh transfers, such as women with pre-conception hypertension or women who had a prior delivery of an infant with LBW. We propose that until further analyses are performed, consideration should be given to either milder ovarian stimulation (43, 44), cryopreservation of all embryos with subsequent conception via frozen embryo transfer (45), or single embryo transfer, especially in cases where the risk of LBW based on other maternal factors is high.

Our study has some major strengths. We analyzed a large dataset, with >230,000 cycles used for calculation of live birth rate as a function of oocyte number, and >50,000 cycles used for calculation of birth weight as a function of oocyte number. In fact, this study is the first to utilize a large database from multiple centers in the United States to examine the correlation of oocyte number with birth weight, and the dataset included a large number of cycles with very high number of oocytes retrieved. Oocyte number is a variable which is likely to be accurately reported and will not vary from center to center in contrast to parameters such as

serum estradiol which may vary depending on the assay used. The analysis of birth weight was restricted to singletons as multiplicity is a key factor affecting birth weight. Separate analysis was reported for transfer of 1 versus 2 embryos to determine if the trends observed were similar, as prior studies have found that singleton pregnancies which were not achieved following single embryo transfer were at increased risk of LBW (45), likely due at least in part to "vanishing twins." Analysis of live birth rate and birth weight was restricted to the first autologous cycle and the first oocyte donation cycle reported for each woman. In contrast to some prior studies suggesting that ovarian stimulation is associated with low birthweight which used controls who had conceived spontaneously, our study largely circumvented the bias of poorer outcome due to underlying infertility because all or nearly all couples included in our study were subfertile and conceived via IVF. Unlike a prior very large study which very nicely described the effect of oocyte number on live birth rate but could not report occurrence of cryopreservation of surplus embryos (15), we were able to include the percentage of cycles with cryopreservation as a function of oocyte number. Analyses were adjusted for maternal age and number of prior births. One additional strength of our study is that the birthweight z-score was utilized to account for physiological variation in birth weight due to gestational age at birth and gender of the child.

Our study also has limitations. Although this study's conclusions are consistent with our hypothesis that excessive levels of products of the corpus luteum may contribute to adverse outcomes with IVF, we are unable to directly prove this hypothesis using SART CORS. Oocyte number retrieved is only a proxy for number of corpora lutea. However, it would be difficult to perform a study with large numbers of patients in which the exact number of corpora lutea are counted. There is no information about products of the corpus luteum such as estradiol, progesterone, and relaxin in SART CORS. The dataset for this analysis does not include many factors known to influence fetal growth and birthweight such as gestational weight gain, gestational diabetes, occupational factors, and other social and behavioral variables. In addition, SART CORS does not include information on birth length, head circumference, or other more specific measures of fetal growth. There are also some important caveats to any conclusion that can be drawn from our observations regarding live birth rate as a function of oocyte number, as many of these cycles were likely associated with diminished ovarian reserve rather than attributable to intentional mild ovarian stimulation. Patient factors such as poor oocyte quality may lead to a lower success rate in the cycles with low egg number.

In conclusion, we found that with fresh transfer of 2 autologous embryos, an increase in oocyte number retrieved was associated with an increase in the incidence of LBW and a decrease in the birthweight, even when corrected for gestational age and infant sex using the birthweight z-score. No association was noted between oocyte number retrieved and birthweight in donor oocyte cycles, suggesting that the effect of ovarian stimulation manifests in the endometrium rather than in the oocyte itself. In contrast to this detrimental effect of a higher oocyte number in autologous cycles, there were benefits documented with retrieval of a greater number of oocytes, including a higher live birth rate and a greater chance of having embryos available for cryopreservation for both autologous and donor oocyte cycles. Furthermore, the effect of oocyte number on birthweight in autologous cycles was modest and not seen with single embryo transfer. Although we did not find a large

effect of ovarian stimulation on birth weight in autologous cycles, we believe that the potential detrimental effect of ovarian stimulation on risk of LBW should be explored further to determine if there are subgroups of women at greatest risk.

Conclusions

With fresh transfer of 2 embryos, an increase in oocyte number retrieved was associated with a modest increase in the incidence of LBW and a decrease in the birthweight in autologous but not donor oocyte cycles.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The authors wish to thank the Society for Assisted Reproductive Technology and its members for providing the clinical information which allowed this analysis to be performed. The project described was supported by Award Number P01 HD 065647 from the National Institute of Child Health and Human Development. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute of Child Health and Human Development or the National Institutes of Health.

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Table 1

Live birth rates by number of oocytes retrieved, oocyte source, number of embryos transferred, and supernumerary embryos cryopreserved.

