ORIGINAL ARTICLE: ASSISTED REPRODUCTION

Gestational carrier in assisted reproductive technology

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Objective: To compare clinical outcomes of in vitro fertilization (IVF) cycles with the use of gestational carriers (GCs) with non-GC IVF cycles.
Design: Retrospective cohort study of assisted reproductive technology (ART) cycles performed with (24,269) and without (1,313,452) the use of a GC.
Setting: ART centers.
Patient(s): Infertile patients seeking IVF with or without use of a GC.
Interventions(s): Autologous and donor oocyte cycles, fresh and cryopreserved embryo transfer cycles.
Main Outcome Measure(s): Live birth rate (LBR), twin and high-order multiple birth rates.
Result(s): Approximately 2% of embryo transfers used a GC. Per embryo transfer, GCs had greater pregnancy rate and LBR across all IVF types compared with non-GC cycles in crude models and models adjusted a priori for potential confounders. For women with uterine-factor infertility, embryo transfer with the use of a GC resulted in a higher odds of live birth for autologous fresh embryos and for cryopreserved embryos compared with patients with non–uterine-factor infertility diagnoses.
Conclusion(s): GC benefits LBRs for some patients seeking ART. The highest LBRs occurred when the indication for GC was uterine-factor infertility. (Fertil Steril® 2017;■:■–■. ©2017 by American Society for Reproductive Medicine.)
Key Words: Gestational carrier, gestational surrogacy, assisted reproductive technology, in vitro fertilization

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A gestational carrier (GC) is a woman who carries and delivers a child on behalf of intended parents (IPs) and is selected to carry a pregnancy because of a history of a term healthy live birth (LB) (1–3). The pregnancy is a product of in vitro fertilization (IVF) with the use of sperm and oocytes, commonly from the IPs, followed by transfer of an embryo, or embryos, into the GC's uterus (4, 5). The most common indications for using a GC include absence of the uterus, recurrent pregnancy loss, repeated failure of IVF, poor obstetrical history, medical conditions that result in excessive maternal risk, and same-sex couples (2, 6).

A range of GC live birth rates (LBRs) have been reported; comparison with non-GC IVF outcomes is often lacking, and studies are small (1, 4, 5, 7–14). A recent Centers for Disease Control and Prevention (CDC) study evaluated trends of GC use and outcomes, but neither the indication for GC nor cryopreserved embryo transfer outcomes were included (15). The present study, with the largest sample size analyzed to date, was undertaken to define the utility of GC in both fresh and cryopreserved, and autologous and donor-oocyte assisted reproductive technology (ART) cycles.

MATERIALS AND METHODS

Study Cohort

We conducted a retrospective cohort study comparing GC and non-GC ART cycles performed at 375 SART member centers from January 2004 through December 2013. Data were collected and verified by SART and reported to the CDC as mandated by the Fertility Clinic Success Rate and Certification Act (16, 17). In 2016, 467 clinics

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reported to the CDC, 80% of which were SART members, accounting for 91% of all ART cycles in the United States (18, 19).

The study cohort included cycles reported to the SART Clinic Outcome Reporting System (CORS) with autologous or donor oocytes and fresh or cryopreserved embryo transfers. Cycles using donor sperm were included. This study was approved by the Partners Healthcare System Institutional Review Board.

Definitions of Study Variables

GC cycles were defined as IVF followed by embryo transfer to the GC's uterus, and non-GC cycles were defined by transfer to the IP's uterus. For autologous cycles, the oocyte of the IP was used.

For GC cycles, all patient demographics except uterine age refer to the IP. Patients were grouped into four infertility categories: any uterine factor, exclusively male factor (decreased sperm count, morphology, or motility [20]), unexplained infertility, and nonuterine female factor (decreased ovarian reserve, endometriosis, ovulatory dysfunction, tubal factor, other). In instances where a cycle was reported as cancelled but also had a reported pregnancy outcome associated with that cycle, the authors assumed that the cancellation was reported in error. Fewer than 1% (0.13%) of all cycles reported as cancelled went on to have pregnancies.

