Cumulative live birth rate in women aged ≤37 years after in vitro fertilization with or without preimplantation genetic testing for aneuploidy: a Society for Assisted Reproductive Technology Clinic Outcome Reporting System retrospective analysis

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Objective: To investigate cumulative live birth rates (CLBRs) in cycles with and without preimplantation genetic testing for aneuploidy (PGT-A) among patients aged <35 and 35–37 years.
Design: Retrospective cohort study.
Setting: Society for Assisted Reproductive Technology reporting clinics.
Patient(s): A total of 31,900 patients aged ≤ 37 years with initial oocyte retrievals between January 2014 and December 2015 followed through December 2016.
Intervention(s): None.
Main outcome measure(s): The primary outcome was CLBR among patients aged <35 and 35–37 years. The secondary outcomes included multifetal births, miscarriage, preterm birth, perinatal mortality, and the time to pregnancy resulting in a live birth. Adjusted odds ratios (aORs) adjusting for age, body mass index, total 2 pronuclei embryos, embryos transferred, and follow-up timeframe.
Result(s): Among patients aged <35 years, PGT-A was associated with reduced CLBRs (70.6% vs. 71.1%; aOR, 0.82; 95% CI [confidence interval], 0.72–0.93). No association was found between PGT-A and CLBRs among patients aged 35–37 years (66.6% vs. 62.5%; aOR, 0.92; 95% CI, 0.83–1.01). Overall, there was no significant difference in the miscarriage rate (aOR, 0.97; 95% CI, 0.82–1.14). Multifetal birth rates were lower with PGT-A (9.5% vs. 23.1%); however, PGT-A was not an independent predictor of multifetal birth (aOR, 1.11; 95% CI, 0.91–1.36). The average time to pregnancy resulting in a live birth was 2.37 months (SD 3.20) for untested transfers vs. 4.58 months (SD 3.53) for PGT-A transfers.
Conclusion(s): In women aged <35, the CLBR was lower with PGT-A than with the transfer of untested embryos. In women aged 35–37 years, PGT-A did not improve CLBRs. (Fertil Steril Rep® 2022;3:184–91. ©2022 by American Society for Reproductive Medicine.)
Key Words: Preimplantation genetic testing-aneuploidy, IVF, live birth rate, SART CORS

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The use of preimplantation genetic testing for aneuploidy (PGT-A), formerly known as preimplantation genetic screening, has increased in recent years, now encompassing an estimated 40% of in vitro fertilization (IVF) cycles in the United States (1). This technique has evolved throughout the years and is now largely performed by biopsy of the blastocyst trophectoderm cells with genetic analysis using newer techniques such as next-generation sequencing and array comparative genomic hybridization to test for aneuploidy (2, 3). Because chromosomal abnormalities are assumed to be the major cause of implantation failure and early pregnancy loss, PGT-A has been touted as a method to select the best embryo for transfer in patients with age-related decline in fertility and recurrent pregnancy loss (2, 3). However, chromosomal abnormalities are common even among younger patients with aneuploid embryos, encompassing 34% of the total embryo pool at 35 years of age and 43% of embryos by 37 years of age (4). Because embryo morphology has been shown to be poorly predictive of aneuploidy (3, 5), PGT-A is increasingly used among all patients undergoing IVF regardless of age or diagnosis, and some studies have shown higher implantation rates per embryo transfer, higher pregnancy and live birth rates, and a reduction in the time to pregnancy when PGT-A is used (2, 6, 7). Other benefits of PGT-A include improved patient and provider confidence in elective single embryo transfer, leading to a reduction in multiple birth rates (8).

