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ASSISTED REPRODUCTION TECHNOLOGIES

Factors associated with short interpregnancy interval among women treated with in vitro fertilization

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Abstract

Purpose To evaluate factors associated with interpregnancy interval (IPI) among women treated with in vitro fertilization (IVF).

Methods Women with at least two cycles of IVF between 2004 and 2013 were identified from the SART CORS database and grouped by age at first cycle, infertility diagnosis, IVF treatment parameters, and cycle 1 outcome (singleton or multiple live birth or no live birth, length of gestation, and birthweight). The distributions of IPIs (in months, 0–5, 6–11, 12–17, 18–23, and ≥ 24) were compared across these factors. IPI was fit as a function of these factors by a general linear model, separately for singleton and multiple live births and no live births at cycle 1.

Results The study included 93,546 women with two consecutive IVF cycles where the first cycle resulted in a clinical intrauterine pregnancy or a live birth. Among women with a live birth in cycle 1, there was a general pattern of longer IPI for younger women compared to older women. Women with a multiple birth waited longer before initiating a second cycle than women with a singleton birth. For women with no live birth in the first cycle, nearly three fourths initiated cycle 2 within 6 months, regardless of their age. Short (0–5 months) IPI was associated with preterm delivery, older maternal age, and use of donor oocytes.

Conclusions Age of the mother, outcome of the first pregnancy, and treatment factors affect the length of the interpregnancy interval. Because short IPI has been associated with poor outcomes, women who are at risk for short IPI should be counseled about these outcome risks.

Keywords In vitro fertilization · Short interpregnancy interval · Obstetrical outcomes · Maternal age

Introduction

Short and long interpregnancy intervals (IPIs) have been associated with poor obstetric outcomes in the general population. Specifically, IPI less than 6 months has been associated with neonatal morbidity, including preterm delivery, preterm premature rupture of membranes, low birth weight, and small for gestational age [1–4]. Additionally, IPI less than 12 months has been associated with an increase in maternal morbidity, including placenta previa and placental abruption [5]. Moreover, IPI less than 18 months has even been associated with increased midlife mortality as compared to IPI of 30–41 months [6].

Despite the abundance of studies examining IPI in the general obstetric population, there is a paucity of studies evaluating IPI specifically in the IVF population. This is interesting, as the IVF population includes a large proportion of women who may have time-sensitive diagnoses and may therefore seek a subsequent pregnancy more quickly after an initial pregnancy. Moreover, IVF pregnancies carry an increased risk of adverse outcomes, including preterm delivery, low birth weight, and need for cesarean section, as compared to those spontaneously conceived [7]. Therefore, women undergoing IVF pregnancies who are at risk of having a short IPI should be counseled regarding its potential adverse effect on a subsequent pregnancy. Long IPI has also been associated with morbidities in the general population, but is less commonly seen in the IVF population.

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Our group therefore sought to characterize which women undergoing IVF pregnancies are likely to have a short IPI.

Materials and methods

The Society for Assisted Reproductive Technology Clinic Outcome Reporting System (SART CORS) database was used to examine our study outcome. This study was approved by Institutional Review Board of the Michigan State University. Women who had two or more IVF treatment cycles reported to the SART CORS database between January 1, 2004 and December 31, 2013 were included. Cycles were linked by woman's date of birth, last name, first name, and social security number (when present); we limited cases to where the consecutive cycles occurred at the same clinic. Cycles were linked in a series of steps which involved matching the cycles with exact name and date of birth first (step "E") followed by matches that were progressively less certain due to variations in spelling or format of names, changes in names over time, or data entry error (steps N1–N5). Programmed steps were checked for accuracy by reviewing a portion of the records by hand. The first match step (E) was for exact matches. The second match step (N1) involved coding names using Soundex software (Soundex SQL Server 2000) to facilitate phonetic matches in names entered differently across clinics (e.g., Frazier and Frasier; O'Neill and O'Neal). These matches were accepted if date of birth and/or social security numbers matched. At the N2 level, cycles were matched that differed as the result of addition of special characters or hyphenated names. Cycles were sorted first by date of birth and then by last name and first name. Social security numbers and partner name were used to adjudicate uncertain matches. The first two cycles for each woman were used in the analysis.

