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Second Try: Who Returns for Additional ART Treatment and the Effect of A Prior ART Birth

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Abstract

Objective—To evaluate the effect of a prior assisted reproductive technology (ART) live birth on subsequent live birth rates.

Design—Historical cohort study

Setting—Clinic-based data

Patients—The study population included 297,635 women with 549,278 cycles from 2004 to 2010 from the Society for Assisted Reproductive Technology Clinic Outcome Reporting System. Try 1 refers to ART cycles up to and including the first live birth; try 2 to ART cycles after first live birth.

Interventions—None

Main Outcome Measures—Live birth rates by cycle number, try number, and oocyte source.

Results—Younger women at Try 1 are more likely to return for Try 2. Women returning for try 2 were more likely to have had an ART singleton versus multiple birth (33.2% after a try 1 singleton versus 8.1% after twins and 4.9% after triplets), and less likely to have a diagnosis of diminished ovarian reserve or tubal factors. Live birth rates were significantly higher for try 2 compared to try 1 for autologous fresh cycles, averaging 7.7 percentage points higher over five

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cycles. Live birth rates were not significantly different for try 2 versus try 1 with thawed autologous cycles, or either fresh or thawed donor cycles.

Conclusions—These results indicate that when fresh autologous oocytes can be used, live birth rates per cycle are significantly greater after a prior history of an ART live birth.

Keywords

prior ART live birth; autologous cycles; donor cycles; live birth rates

Introduction

For many women undergoing treatment for infertility, more than one cycle is needed to achieve a live birth. Success rates after the first cycle of assisted reproductive technology (ART) average about 30–34%, but vary by maternal factors, including age and diagnosis [1]. Prior history of a live birth is an established factor positively influencing future reproductive outcomes [2, 3]. The purpose of this analysis was to evaluate the effect of a history of a prior ART live birth on the subsequent ART live birth rates using linked cycles for individual women. This is the most recent in a series of analyses using linked cycles of ART [1, 4, 5].

Materials and Methods

The data source for this study was the Society for Assisted Reproductive Technology Clinic Outcome Reporting System (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). The study was approved by the Committees for the Protection of Human Subjects at Dartmouth College, and Michigan State University, respectively, and was analyzed using SAS 9.2 software (Cary, NC).

Cycles reported to the SART CORS between 2004 and 2010 were included, linked by the woman's birth date, first and last names, and social security number (when present). Linkages across clinics also included partner's name and the sequence of ART outcomes. Identifying variables (including names, dates, and social security numbers) were removed and the de-identified analytic file generated. Cycles were excluded if they used gestational carriers, or were designated as for research or for embryo banking; all subsequent cycles from the same woman were also excluded. Women were excluded if they reported prior ART cycles before their first cycle in the SART CORS or if the first cycle was reported in 2010. Cycles were numbered sequentially, regardless of cycle type (fresh or thawed, autologous or donor); therefore, cycles within a woman used in a subanalysis (such as when using of fresh autologous oocytes) may not be numbered consecutively.

The study population was grouped as try 1 and try 2. Women in try 1 included those with cycles up to and including their first ART live birth as reported in the SART CORS. Excluded from try 1 were women who used frozen embryo transfer (FETs) at their first ART cycle. Women in try 2 included those who had a prior ART birth reported in the SART CORS and were returning for subsequent treatment. Due to the time delay in returning for additional ART treatment after a live birth, the data was limited to women who had a live birth at their last cycle in years 2004–2007 in determining the characteristics of women who returned for try 2. Because of small numbers of women with greater than five cycles, only data from the first five cycles for any individual woman were used. For each try, pregnancy outcome (live birth yes/no) was classified by cycle number, reporting year, age category, and diagnosis. Data on live births were limited to births with a gestation of at least 22 weeks

and birthweights of at least 300 grams. Because the live birth rates differ by reporting year, the Cochran-Mantel-Haenszel statistic was used to test for independence, adjusted for reporting year, age category, and diagnosis.

Results

The study population included 297,635 women with 549,278 cycles and 163,908 live births in try 1. When limited to women who had a live birth during their last cycle of ART between 2004 and 2007, the study population included 101,339 women in try 1 and 25,541 women in try 2 (see Table 1). The characteristics of the women in these two groups are shown in Table 2. Younger women at Try 1 were more likely to return for a second try than older women. A return for try 2 was less likely with higher gravidity, after a prior ART multiple birth, or when there was a diagnosis of diminished ovarian reserve or tubal factors.

Of the 14,983 women who had a single diagnosis at the time of birth at both tries, 86.7% had the same diagnosis. Among women with donor cycles, at the first cycle of try 1 where there was only a single diagnosis, 76.2% had diminished ovarian reserve.