However, the use of PGT-A for the improvement of live birth rates is controversial, and a recent randomized controlled trial found no difference in the ongoing pregnancy per embryo transfer or intention to treat after randomization to PGT-A or morphology alone (9). A recent Cochrane review found insufficient good-quality evidence that live birth rates after the first embryo transfer, cumulative live birth rates (CLBRs), and miscarriage rates are significantly different between IVF with and without PGT-A and concluded that there is currently insufficient evidence to support the use of PGT-A in routine clinical practice (10). Preimplantation genetic testing for aneuploidy is not without risks, and these include the increased cost of testing, the possibility of embryo damage during or following biopsy, and the possibility of testing error; even if the testing is correct, a trophectoderm biopsy with a percentage of aneuploid cells may not reflect the potential of the embryo to lead to a healthy live birth and, thus, good embryos may be discarded (11–13). Furthermore, embryos of insufficient morphologic grade may be discarded before biopsy, lowering the total number of embryos available for transfer. Data suggest that embryos of lower morphologic grade do have appreciable live birth rates and should be considered for transfer (14). In a recent review, Kemper et al. (15) evaluated randomized controlled trials comparing IVF with and without PGT-A and found that only 2 trials examined the CLBRs per started cycle. They discussed that although PGT-A may lead to an improved live birth rate for the first embryo transferred, it cannot restore euploidy to aneuploid embryos and, therefore, will never increase the CLBR from a pool of transferrable embryos. Therefore, they made a call for more studies examining the CLBR after PGT-A (15).

The Society for Assisted Reproductive Technology (SART) database encompasses data from a majority (86% in 2018) of IVF clinics in the United States and is a rich resource of current practice patterns around the country. We sought to investigate CLBRs in cycles with and without PGT-A using the SART database, examining the youngest patients (those aged $\leq$35 years and those aged 35–37 years). Our hypothesis was that there would be no difference in CLBRs between cycles with and without PGT-A in this patient population.

MATERIALS AND METHODS

The data used for this retrospective analysis were obtained from the SART Clinic Outcome Reporting System (CORS) and included patients aged 21–37 years who had their first autologous IVF retrieval cycle between January 2014 and December 2015. Data were collected through voluntary submission, were verified by SART, and were 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). In 2004, after a contract change with the Centers for Disease Control and Prevention, SART gained access to the SART CORS data system for the purposes of conducting research.

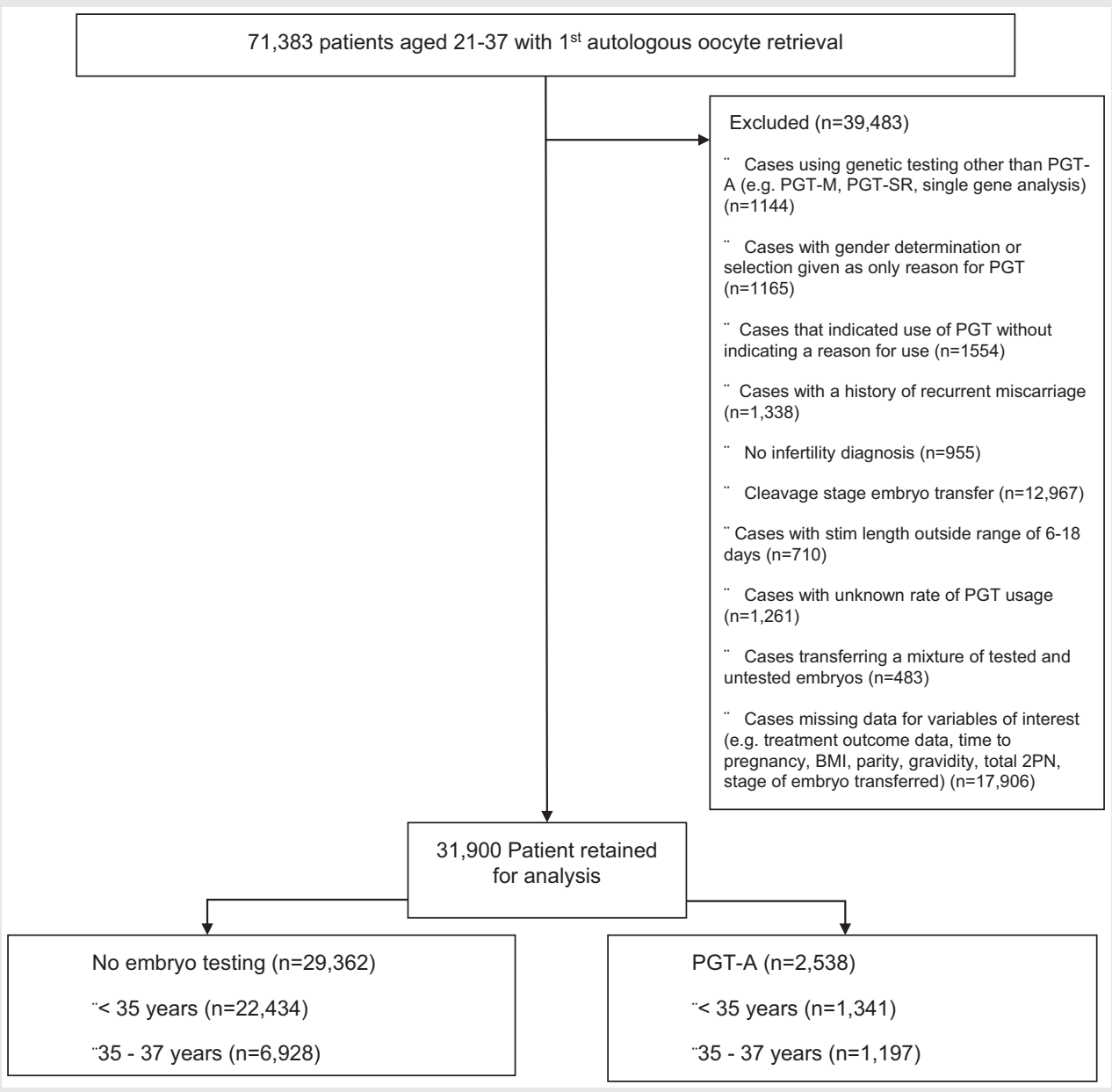
The data in the SART CORS are validated annually, with 7%–10% of clinics receiving on-site visits for chart review on the basis of an algorithm for clinic selection. During each visit, data reported by the clinic were compared with the information recorded in patients' charts. In 2019, records for 2,014 cycles at 34 clinics were randomly selected for full validation, along with 213 fertility preservation cycles selected for partial validation. The full validation included a review of 1,300 cycles for which pregnancy was reported. Nine out of 11 data fields selected for validation were found to have discrepancy rates of $\leq$5% (16). The exceptions were the diagnosis field, which, depending on the diagnosis, had a discrepancy rate between 2.5% and 17.8%, and the start date, which had an 8.4% discrepancy rate (16). Obstetrical outcomes from Massachusetts assisted reproductive technology records from 2004–2008 have been validated to have >95% agreement with vital records (17).