The N3 level checked for those patients with the same first and last name and date of birth that agreed by month but differed by plus or minus 1 year. At the N4 level, we checked those patients with the same first and last name and a date of birth containing the same month and day but a different year. At N5, we reviewed patients with the same date of birth and first name, but whose last names differed, which might occur due to marriage or divorce. At steps N3–N5, all close matches were again adjudicated by social security numbers or partner name.

The investigators were provided with a de-identified file where each woman was identified by one or more research ID numbers and dates were converted into ages or durations. To be included in the study, the woman had to have at least two reported IVF cycles in the database. The first cycle to report either a positive clinical intrauterine gestation or a live birth was labeled as cycle 1, and the first subsequent cycle as cycle 2. The second cycle did not have to result in a positive outcome. Research cycles, cycles restricted to embryo banking, and gestational carriers were excluded.

Statistical modeling

The women were grouped by the outcome of the first IVF cycle as a singleton or multiple live birth or as no live birth. Within these groups, the data were categorized by interpregnancy intervals and maternal age (age at first cycle) (Table 1), infertility diagnosis (Table 2), and length of gestation and birthweight categories (Table 3). Interpregnancy interval was defined as the time from outcome of the first cycle to the start of treatment for the second cycle. Outcomes across interpregnancy intervals were compared using χ^2; results were considered significant with $P < 0.05$. Within each of these analyses, the excess (percent above) or deficit (percent below) was generated, as [(observed − overall)/overall] where overall was the average over all ages.

We modeled the length of the interpregnancy interval by a general linear model as a function of mother's age (categorized), the infertility diagnoses, oocyte source (autologous vs. donor), and birthweight in the first cycle (categorized), separately for singleton, multiple live birth, or no live birth in the first cycle (Table 4). The data were analyzed using SAS 9.4 (Cary, NC) and Excel (Microsoft Corp, Redmond, WA).

Results

The final dataset for analysis included 49,804 women with a singleton live birth, 5993 with a multiple live birth, and 37,749 women with no live birth in cycle 1. The distributions of women across interpregnancy intervals by maternal age and outcome in cycle 1 are presented in Table 1. For multiple births, the distributions are shifted to the right, with a higher proportion of women waiting longer before initiating a second cycle. For women with no live birth in the first cycle, nearly three fourths attempted a subsequent pregnancy shortly after the end of the first pregnancy; the distribution of IPI was 75.3% (0–5 months), 16.3% (6–11 months), 4.2% (12–17 months), 1.8% (18–23 months), and 2.3% (≥ 24 months).

Among women with a live birth in cycle 1, there is a general pattern of longer IPI for younger women and shorter IPI for older women. Among singleton live births, women aged ≥ 41 were more than twice as likely to have an IPI of < 12 months compared to the youngest women (18–29 years) (39.7% for ages 41–43 and 38.0% for ages ≥ 44 years vs. 17.7%). In multiple births, a similar increase is seen (19.0 and 27.5% in the two oldest groups vs. 10.0% for women ages 18–29 years). In contrast, among women with no live birth in cycle 1, more than 70% of women in every age group had an IPI of 0–5 months, ranging from 76.6 to 70.4% from youngest to oldest age group.

The distributions of women across interpregnancy intervals by infertility diagnoses and outcome in cycle 1 (singleton births, multiple births, and no live births) are shown in