The rate of return for try 2 did not vary substantially by the number of cycles in try 1, ranging from 24.6% with one cycle in try 1 to 28.6% with five or more cycles in try 1.

The number of embryos transferred varied from cycle to cycle, but overall declined by about 8% in try 2 versus try 1. Among women with a single embryo transferred in try 1, 38% also had a single embryo transfer in try 2, and 62% had more than one embryo transferred. Among women who had two embryos transferred in try 1, 66% also had two embryos transferred in try 2, 17% had one and 17% had more than two transferred in try 2. Among women with three embryos transferred in try 1, 40% had fewer transferred in try 2.

Live birth rates by cycle number, try number, and oocyte source are shown in Table 3. Live birth rates were significantly higher for try 2 compared to try 1 for fresh autologous cycles, averaging 7.7 percentage points higher. In contrast, thawed autologous cycles did not result in significantly different live birth rates between try 2 and try 1, nor did fresh or thawed donor cycles.

Discussion

These findings indicate that with fresh autologous cycles there is a significantly higher live birth rate after a prior ART birth. These findings confirm earlier reports that a prior ART birth is associated with a higher success rate with subsequent attempts [2, 3]. The higher birth rate, however, was not seen when comparing outcomes with the use of donor eggs or frozen embryo transfer.

It has long been assumed that couples returning for a second baby would have a higher rate of success than couples undergoing their first attempt at an ART birth. For example, in their most recent guidelines on the number of embryos to transfer, the Practice Committee of the American Society for Reproductive Medicine includes in their favorable prognostic category “Patients who have had previous success with IVF [in vitro fertilization]...” [6]. Our findings confirm this assumption, although, by design, we used a limited timeframe (ART treatment and live birth between 2004 and 2007, and return for additional cycles by 2010).

The decision to have more children includes many factors—parental ages, economics, and plans for ultimate family size. Of note, women who had a prior ART multiple birth were much less likely to return for additional ART cycles (8.1% who had twins and 4.9% with

triplets in try 1 returned for try 2, compared to 33.2% with singletons). This finding may also reflect the special challenges of multiples [7, 8].

There are many reasons why patients discontinue ART treatment, including financial stress, decisions to adopt, or because there is a perceived chance that success is low [9–15]. For patients who have already had an ART singleton birth, there may be a greater incentive to continue treatment if they consider themselves likely to have another live birth. In addition to a prior birth, factors that can contribute to higher success rates include retrieval of a greater number of eggs, good fertilization rate, good embryo morphology, and having embryos to cryopreserve [2, 3, 16, 17]. The use of donor eggs also correlates with better live birth rates [1]. In our analyses, the highest live birth rates were with fresh donor cycles, averaging 47–49% for try 1 and 49–56% for try 2.

We found that patients with diminished ovarian reserve were less likely to return for a second live birth than those with other diagnoses. One reason may be that these women were older than women with other diagnoses at their first cycle. These patients may also have undergone more cycles prior to their first live birth. The chance of success for women with diminished ovarian reserve using autologous oocytes is lower and thus fewer of these patients find encouragement to return [1]. Women with tubal factor infertility were also less likely to return for try 2. The explanation for this is less clear, but may reflect a high percentage of patients with tubal reversal who had already had one or more spontaneously conceived children prior to the ligation.

There was no significant difference in live birth rates between try 1 and try 2 for thawed cycles. Women who return for thawed cycles have embryos cryopreserved, which may reflect a better prognosis in try 1. There also could be a difference in motivation between patients who return for thawed embryos and those who come back to undergo a fresh cycle. Patients returning for thawed embryos may do so because they don't want the embryos discarded or donated, preferring to use the embryos themselves. These cycles are less expensive and therefore pose less of a financial barrier for returning.

These findings have several limitations. The higher live birth rates in try 2 may have been due to factors not captured in this dataset. For example, treatment parameters which were successful beyond those recorded in the SART CORS may have been utilized again in try 2. Because the population of women who returned for additional ART cycles after having an ART live birth represents a self-selected sample, they may include other biases. In addition, our study population was limited in timeframe. If patients wait longer, there could be additional influences of age and changes in diagnosis which may affect try 2 live birth rates.

The findings presented in this analysis confirm that, within a certain timeframe, a history of a prior ART live birth is associated with improved chances of success in subsequent cycles.

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Table 1**Linked Cycles of ART Treatment, 2004 – 2010**

	Women	Cycles	
Women in SART CORS database	445,264	846,914	
	147,629		
Excluded*			
Try 1: Women with cycles	297,635	549,278	Used to compare live birth rates between women who had first try and those who returned for second try
Try 1: Number of women with live birth	163,908		
Try 1: Number with live birth prior to 2008	101,339	167,817	Used to compare women with successful first try to women who returned for second try
Try 2: women who returned for additional ART treatment**	25,541	44,277	Used for both comparisons described above
Try 2: Number of women with live birth	14,533		

* Try 1: A woman was excluded if she had a prior ART treatment.