The study was determined to be exempt from review by the University of Iowa institution review board (Determination of Human Subjects IRB ID# 201608711). The SART maintains the Health Insurance Portability and Accountability Act of 1996–compliant business associates agreements with reporting clinics.

Study Population

The dataset contained 71,610 patients aged 21–37 years. Patients were excluded if they did not have an infertility diagnosis, had a history of recurrent miscarriage, used genetic testing other than PGT-A, had a cleavage-stage embryo transfer, or were missing data on a variable of interest. Cases indicating "some" embryos for preimplantation genetic testing that had an embryo transfer during the fresh cycle were excluded from analysis because it was not possible to determine from the data available if tested or untested embryos were transferred in the fresh cycle. After these patients

FIGURE 1



Study sample selection. 2PN = 2 pronuclei; BMI = body mass index; PGT = preimplantation genetic testing; PGT-A = preimplantation genetic testing for aneuploidy; PGT-M = preimplantation genetic testing for monogenic disease; PGT-SR = preimplantation genetic testing for structural rearrangement.

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were excluded, the final population analyzed comprised 31,900 patients (Fig. 1).

Cycle Linkage

In addition to each patient's first autologous retrieval cycle, the dataset included all linked subsequent cycles wherein embryos cryopreserved in the first retrieval cycle were transferred through December 2016. The patients were followed through a live birth resulting from a linked transfer cycle, or if no live birth occurred, through the end of their final transfer cycle within the period from January 2014 to December 2016. The cycle linkage is tracked by SART using cycle Identifications (IDs), with each retrieval and thaw cycle assigned a unique ID. Linked thaw cycle IDs are recorded for each retrieval cycle, whereas linked retrieval cycle IDs are recorded for each transfer cycle. Subsequent linked transfer cycles for each patient were identified by matching on both

patient and retrieval cycle IDs, thereby excluding thaw cycles that resulted from retrieval cycles other than the first autologous cycle. We restricted transfer cycles to only those using embryos from the initial retrieval cycle by excluding cycles that reported ≥2 retrieval cycle IDs. In addition to identifying linked cycles through cycle IDs, we confirmed that retrieval cycle fields (such as number retrieved) matched between the initial autologous transfer and all linked subsequent transfers. Linked cycles for each patient were chronologized on the basis of cycle number (from 1 to the highest, where cycle number 1 indicates a patient's first reported IVF cycle, and clinics assign subsequent cycle numbers chronologically).