Table 1 Maternal age (%) by interpregnancy interval group

			Interpregnancy interval (months)						Excess (+ %) or deficit (− %) relative to "all ages"*				
Cycle 1 outcome	Age group	*N*, women	0–5	6–11	12–17	18–23	≥24	*P* value	0–5	6–11	12–17	18–23	≥24
All live births	All ages	55,797	3.3	20.0	29.8	18.7	28.1		3.3	20.0	29.8	18.7	28.1
	18–29 years	8694	2.5	15.2	27.0	19.3	36.0	< 0.0001	− 24.1	− 24.2	− 9.5	3.2	27.9
	30–34 years	21,487	2.2	16.1	29.4	20.3	31.9		− 32.2	− 19.4	− 1.3	8.2	13.5
	35–37 years	12,145	3.1	20.4	31.5	18.8	26.1		− 4.3	1.8	5.6	0.5	− 7.0
	38–40 years	7670	4.8	26.5	31.2	16.9	20.6		44.8	32.4	4.6	− 9.7	− 26.7
	41–43 years	3623	7.0	32.7	30.3	13.9	16.1		113.3	63.3	1.5	− 25.7	− 42.8
	≥44 years	2178	6.3	31.7	30.2	15.1	16.7		91.4	58.4	1.2	− 19.4	− 40.6
Multiple births	All ages	49,804	3.3	21.3	31.1	18.8	25.5		3.3	21.3	31.1	18.8	25.5
	18–29 years	7246	2.5	16.7	29.2	19.8	31.7	< 0.0001	− 24.2	− 21.5	− 6.0	5.3	24.4
	30–34 years	18,949	2.2	17.2	31.1	20.5	29.0		− 32.9	− 19.1	0.0	8.9	13.7
	35–37 years	11,099	3.1	21.3	32.4	18.8	24.4		− 7.3	0.0	4.1	0.0	− 4.1
	38–40 years	7121	4.8	27.5	31.6	16.9	19.2		42.8	29.3	1.8	− 10.3	− 24.6
	41–43 years	3397	7.2	33.9	30.4	13.7	14.9		117.3	59.3	− 2.4	− 27.4	− 41.7
	≥44 years	1992	6.3	32.7	30.0	15.0	16.0		88.3	54.0	− 3.4	− 20.6	− 37.2
Singleton births	All ages	5993	2.9	9.8	19.3	18.0	50.0		2.9	9.8	19.3	18.0	50.0
	18–29 years	1448	2.3	7.7	15.8	16.9	57.3	< 0.0001	− 19.1	− 21.9	− 18.0	− 6.2	14.6
	30–34 years	2538	2.2	8.3	17.0	18.5	54.0		− 25.4	− 15.3	− 11.8	3.0	7.9
	35–37 years	1046	3.7	11.1	22.3	18.7	44.2		28.4	13.0	15.5	4.3	− 11.7
	38–40 years	549	4.7	13.8	25.1	17.5	38.8		63.1	41.1	30.3	− 2.7	− 22.4
	41–43 years	226	3.5	15.5	28.8	17.7	34.5		21.9	57.8	49.1	− 1.5	− 31.0
	≥44 years	186	6.5	21.0	31.7	16.7	24.2		122.2	113.7	64.4	− 7.3	− 51.6
No live births	All ages	37,749	75.3	16.3	4.2	1.8	2.3		75.3	16.3	4.2	1.8	2.3
	18–29 years	4341	76.6	14.3	4.3	1.9	2.9	< 0.0001	1.8	− 12.8	2.0	6.9	23.7
	30–34 years	10,860	75.1	15.9	4.1	2.1	2.8		− 0.2	− 2.8	− 2.1	17.4	18.1
	35–37 years	7885	75.2	16.5	4.1	1.8	2.5		− 0.1	0.7	− 3.9	− 2.1	8.1
	38–40 years	7564	76.1	16.2	4.2	1.6	1.9		1.1	− 0.8	− 0.1	− 10.5	− 21.1
	41–43 years	4852	75.7	17.1	4.3	1.3	1.6		0.5	4.5	2.5	− 28.5	− 29.8
	≥44 years	2247	70.4	21.1	4.9	1.9	1.7		− 6.4	28.8	14.9	7.0	− 26.1