		One Embryo Transferred				Two Embryos Transferred			
			Live Birth Rate				Live Birth Rate		
Oocyte Source And Day of Transfer	#Oocytes Retrieved	% Cycles with Cryopreservation	Overall Rate	Embryos Cryopreserved		% Cycles with Cryopreservation	Overall Rate	Embryos Cryopreserved	
				None	Any			None	Any
Autologous, Day 2–3 (N=103,852)			14.8	12.1	34.5		38.9	31.9	48.8
	1–5	2.5	10.7	10.3	24.3	6.3	24.1	22.8	43.3
	6–10	13.3	17.1	14.3	35.5	31.1	37.8	33.0	48.5
	11–15	31.6	23.2	17.6	35.1	52.8	44.3	38.2	49.6
	16–25	53.1	26.7	16.6	35.7	66.1	45.9	39.7	49.1
	≥26	72.2	35.7	23.5	40.5	77.4	44.9	38.6	46.8
	p value for trend	<0.0001	<0.0001	<0.0001	0.002	<0.0001	<0.0001	<0.0001	0.81
	Adjusted p-value	<0.0001	0.01	0.07	0.06	<0.0001	<0.0001	<0.0001	0.02
Donor, Day 2–3 (N=14,744)			26.6	21.5	35.5		48.0	40.9	51.3
	1–5	4.9	15.1	14.8	22.2	22.1	36.2	32.4	49.6
	6–10	22.0	23.6	21.9	29.6	48.7	43.4	37.5	49.5
	11–15	41.3	27.5	21.9	35.6	65.8	48.0	42.5	50.9
	16–25	65.5	33.5	31.3	34.6	76.9	49.9	45.8	51.1
	≥26	77.6	46.3	46.7	46.2	87.2	52.2	43.4	53.5
	p value for trend	<0.0001	<0.0001	0.001	0.11	<0.0001	<0.0001	<0.0001	0.02
	Adjusted p-value	<0.0001	0.0006	0.001	0.11	<0.0001	<0.0001	<0.0001	0.02
Autologous, Day 5–6 (N=90,775)			40.3	24.7	50.2		52.2	44.7	56.9
	1–5	10.0	20.5	18.6	37.0	18.1	40.3	37.3	53.8
	6–10	36.7	33.4	24.9	48.0	41.1	49.1	43.7	56.8

		One Embryo Transferred				Two Embryos Transferred			
			Live Birth Rate				Live Birth Rate		
Oocyte Source And Day of Transfer	**#Oocytes Retrieved**	**% Cycles with Cryopreservation**	**Overall Rate**	**Embryos Cryopreserved**		**% Cycles with Cryopreservation**	**Overall Rate**	**Embryos Cryopreserved**	
				None	**Any**			**None**	**Any**
	11–15	60.2	40.3	26.0	49.9	57.6	52.5	45.6	57.5
	16–25	77.2	46.3	27.9	51.7	69.4	53.8	45.8	57.4
	≥26	87.3	46.8	26.5	49.7	80.2	53.2	44.9	55.2
	p value for trend	<0.0001	<0.0001	<0.0001	0.12	<0.0001	<0.0001	0.0001	0.07
	Adjusted p-value	<0.0001	0.09	0.02	0.37	<0.0001	0.03	0.07	0.001
Donor, Day 5–6 (N=22,444)			54.0	38.4	56.6		63.2	55.4	65.6
	1–5	22.2	25.0	28.6	12.5	29.6	45.4	34.2	71.9
	6–10	61.9	49.8	34.5	59.2	54.1	56.5	51.0	61.2
	11–15	81.6	55.5	44.0	58.1	67.8	60.7	56.2	62.8
	16–25	88.5	53.5	34.9	55.9	78.9	64.2	57.2	66.1
	≥26	94.3	56.2	51.0	56.5	87.5	66.1	56.7	67.4
	p value for trend	<0.0001	0.03	0.17	0.78	<0.0001	<0.0001	0.002	<0.0001
	Adjusted p-value*	<0.0001	0.79	0.20	0.75	<0.0001	<0.0001	0.002	0.0004

* The p value for trend was adjusted for female age and prior births. The overall rate was also adjusted for presence or absence of cryopreserved embryos.

Table 2

Birth outcomes by number of oocytes retrieved, oocyte source, and day of transfer for cycles with transfer of one embryo.

Oocyte Source	Day of Transfer	# Oocytes Retrieved	N	Length of Gestation (mean weeks, SD)	Birthweight (Mean grams, SD)	Z-score (Mean, SD)	Percent SGA	Percent LBW
Autologous	Days 2–3	1–5	1132	38.5±2.0	3261±559	−0.04±0.96	9.1	8.3
Oocytes		6–10	773	38.5±2.0	3279±566	0.01±0.97	7.3	7.6
		11–15	396	38.2±2.4	3161±625	−0.12±0.97	9.6	12.6
		16–25	300	38.6±1.9	3289±582	−0.04±1.04	10.7	8.7
		≥26	104	38.7±1.7	3339±526	0.06±0.88	5.8	6.7
		p Value for trend		0.69	0.84	0.72	0.83	0.44
		Adjusted p value*		0.90	0.86	0.85	0.89	0.34
Donor	Days 2–3	1–5	27	38.6±1.6	3223±585	−0.15±1.14	14.8	14.8
Oocytes		6–10	58	38.0±2.8	3318±688	0.23±1.04	8.8	8.8
		11–15	59	38.2±2.6	3323±668	0.20±0.94	5.1	6.8
		16–25	64	38.3±2.6	3395±549	0.21±0.96	7.8	6.3
		≥26	31	38.3±2.2	3207±612	−0.06±0.98	6.5	16.1
		p Value for trend		0.85	0.86	0.75	0.31	0.73
		Adjusted p value*		0.82	0.80	0.77	0.25	0.65
Autologous	Days 5–6	1–5	241	38.0±2.2	3276±593	0.20±0.96	4.2	7.1
Oocytes		6–10	1001	38.1±2.1	3285±552	0.14±0.97	5.9	7.2
		11–15	1545	38.1±2.1	3262±577	0.11±0.93	5.4	7.3
		16–25	2336	38.1±2.1	3251±578	0.08±0.96	7.2	8.1
		≥26	942	37.9±2.4	3231±620	0.12±0.95	6.4	9.6
		p Value for trend		0.04	0.02	0.23	0.10	0.02
		Adjusted p value*		0.05	0.07	0.54	0.18	0.04
Donor	Days 5–6	1–5	9	38.8±1.1	3461±552	0.18±1.17	11.1	0.0
Oocytes		6–10	140	37.9±2.6	3177±640	0.03±0.97	8.0	12.1
		11–15	345	38.1±2.5	3259±620	0.11±0.94	4.7	11.9
		16–25	752	38.3±2.1	3268±588	0.07±1.00	8.9	10.0
		≥26	481	38.1±2.4	3255±614	0.10±0.93	6.9	8.9