Measures

Cases were classified as using PGT-A if they were recorded as using preimplantation genetic testing for "all" or "some" embryos and if aneuploidy screening was identified as the indication. Cases meeting these criteria with preimplantation genetic testing for some embryos that did not have a transfer in the fresh cycle were classified as PGT-A on the basis of the assumption that tested embryos were transferred in subsequent frozen embryo cycles because clinics may only perform PGT-A on good-quality embryos or patients opted to limit the number of embryos biopsied for preimplantation genetic testing. As stated above, cases indicating "some" embryos for preimplantation genetic testing that had an embryo transfer during the fresh cycle were excluded from the analysis.

Our primary outcome was cumulative live birth, which SART defines as up to 1 live birth resulting from a retrieval cycle and linked transfer cycles (18). Secondary outcomes included multifetal births, miscarriage, preterm birth, perinatal mortality, and the time to pregnancy resulting in a live birth. Miscarriage was defined as a pregnancy loss within 18 weeks after embryo transfer. Preterm birth was assessed at 2 levels, defined as delivery before 28 and 32 weeks of gestation. Perinatal mortality was defined as the death of a live born infant before the completion of the 28th day of life. The time to pregnancy resulting in a live birth was selected as an outcome to avoid the confounding impact of preterm delivery on the time to live birth. We calculated the time to pregnancy resulting in a live birth by adding 10 days (the standard amount of time from embryo transfer to the pregnancy test) to the number of days between the start of medication in the retrieval cycle and the embryo transfer that resulted in the live birth.

A detailed description of data collection and summary for fields of race, infertility diagnosis, and intracytoplasmic sperm injection (ICSI) use has been described elsewhere (19). Of note, the precise length of patient follow-up was not available within the dataset because of the de-identification process. Because the treatment for all patients was followed through 2016, we used the year of the initial retrieval cycle (2014 or 2015) as a proxy for the length of follow-up, with patients who had their initial cycle in 2014 having the potential for up to 3 years of follow-up, whereas those who had their initial cycle in 2015 only had the potential for up to 2 years of follow-up.

Statistical Analyses

Because live birth rates are relatively stable in women aged <35 years but decline steadily past the age of 35 years (20), we grouped women into 2 cohorts on the basis of their age (<35 or 35–37 years) at the beginning of their retrieval cycle. These age-based cohorts match those routinely used by SART to report IVF outcomes. The sample was described using the *t*-test, Mann-Whitney *U* test, and χ^2. Statistical analyses were performed with SPSS version 26 and SAS 9.4. Generalized linear mixed models were used to assess the impact of PGT-A on the CLBR, multifetal delivery rate, miscarriage rate, and time to pregnancy. Age, diagnosis, weight, body mass index (BMI), total follicle-stimulating hormone dosage in the stimulation cycle, use of ICSI, number of 2 pronuclei (2PN) embryos, number of embryos cryopreserved, use of assisted hatching, number of embryos transferred, and length of follow-up were assessed as potential covariates for the regression model. We did not include race in the regression model because a large proportion of the sample was missing data on race. The Bayesian information criteria were used to select covariates for inclusion in the final model after models of all possible covariate subsets were fit. The final regression included the following covariates: age, BMI, the number of 2PN, the number of embryos transferred, and the length of follow-up.

The infant outcomes were assessed for singleton and multifetal live births.