*Calculated as [observed/overall] − 1

Table 2 Diagnoses (%) by interpregnancy interval group

Cycle 1 outcome	Diagnosis	*N*, women	Interpregnancy interval (months)						Excess (+ %) or deficit (− %) relative to "all diagnoses"*				
			0–5	6–11	12–17	18–23	≥24	*P* value	0–5	6–11	12–17	18–23	≥24
Singleton births	All diagnoses	49,804	3.3	21.3	31.1	18.8	25.5		3.3	21.3	31.1	18.8	25.5
	Male factor (%)	19,745	3.0	19.7	30.9	19.6	26.8	< 0.0001	− 9.7	− 7.3	− 0.6	4.0	5.1
	Endometriosis (%)	5880	2.6	19.6	30.9	19.6	27.3	< 0.0001	− 23.5	− 7.9	− 0.5	4.2	7.2
	Ovulation disorders (%)	8485	3.0	19.3	30.9	19.7	27.1	< 0.0001	−11.2	− 9.4	− 0.4	4.5	6.5
	Diminished ovarian reserve (%)	8586	4.7	27.5	31.5	16.8	19.6	< 0.0001	40.5	29.4	1.2	− 10.9	− 23.3
	Tubal ligation (%)	643	6.5	22.6	25.3	15.1	30.5	< 0.0001	96.0	6.1	− 18.4	− 19.9	19.6
	Tubal hydrosalpinx (%)	664	2.9	19.3	31.3	18.5	28.0	0.49	− 14.1	− 9.3	0.8	− 1.7	9.9
	Tubal other (%)	5784	3.3	20.7	29.3	18.1	28.7	< 0.0001	− 2.0	− 2.8	− 5.7	− 4.3	12.6
	Uterine (%)	1902	3.2	23.9	31.9	18.3	22.8	0.011	− 5.4	12.3	2.7	− 2.9	− 10.7
	Unexplained (%)	6703	3.1	20.9	33.3	18.9	23.8	0.0001	− 6.5	− 1.5	7.1	0.3	− 6.8
	Other (%)	6023	3.9	23.0	30.9	17.9	24.3	0.0002	15.6	8.1	− 0.6	− 4.8	− 4.5
Multiple births	All diagnoses	5993	2.9	9.8	19.3	18.0	50.0		2.9	9.8	19.3	18.0	50.0
	Male factor (%)	2524	2.7	8.8	18.6	18.5	51.4	0.069	− 5.8	− 10.8	− 3.5	2.7	2.8
	Endometriosis (%)	784	2.0	8.3	18.2	18.4	53.1	0.15	− 29.7	− 15.5	− 5.4	2.2	6.1
	Ovulation disorders (%)	1213	3.1	9.2	18.9	17.9	50.9	0.85	7.9	− 6.7	− 2.1	− 0.5	1.8
	Diminished ovarian reserve (%)	821	3.7	13.5	23.8	19.1	40.0	< 0.0001	25.9	37.8	23.1	6.4	− 20.1
	Tubal ligation (%)	87	11.5	14.9	20.7	5.7	47.1	< 0.0001	295.9	52.3	7.3	− 68.0	− 5.8
	Tubal hydrosalpinx (%)	96	8.3	8.3	22.9	9.4	51.0	0.0051	187.0	− 15.1	18.8	− 47.8	2.0
	Tubal other (%)	679	3.8	10.3	18.9	17.7	49.3	0.62	31.9	− 2.8	− 5.7	− 4.3	12.6
	Uterine (%)	178	5.1	11.2	22.5	18.0	43.3	0.20	74.1	14.5	16.5	0.0	− 13.5
	Unexplained (%)	703	2.4	10.0	18.3	16.4	52.9	0.48	− 16.7	1.5	− 4.9	− 9.0	5.8
	Other (%)	671	2.4	11.5	20.4	21.5	44.3	0.0092	− 17.9	17.0	5.8	19.4	− 11.5
No live births	All diagnoses	37,749	75.3	16.3	4.2	1.8	2.3		75.3	16.3	4.2	1.8	2.3
	Male factor (%)	13,299	75.0	16.5	4.3	1.8	2.3	0.80	− 0.4	1.2	2.9	0.9	− 2.0
	Endometriosis (%)	3867	73.9	16.5	4.4	2.4	2.8	0.0054	− 1.8	0.8	4.1	34.5	20.1
	Ovulation disorders (%)	6266	75.1	16.3	4.1	1.8	2.7	0.24	− 0.3	− 0.2	− 3.2	0.9	17.0
	Diminished ovarian reserve (%)	8944	74.0	18.1	4.5	1.7	1.7	< 0.0001	− 1.7	11.0	6.7	− 6.8	− 29.5
	Tubal ligation (%)	865	71.3	17.7	5.1	2.7	3.2	0.025	− 5.3	8.2	20.5	48.7	37.9
	Tubal hydrosalpinx (%)	483	72.7	16.8	6.2	1.9	2.5	0.27	− 3.5	2.6	47.1	4.2	5.9
	Tubal other (%)	4699	71.2	18.2	5.4	2.2	3.0	< 0.0001	− 5.5	− 2.8	− 5.7	− 4.3	12.6
	Uterine (%)	1998	71.2	19.6	5.3	2.0	1.9	< 0.0001	− 5.4	20.0	24.5	12.0	− 19.0
	Unexplained (%)	4745	80.8	12.8	3.2	1.2	2.0	< 0.0001	7.3	− 21.5	− 23.1	− 34.0	− 16.5
	Other (%)	5073	74.9	16.3	4.2	2.1	2.4	0.52	− 0.5	− 0.3	0.4	16.9	3.3