Clinical outcomes included biochemical pregnancy (transient serum β-hCG rise), implantation (the maximum number of fetal heartbeats seen on ultrasound or infants born, whichever was greater, divided by the number of embryos transferred), clinical pregnancy (visualization of gestational sac on ultrasound [US]), clinical miscarriage (spontaneous loss of a clinical pregnancy at $<$20 weeks of gestation), stillbirth (spontaneous loss of a fetus at $\geq$20 weeks gestation, absence of fetal cardiac activity on US, or birth weight (BW) $<$300 g), LB (birth of a neonate at $\geq$22 weeks of gestation weighing $\geq$300 g), gestational age (GA), and BW.

Statistical Analysis

Generalized estimating equations (GEEs) were used to account for the correlation between multiple cycles from the same IP within the same clinic. A binomial distribution and logit link were applied for dichotomous outcomes (e.g., LB), yielding odds ratios (ORs) and 95% confidence intervals (CIs). For GA and BW, linear regression was used. Robust standard errors were used in all models. Models were a priori adjusted for potential confounding variables including oocyte age ($<$35, 35–37, 38–40, 41–43, and $>$43 y), number of embryos transferred (continuous), day of embryo transfer (day 2–3, day 5–6, vs. other), number of embryos cryopreserved (continuous), body mass index (BMI; $<$22.5, 22.5–25, 26–30, 31–35, and $>$35 kg/m^2, or missing), infertility diagnosis, previous cycles, clinical miscarriage, LB, and use of intracytoplasmic sperm injection, assisted hatching, and preimplantation genetic screening (PGS). For cycles missing oocyte age, number of embryos transferred, or number of embryos cryopreserved, the median value for the clinical parameter was substituted. Missing day of transfer was imputed (day 3 if 6–8 cells at transfer, day 5 if blastocyst at transfer). A missing indicator variable was used for cycles missing BMI. Cycles missing an infertility diagnosis were set to female factor, because this was the group with the most number of cycles. Tests for heterogeneity among groups were calculated via the likelihood ratio test. Comparison of BWs was restricted to singleton LBs and adjusted for oocyte age, day of embryo transfer, number of embryos transferred, and GA. Analyses were performed with the use of Statistical Analysis Software (SAS) version 9.3 (SAS Institute).

RESULTS

A total of 1,337,721 cycles were analyzed, including 24,269 GC and 1,313,452 non-GC cycles. Donor oocytes were used in 11% of non-GC cycles and 46% of GC cycles (Table 1).

Oocyte age was older in autologous GC cycles (mean age 37.6 y) than in non-GC cycles (35.2 y) (Table 2). Carriers (uterine age) were younger than donors (oocyte age) for autologous GC cycles using fresh and cryopreserved embryos. The most common infertility diagnosis in non-GC autologous fresh and cryopreserved embryo transfers was male factor. The most common infertility diagnosis for autologous fresh and cryopreserved embryos transferred into GCs was "other," followed by uterine factor. Within the "other" infertility diagnosis category, $>$98% were patients with a medical indication for GC (immunologic or chromosomal disorders, cancer diagnoses, or other serious systemic disease), and the remaining patients used a GC for non-infertility reasons (e.g., same-sex couple or PGS).

Donor oocyte recipients (uterine age) were older than oocyte donors (oocyte age), with a greater difference between uterine age and oocyte age for non-GC cycles ($>$10 y) than for GC cycles ($<$5 y). The most common infertility diagnosis in donor-oocyte non-GC cycles was diminished ovarian reserve. In donor-oocyte GC cycles, the most common infertility diagnosis was "other," followed by diminished ovarian reserve. Uterine factor was more prevalent as an infertility diagnosis in donor-oocyte GC cycles than in donor-oocyte non-GC cycles.

Clinical Outcomes

When autologous oocytes were used, clinical pregnancy rate, LBR, and twin birth rate were higher in GC cycles than in

TABLE 1

Number of cycles of each type analyzed.

Cycle type	Non-GC cycles	GC cycles	Total
Autologous oocyte			1,182,495
Fresh cycles	914,086	7,779	
Frozen cycles	255,419	5,211	
Donor oocyte			155,226
Fresh cycles	93,154	6,312	
Frozen cycles	50,793	4,967	
Total	1,313,452	24,269	1,337,721

Note: GC = gestational carrier.

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