RESULTS

There were nearly 11 times as many patients who had untested embryos compared with the number of patients having PGT-A–tested embryos in this study group (29,362 untested vs. 2,538 using PGT-A). Patients using PGT-A–tested embryos were older than patients using untested embryos (33.5 ± 3.0 vs. 31.8 ± 3.3) (Table 1). Overall, infertility diagnoses were clinically similar between the groups, although more patients in the PGT-A group had multiple diagnoses (36.8% vs. 22.2%), a higher rate of diminished ovarian reserve (5.2% vs. 3.2%), and a lower rate of male infertility (18.3% vs. 25.4%). Data on patient race were only available for 66.2% of the sample. Among patients with race reported, racial backgrounds were similar when comparing the groups, although those having untested embryos were more likely to be of Black (3.6% vs. 7.1%) or Hispanic/Latino (5.6% vs. 7.5%) background and those using PGT-A were more likely to be of Asian background (19.6% vs. 12.0%) (Table 1).

There were differences in the cycle characteristics when comparing untested and PGT-A groups. Women using PGT-A had a higher total follicle-stimulating hormone dosage (3,015 ± 1,337 vs. 2742 ± 1289) and used ICSI more frequently (93.0% vs. 74.4%) than those using untested cycles (Table 1).

We statistically adjusted all comparisons by controlling for a woman's age, BMI, the total number of 2PN embryos, the number of embryos transferred in the final transfer cycle, and the length of follow-up. Overall, PGT-A was not associated with CLBR (adjusted odds ratio [aOR], 0.92; 95% confidence interval [CI], 0.83–1.01), miscarriage (aOR, 0.97; 95%

TABLE 1

Patient and cycle characteristics (n = 31,900).

Patient and cycle characteristics	Full sample			< 35 y of age			35–37 y of age		
	PGT-A (n = 2,538)	Untested (n = 29,362)	*P* value	PGT-A (n = 1,341)	Untested (n = 22,434)	*P* value	PGT-A (n = 1,197)	Untested (n = 6,928)	*P* value
Age (y)	33.5 ± 3.0	31.8 ± 3.3	<.001	31.3 ± 2.4	30.6 ± 2.7	<.001	36.1 ± 0.8	35.9 ± 0.8	<.001
BMI	23.0 (21.0–26.6)	24.4 (21.6–28.7)	<.001	23.0 (20.9–26.6)	24.2 (21.6–28.6)	<.001	23.1 (21.0–26.7)	24.8 (21.9–29.2)	<.001
Gravidity	0 (0–1)	0 (0–1)	<.001	0 (0–1)	0 (0–1)	.028	0 (0–1)	0 (0-1)	.750
Parity	0 (0–0)	0 (0–0)	<.001	0 (0–0)	0 (0–0)	.287	0 (0–0)	0 (0-0)	.879
Diagnosis			<.001			<.001			<.001
Male infertility	18.3[a]	25.4[a]		19.9[a]	26.5[a]		16.5[a]	21.7[a]	
Endometriosis	3.1[a]	4.6[a]		4.0	4.8		2.1[a]	4.0[a]	
Anovulation	9.2[a]	12.5[a]		11.4[a]	13.8[a]		6.8	8.4	
Diminished ovarian reserve	5.2[a]	3.2[a]		3.5[a]	2.4[a]		7.0	6.0	
Tubal factor	3.9[a]	8.6[a]		4.7[a]	8.2[a]		3.1[a]	9.9[a]	
Uterine factor	1.3	1.2		1.2	1.1		1.5	1.7	
Unexplained	16.0[a]	18.3[a]		13.8[a]	17.5[a]		18.5	20.8	
Multiple	36.8[a]	22.2[a]		36.5[a]	22.0[a]		37.1[a]	11.8[a]	
Other	6.1[a]	3.9[a]		5.0[a]	3.6[a]		7.4[a]	4.6[a]	
Patient Race			<.001			<.001			<.001
White	69.8	71.3		73.7	72.9		65.3	66.0	
Black	3.6[a]	7.1[a]		2.7[a]	6.6[a]		4.6[a]	8.6[a]	
Hispanic/Latino	5.6[a]	7.5[a]		4.9[a]	7.0[a]		6.4[a]	9.3[a]	
Asian	19.6[a]	12.0[a]		17.4[a]	11.5[a]		22.2[a]	13.6[a]	
Other/multiracial	1.4	2.1		1.3	2.0		1.5	2.4	
Oocytes retrieved	18 ± 10	16 ± 8	<.001	20 ± 10	17 ± 9	<.001	17 ± 9	15 ± 8	<.001
2PN embryos	10 (7–15)	9 (6–13)	<.001	11 (8–16)	9 (6–13)	<.001	10 (6–14)	8 (6–12)	<.001
Assisted hatching	75.5	34.8%	<.001	79.9	34.3	<.001	70.5	36.6	<.001
ICSI	93.0	74.4%	<.001	94.3	75.1	<.001	91.6	72.3	<.001
FSH dosage (IU/stimulation cycle)	3,015 ± 1,337	2,742 ± 1,289	<.001	2,820 ± 1,205	2,582 ± 1,152	<.001	3,134 ± 1,272	3,088 ± 1,284	.266
Embryos transferred in first transfer cycle			<.001			<.001			<.001
SET	85.7	49.4		85.7	52.4		85.8	39.7	
DET	14.2	49.9		14.2	47.1		14.1	59.0	
MET	0.1	0.7		0.1	0.5		0.1	1.3	
Embryos transferred in final transfer cycle			<.001			<.001			<.001
SET	81.6	44.4		80.6	46.7		82.8	37.1	
DET	18.2	54.4		19.3	52.4		17.0	60.8	
MET	0.1	1.2		0.1	0.9		0.2	2.1	
Total embryos transferred across all transfer cycles	1 (1–2)	2 (1–2)	<.001	1 (1–2)	2 (1–2)	<.001	1 (1–2)	2 (1–2)	<.001