Oocyte Source	Day of Transfer	# Oocytes Retrieved	N	Length of Gestation (mean weeks, SD)	Birthweight (Mean grams, SD)	Z-score (Mean, SD)	Percent SGA	Percent LBW
		p Value for trend		0.54	0.81	0.78	0.52	0.16
		Adjusted p value*		0.56	0.76	0.89	0.57	0.14

* The p value for trend was adjusted for female age and prior births.

Fertil Steril. Author manuscript; available in PMC 2016 April 01.

Table 3

Birth outcomes by number of oocytes retrieved, oocyte source, and day of transfer for cycles with transfer of two embryos.

Oocyte Source	Day of Transfer	# Oocytes Retrieved	N	Length of Gestation (mean weeks, SD)	Birthweight (Mean grams, SD)	Z-score (Mean, SD)	Percent SGA	Percent LBW
Autologous	Days 2–3	1–5	3007	38.3±2.1	3263±580	0.02±0.96	8.1	8.3
Oocytes		6–10	7352	38.4±2.1	3257±581	−0.02±0.97	8.9	8.7
		11–15	6388	38.4±2.2	3244±591	−0.05±0.96	9.3	8.8
		16–25	5538	38.3±2.3	3229±605	−0.04±0.95	8.4	9.7
		≥26	1310	38.2±2.3	3193±608	−0.07±0.98	9.5	11.5
		p Value for trend		0.002	<0.0001	0.0009	0.43	0.0001
		Adjusted p value*		0.01	0.0001	0.005	0.31	0.0002
Donor	Days 2–3	1–5	138	37.9±2.9	3222±723	0.05±1.08	14.0	14.6
Oocytes		6–10	810	38.1±2.3	3229±619	0.06±0.95	8.3	11.4
		11–15	1150	38.2±2.3	3280±630	0.12±1.02	8.0	10.1
		16–25	1596	38.1±2.5	3220±646	0.04±0.99	7.8	11.4
		≥26	710	38.2±2.1	3291±586	0.13±0.97	7.6	8.9
		p Value for trend		0.59	0.41	0.42	0.17	0.21
		Adjusted p value*		0.62	0.39	0.37	0.16	0.19
Autologous	Days 5–6	1–5	453	38.0±2.1	3260±603	0.18±0.98	6.7	8.8
Oocytes		6–10	4207	37.9±2.1	3243±583	0.15±0.99	6.8	9.4
		11–15	6789	37.9±2.3	3209±603	0.07±0.95	6.9	9.9
		16–25	9081	37.9±2.4	3194±625	0.05±0.97	7.8	10.8
		≥26	2951	37.8±2.6	3178±641	0.07±0.96	7.4	12.3
		p Value for trend		0.006	<0.0001	<0.0001	0.06	<0.0001
		Adjusted p value*		0.01	<0.0001	<0.0001	0.06	<0.0001
Donor	Days 5–6	1–5	36	38±2.7	3260±694	0.20±1.05	5.6	8.3
Oocytes		6–10	589	38±2.7	3226±677	0.10±1.03	8.9	10.5
		11–15	1356	38±2.4	3255±615	0.13±0.99	6.1	9.3
		16–25	2743	38±2.4	3236±638	0.11±1.00	7.3	10.6
		≥26	1768	38±2.5	3223±660	0.07±0.96	8.1	10.7

Oocyte Source	Day of Transfer	# Oocytes Retrieved	N	Length of Gestation (mean weeks, SD)	Birthweight (Mean grams, SD)	Z-score (Mean, SD)	Percent SGA	Percent LBW
		p Value for trend		0.80	0.51	0.14	0.34	0.73
		Adjusted p value*		0.80	0.58	0.19	0.37	0.77

* The p value for trend was adjusted for female age and prior births.

Fertil Steril. Author manuscript; available in PMC 2016 April 01.