*Calculated as [observed/overall] − 1

Table 3 Length of gestation (%) and birthweight (%) by interpregnancy interval group

			Interpregnancy interval (months)						Excess (+ %) or deficit (− %) relative to "all"* Interpregnancy interval (months)				
Cycle 1 outcome		*N*, women	0–5	6–11	12–17	18–23	≥ 24	*P* value	0–5	6–11	12–17	18–23	≥ 24
Singleton births	All	49,804	3.3	21.3	31.1	18.8	25.5		3.3	21.3	31.1	18.8	25.5
	% weeks' gestation												
	22–27 weeks	432	19.9	22.5	17.6	13.4	26.6	< 0.0001	497.3	5.6	− 43.4	− 28.7	4.5
	28–32 weeks	997	4.9	19.1	26.5	18.9	30.7		47.5	− 10.4	− 14.8	0.1	20.4
	33–36 weeks	6964	3.6	21.1	30.2	18.7	26.4		7.7	− 0.8	− 2.8	− 0.7	3.6
	≥ 37 weeks	41,411	3.1	21.3	31.5	18.9	25.2		− 7.6	0.3	1.3	0.4	− 1.1
	% Birthweight												
	300–999 g	390	21.8	22.1	19.5	13.1	23.6	< 0.0001	553.9	3.7	− 37.3	− 30.6	− 7.4
	1000–1499 g	362	6.6	20.4	20.2	20.7	32.0		98.9	− 3.8	− 35.1	10.0	25.7
	1500–2499 g	3624	3.8	20.1	30.0	19.5	26.6		12.6	− 5.2	− 3.5	3.7	4.3
	≥ 2500 g	45,428	3.1	21.3	31.4	18.8	25.4		− 6.5	0.4	0.9	− 0.1	− 0.5
Multiple births	All	5993	2.9	9.8	19.3	18.0	50.0		2.9	9.8	19.3	18.0	50.0
	% weeks' gestation												
	22–27 weeks	392	21.2	19.4	18.1	14.8	26.5	< 0.0001	629.3	97.6	− 6.1	− 17.7	− 47.0
	28–32 weeks	860	1.5	10.7	17.3	18.4	52.1		− 47.9	9.0	− 10.2	2.2	4.1
	33–36 weeks	3406	1.4	9.0	19.2	18.1	52.3		− 50.4	− 8.4	− 0.5	0.8	4.5
	≥ 37 weeks	1335	2.2	8.5	21.1	18.3	49.9		− 25.2	− 13.0	9.5	1.7	− 0.3
	% birthweight**												
	300–999 g	305	26.9	19.7	18.7	14.1	20.7	< 0.0001	826.0	100.5	− 3.1	− 21.5	− 58.7
	1000–1499 g	267	2.2	12.0	18.0	19.9	47.9		− 22.6	22.2	− 6.8	10.5	− 4.2
	1500–2499 g	2305	1.9	9.2	18.0	17.7	53.2		− 34.3	− 6.7	− 6.4	− 1.7	6.4
	≥ 2500 g	3116	1.3	9.1	20.4	18.4	50.7		− 53.6	− 6.8	5.6	2.5	1.4