Note: Data are presented as mean ± SD, median (interquartile range), or percentage. 2PN = 2 pronuclei; BMI = body mass index; DET = double embryo transfer; FSH = follicle-stimulating hormone; ICSI= intracytoplasmic sperm injection; MET = multiple embryo transfer; PGT-A = preimplantation genetic testing for aneuploidy, SET = single embryo transfer.

[a] Significant at .05 level in the post hoc z-test.

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TABLE 2

Outcomes comparing PGT-A to untested embryos.

Full Sample

Outcomes	PGT-A	Untested	aOR (95% CI)
Cumulative live birth rate (%)	68.7	69.0	0.92 (0.83ç1.01)
Multifetal births (%)	9.5	23.1	1.11 (0.91–1.36)
Miscarriages (%)	7.4	7.6	0.97 (0.82–1.14)
<35 y old			
	PGT-A	Untested	aOR (95% CI)
Cumulative live birth rate (%)	70.6	71.1	0.82 (0.72–0.93)
Multifetal births (%)	8.7	23.2	0.83 (0.64–1.10)
Miscarriages (%)	7.0	7.0	1.08 (0.86–1.35)
35–37 y old			
	PGT-A	Untested	aOR (95% CI)
Cumulative live birth rate (%)	66.6	62.5	1.14 (0.99–1.31)
Multifetal births (%)	10.5	22.8	1.67 (1.23–2.26)
Miscarriages (%)	7.9	9.5	0.77 (0.61–0.98)

Note: Odds ratios were adjusted for age, BMI, number of 2 pronuclei embryos, number of embryos transferred in the final transfer cycle, and length of follow-up. aOR = adjusted odds ratio; CI = confidence interval; PGT-A = preimplantation genetic testing for aneuploidy.

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CI, 0.82–1.14), or multifetal births (aOR, 1.11; 95% CI, 0.91–1.36) (Table 2).

For patients aged <35 years, the crude CLBR for PGT-A (70.6%) and untested (71.1%) embryos was similar, however, after adjusting for covariates, PGT-A was associated with a lower CLBR (aOR, 0.82; 95% CI, 0.72 –0.93) (Table 2). There was not a significant difference in miscarriage rate between PGT-A and untested groups (aOR, 1.08; 95% CI, 0.86–1.35). Although PGT-A was associated with lower rates of multifetal births (8.7 % vs. 23.2%), it was not an independent predictor of multifetal birth within this age group (aOR, 0.83; 95% CI, 0.64 –1.10).