Cycles were excluded if: (1) they occurred in 2010 or (2) were used for research or for embryo banking or (3) a gestational carrier was used; all subsequent cycles were also excluded.

** Cycles were excluded for the same reasons as in first try

Table 2

Characteristics of Women by Try Number

		Try 1: Live birth prior to 2008 (Last Cycle)	Try2 (First Cycle)	% Women with a live birth at Try 1 who return for Try 2*
	Number of Women	101,339	25,541	25.2
Race and Ethnicity (%)	White	51.5	53.3	25.9
	Black	3.2	2.4	18.8
	Hispanic	4.3	3.2	18.5
	Asian	5.3	4.7	22.4
	Mixed	0.4	0.5	26.9
	Other	0.3	0.2	17.5
	Unknown	35.1	35.8	26.1
Age (years) (%)	30	53.5	39.7	27.6
	31–37	21.7	24.7	24.7
	38–40	13.7	19.9	22.2
	41	11.1	15.7	18.4
Diagnosis (%)	Multiple diagnoses	35.6	35.6	23.4
	Single diagnosis	64.4	64.4	26.2
	Male factor	31.5	35.1	29.3
	Endometriosis	8.5	8.2	26.3
	Polycystic Ovarian Syndrome	11.7	12.5	27.7
	Diminished Ovarian Reserve	16.0	14.6	20.5
	Uterine Factors	1.4	1.3	27.0
	Tubal Factors	0.7	0.3	18.6
	Other	10.6	9.6	24.1
	Unexplained	19.5	18.5	26.3
Oocyte Source (%)	Autologous	86.9	90.1	25.8
	Donor	13.1	9.9	21.3
Embryo State (%)	Fresh	89.4	41.7	25.1
	Thawed	10.6	58.3	25.7
Number of Cycles (%)	1	62.1		24.6
	2	22.0		25.4
	3	9.2		26.9
	4	3.9		26.9
	5+	2.8		28.6
Gravidity	0	52.0		29.6
	1	24.1		23.4
	2	12.2		18.9
	3	11.7		16.2
		Try 2-1 st cycle		Try 2-last cycle
Plurality of ART Live Birth (%)		N=8833		N=14,533

	Try 1: Live birth prior to 2008 (Last Cycle)	Try2 (First Cycle)		% Women with a live birth at Try 1 who return for Try 2*
Singleton	68.4	75.1	73.9	33.2
Twins	29.7	23.7	24.9	8.1
Triplets+	1.9	1.2	1.2	4.9

*
all p-values are <0.0001 except fresh/thawed p=0.23

Table 3

Live Birth Rates by Cycle Number, Try Number, and Oocyte Source

	Cycle #	Try 1		Try 2		C-M-H P Value*
		N	LB (%)	N	LB (%)	
All Cycles	1	297,635	33.1	25,541	34.0	0.66
	2	135,180	27.0	10,593	32.6	<0.0001
	3	61,914	25.8	4,517	30.6	<0.0001
	4	28,583	25.1	1,972	29.4	0.011
	5	13,216	24.0	894	27.3	0.15
Fresh	1	278,405	32.0	10,157	37.8	<0.0001
Autologous	2	89,985	24.5	6,003	34.6	<0.0001
Cycles	3	40,169	23.1	2,754	30.5	<0.0001
	4	17,508	21.4	1,205	29.7	<0.0001
	5	7,561	19.1	535	25.8	0.019
Thawed	1	---	---	12,853	30.7	---
Autologous	2	33,820	28.4	3,514	27.3	0.40
Cycles	3	13,958	25.0	1,283	26.6	0.31
	4	6,194	23.4	510	22.9	0.56
	5	2,732	21.3	223	23.8	0.41
Fresh Donor	1	19,230	48.7	506	53.0	0.41
Cycles	2	7,358	49.2	361	56.8	0.23
	3	5,104	48.7	229	52.8	0.065
	4	3,125	48.2	138	51.4	0.96
	5	1,789	47.7	69	49.3	0.94
Thawed Donor	1	---	---	2,025	31.5	---
Cycles	2	4,017	29.4	715	29.7	0.65
	3	2,683	27.1	251	30.7	0.71
	4	1,756	26.3	119	28.6	0.81
	5	1,134	25.4	67	28.4	0.76

* Cochran-Mantel-Haenszel p-value adjusted for reporting year, age group, and diagnosis