*Calculated as [observed/overall] – 1

**For multiple births, the larger birthweight of the sibling set was used

Table 4 Regression models of factors associated with interpregnancy intervals

	Singleton live birth—cycle 1			Multiple live birth—cycle 1			No live birth—cycle 1		
	Regression coefficient (months)	SE (months)	*P* value	Regression coefficient (months)	SE (months)	*P* value	Regression coefficient (months)	SE (months)	*P* value
Intercept	23.0	0.2	< 0.0001	33.0	0.9	< 0.0001	6.9	0.2	< 0.0001
Age 18–29 years	0	Reference		0	Reference		0	Reference	
Age 30–34 years	− 0.7	0.1	< 0.0001	− 1.3	0.4	0.0040	0.0	0.1	0.85
Age 35–37 years	− 2.3	0.2	< 0.0001	− 4.2	0.5	< 0.0001	− 0.2	0.1	0.079
Age 38–40 years	− 4.0	0.2	< 0.0001	− 6.3	0.7	< 0.0001	− 0.6	0.1	< 0.0001
Age 41–43 years	− 5.7	0.2	< 0.0001	− 7.1	1.1	< 0.0001	− 0.9	0.1	< 0.0001
Age ≥ 44 years	− 5.4	0.3	< 0.0001	− 9.2	1.2	< 0.0001	− 0.8	0.2	< 0.0001
Autologous, both pregnancies	0	Reference		0	Reference		0	Reference	
Autologous, and then donor	6.2	0.7	< 0.0001	− 2.4	3.5	0.48	5.8	0.2	< 0.0001
Donor, and then autologous	0.4	0.4	0.34	2.5	1.4	0.076	1.4	0.3	< 0.0001
Donor, both pregnancies	0.9	0.2	< 0.0001	0.0	0.8	0.97	1.5	0.1	< 0.0001
Fresh, both times	0	Reference		0	Reference		0	Reference	
Fresh, then thawed	0.2	0.1	0.027	0.4	0.5	0.36	− 0.3	0.1	< 0.0001
Thawed, then fresh	1.5	0.3	< 0.0001	0.0	1.6	0.98	1.1	0.1	< 0.0001
Thawed, both times	1.2	0.2	< 0.0001	2.2	0.7	0.0015	0.3	0.1	0.0028
Diminished ovarian reserve	− 0.6	0.3	0.019	− 0.2	1.0	0.87	− 0.5	0.2	0.0032
Birthweight 300–999 g	− 1.3	0.5	0.013	− 8.5	0.8	< 0.0001	N/A	N/A	N/A
Birthweight 1000–1499 g	1.7	0.6	0.0028	− 1.5	0.8	0.083	N/A	N/A	N/A
Birthweight 1500–2499 g	0.6	0.2	0.0007	0.5	0.4	0.15	N/A	N/A	N/A
Birthweight 2500+ grams	0	Reference		0	Reference		0	Reference	

Models adjusted for all other diagnoses and reporting year; no live birth also adjusted for heartbeats on ultrasound at 6 weeks

Table 2. Among women with a live birth in cycle 1, those with a diagnosis of tubal ligation or diminished ovarian reserve were more likely to have a shorter IPI.

The distributions of live births across interpregnancy interval by weeks of gestation and birthweight are shown in Table 3. Women with live births which were the most premature (22–27 weeks) and lowest birthweight (300–999 g) were much more likely to have an IPI of 0–5 months (among all live births, 19.9% for 22–27 weeks and 21.8% for 300–999 g vs. 3.3% overall); the pattern was similar for singleton and multiple births.