Among women aged 35–37 years, there was no significant difference in the CLBR for PGT-A (66.6%) and untested embryos (62.5%) (aOR, 1.14; 95% CI, 0.99–1.31) (Table 2). Unlike patients aged <35 years, among patients aged 35–37 years, PGT-A was associated with a significant reduction in miscarriage (aOR, 0.77; 95% CI, 0.61–0.98). In this age group, PGT-A was also found to be associated with an increase in multifetal birth (aOR, 1.67; 95% CI, 1.23 –2.26). Although multifetal births were higher among the untested group (23.2% vs. 10.5%), when examined by the number of embryos transferred, a greater proportion of double embryo transfers in the PGT-A group resulted in multifetal birth (51.4%) compared with the untested group (34.7%). Rates of multifetal birth among single embryo transfers were similar between PGT-A and the untested embryos (1.2% vs. 1.5%).

Singleton live births in women aged ≤37 years who underwent PGT-A testing had an average infant birthweight of 3,340 grams compared with an average of 3,258 grams in singleton live births from untested embryos. Preterm birth (at 28 and 32 weeks) and perinatal mortality were similar in both singleton (1.1% vs. 1.2%, 2.4% vs. 2.6%, and 0.5% vs. 0.6%) and twin and high-order multiple live births (6.6% vs. 5.7%, 16.2% vs. 14.7%, and 1.8% vs. 1.9%) from PGT-A compared with the untested embryos (Table 3).

The average time from onset of IVF cycles to a pregnancy resulting in a live birth was significantly shorter in untested transfer cycles (mean difference 2.2 months, 95% CI, 2.1–2.3 months). For patients aged <35 years, the time to pregnancy resulting in a live birth was 2.38 months (SD 3.19) for untested transfer cycles and 4.53 months (SD 3.49) for PGT-A transfers. For patients aged 35–37 years, the average time to pregnancy using untested embryos was 2.35 months (SD 3.25) and that using PGT-A cycles was 4.63 months (SD 3.57).

DISCUSSION

Our study, which found lower CLBRs in patients aged <35 years and no improvement in those aged 35–37 years, adds to the conflicting data promoting PGT-A as a tool to improve live birth rates after IVF. Recently, in a 2019 randomized control trial, the use of PGT-A did not improve ongoing pregnancy rates per transfer in women aged 25–40 years undergoing IVF compared with embryos selected by morphology alone (9). The American Society for Reproductive Medicine committee opinion on the use of PGT-A states that currently, there is insufficient evidence to recommend the routine use of blastocyst biopsy with aneuploidy testing in all infertile patients (21). Despite the insufficient level of evidence supporting the use of PGT-A, an increasing number of laboratories are performing PGT-A routinely (9, 15). At the time this data was released from SART reporting clinics in 2019, 43% of cycles were reported to be using PGT-A.

In our large national cohort, after controlling for covariates, not only did we find no improvement in the live birth rate but, for women aged <35 years, PGT-A was associated with a decreased CLBR compared with that for women who did not use PGT-A. This is, to our knowledge, the first large prospectively captured SART database study that reports a lower cumulative LBR in women that used PGT-A. Although other studies have demonstrated that the use of PGT-A may be beneficial in patients over the age of 35 years, the use of

TABLE 3

Infant outcomes for cycles resulting in live birth by pregnancy type.

	Singleton pregnancies (17,373 infants in 17,373 pregnancies)			Twin and higher-order multiple pregnancies (9,811 infants in 4,870 pregnancies)		
Infant outcomes	**PGT-A**	**Untested**	***P* value**	**PGT-A**	**Untested**	***P* value**
Birthweight[a]	3,340 ± 599	3,258 ± 762	<.001	2,308 ± 613	2,311 ± 634	.927
Preterm birth before 28 weeks[b]	1.1	1.2	.828	6.6	5.7	.714
Preterm birth before 32 weeks[b]	2.4	2.6	.630	16.2	14.7	.608
Perinatal mortality[a]	0.5	0.6	.628	1.8	1.9	.885

Note: Data are presented as mean ± SD or percentage. PGT-A = preimplantation genetic testing for aneuploidy.
[a] Outcomes reported per infant.
[b] Outcomes reported per pregnancy.

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PGT-A in younger patients is controversial because several randomized control trials have not found a significant difference in pregnancy rates with the use of PGT-A vs. controls (9). Our study supports that this practice is not beneficial and may even be detrimental with routine use in this younger age group. This could potentially be explained by women aged 26–38 years having higher rates of euploid embryos (4), the potential damage caused by the current invasive biopsy techniques (15), the risk of false-positive PGT-A results, the uncertainty of self-correction, and/or accuracy of mosaic diagnosis leading to discarding of viable embryos that could have resulted in healthy infants (21, 22). Ultimately, we are screening a low-risk population and decreasing the cohort of usable embryos for transfer. Just recently, a randomized controlled trial was published evaluating the CLBR with PGT-A vs. conventional IVF, and it demonstrated that among women with a good prognosis for a live birth, conventional IVF was noninferior to PGT-A (23) and resulted in a higher CLBR. We report similar findings from a large national dataset specifically examining the CLBR.

Our study evaluated the use of PGT-A on miscarriage rates and found no significant difference compared with untested embryos in the patient group aged <35 years. However, in women aged 35–37 years, the miscarriage rate was significantly lower in the PGT-A group compared with that in the untested embryo group. Similarly, Murphy et al. (24) found no significant difference in the rate of miscarriage per transfer in PGT-A embryos compared with that in controls, supporting that the cause of miscarriage is not solely based on the chromosome status of the embryo. Based on these studies, we should be cautious and avoid proposing to patients that PGT-A will decrease miscarriage rates in younger patients.

Our study showed a marked reduction in multiple birth rates in PGT-A cycles. We hypothesize that this is related to increased provider and patient confidence in the use of elective single embryo transfer after PGT-A cycles because the relationship was not statistically significant among patients aged <35 years, and PGT-A was actually found to be associated with increased multifetal births among those aged 35–37 years in our multivariate models that included the number of embryos transferred. We have previously analyzed the SART CORS dataset during this same time frame in which we excluded all PGT-A cycles and demonstrated that elective single embryo transfer was associated with increased CLBR compared with double embryo transfer (74% vs. 57% [aOR, 1.32; 95% CI, 1.26–1.38]) (19). This reinforces that even without PGT-A, a high CLBR can be achieved when transferring 1 embryo in the initial transfer cycle (19). When we assessed infant outcomes, there was a statistically significant difference with lower birth weight in the untested group (3,258 grams vs. 3,340 grams) among singleton pregnancies, although an 82-gram (2.9 ounces) difference may not translate into clinical significance. There were no other differences in infant outcomes among singletons or twin or higher-order multiples.

A strength of our study is the use of a large prospectively collected dataset from the SART Reporting Clinics database that captures >85% of all IVF cycles performed in the United States. Cumulative IVF outcomes can be determined through linkages between the initial cycle and subsequent embryo transfers, allowing for the study of the full reproductive potential of an IVF stimulation cycle. This study supports the current advocacy for detailing CLBRs when investigating PGT-A efficacy (15). We acknowledge that this study includes data that is several years delayed; however, live birth outcomes for transfers occurring in 2016 were not finalized until 2019. This was one of the first datasets released, which included linked cycles as well as a patient's first autologous cycle. As a result, there were multiple delays in obtaining the dataset. In addition to the delay of outcome data necessitated by our primary outcome of cumulative live birth, studies assessing this outcome may be limited by missing cycle linkage data. The SART database relies on clinics to accurately report the appropriately linked retrieval cycles for embryos transferred in a thawed cycle. It is possible that some subsequent transfers of embryos from the initial retrieval cycle of interest were missing from our dataset if clinics did not accurately enter linked thawed transfer cycles into the database. We are unable to estimate a frequency for linkage data entry errors in our dataset because inclusion criteria required that all thaw cycles in our dataset be linked to a patient's initial autologous retrieval cycle and because there are a number of reasons patients may complete a retrieval cycle without returning for subsequent transfers (25).

We did not include patients aged ≥38 years of age for several reasons. Foremost, our goal was to understand the CLBR in this younger patient population that has a lower risk of aneuploidy, in which we questioned the utility of PGT-A. Additionally, because of the higher rate of embryo banking cycles in older patients, there was a greater likelihood of incorrect reporting of cycle numbers, making it challenging to assess the CLBR from 1 retrieval.

CONCLUSION

The use of PGT-A has undergone many technical developments and has been increasing in clinical practice in recent years. Our results from national data provide a framework that using PGT-A for women aged <38 years does not lead to an improved CLBR compared with transferring untested embryos.

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