The results of the regression analyses of factors associated with interpregnancy interval for singleton and multiple live births in cycle 1 are presented in Table 4. In these analyses, the regression coefficients are expressed in months. Among singleton births, maternal age in cycle 1 was the most important factor, decreasing the baseline IPI by less than 1 month for women ages 30–34 to 5.4 months for women ages ≥ 44. Compared to birthweights of ≥ 2500 g in cycle 1, women whose infants had the lowest birthweights (300–999 g) had shorter IPIs by about 1.3 months, whereas birthweights of 1000–1499 g were associated with a greater IPI by 1.7 months and birthweights of 1500–2499 g with an IPI 0.6 months greater. When the source of the oocyte changed from autologous to donor, there was an average delay of 6.2 months. Also, when frozen embryos were used in the first cycle, there was a delay of 1 month in the second cycle, whether the second cycle embryo was fresh or thawed.

Among multiple births, maternal age in cycle 1 was again the most important factor, decreasing the baseline IPI by about 1.3 months for women ages 30–34 to 9.2 months for women ages ≥ 44. Compared to birthweights of ≥ 2500 g in cycle 1, women whose infants had the lowest birthweights (300–999 g) had shorter IPIs by about 8.5 months, whereas other birthweights had nonsignificant effects. When frozen embryos were used in both cycles, there was an average delay of 2.2 months.

Among women without a live birth and the source of the oocyte changed from autologous to donor, there was an average delay of 5.8 months. When frozen embryos were used, there was a delay of 0.3 to 1.1 months. Since singleton and multiple are reported at delivery, we added ultrasound fetal hearts to the model; where there was more than one fetal heart, there was a delay of 1.3 ± 0.1 months, and when there were no fetal hearts, there was a reduction in the IPI of 0.7 ± 0.1 months compared to when there was one fetal heart.

Discussion

These analyses reveal specific characteristics associated with the length of the IPI in women undergoing IVF pregnancies. No live birth, a singleton birth in the first pregnancy, and older maternal age were associated with short IPI. Of note, those women with a live birth who had the shortest IPI were those with the lowest birthweight and gestation in the first pregnancy, likely reflecting perinatal or neonatal death. It seems logical that a couple seeking a child with a poor obstetric outcome, such as perinatal or neonatal death, would be more likely to seek treatment for a subsequent pregnancy sooner. However, these patients are at increased risk for recurrence of preterm delivery in a subsequent pregnancy [8], and discussion of this risk should be included in the counseling prior to initiating treatment, with consideration for evaluation by a maternal fetal medicine specialist. Moreover, given the elevated risk of recurrence of preterm delivery and potential associated maternal morbidities, such as preeclampsia, these patients should be counseled about the additional risks associated with short IPI prior to their decisions regarding IVF treatment.

The strengths of this study include a very large subject pool with use of the SART CORS database, which contains reported data from diverse geographical areas and clinic types within the USA. Limitations include its retrospective nature, as well as the limitations of the SART-CORS database; no additional demographic or clinical information from the subjects could be obtained other than what was provided through the database. In addition, other non-IVF pregnancies, whether spontaneous or the result of intrauterine insemination, may have occurred in between both pregnancies examined in this study. Unfortunately, these pregnancies were not identifiable in the SART CORS database. The absence of these data may have falsely increased the calculated IPI in those patients with non-IVF pregnancies between both examined pregnancies. However, we believe the absolute number of women to whom this applies is low, given that IVF is typically a second- or third-line infertility treatment and is often required to achieve all pregnancies, if deemed necessary. Additionally, the database used did not allow for the tracking of patients who switched fertility clinics between treatments.

In conclusion, women without a live birth or with a preterm delivery followed by neonatal or perinatal demise in the first pregnancy, a singleton birth, and older maternal age are more likely to have a short IPI. These women should be counseled about the risks associated with short IPI, in addition to potential risks associated with prior obstetric morbidity.

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Compliance with ethical standards

This study was approved by Institutional Review Board of the Michigan State University.

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