ORIGINAL ARTICLE: ASSISTED REPRODUCTION

Pregnancy rates in donor oocyte cycles compared to similar autologous in vitro fertilization cycles: an analysis of 26,457 fresh cycles from the Society for Assisted Reproductive Technology

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Objective: To use a large US IVF database and compare pregnancy outcomes in fresh donor oocyte versus autologous IVF cycles in women age 20–30 years.
Design: Retrospective cohort study.
Setting: Not applicable.
Patient(s): Women undergoing fresh autologous ovarian stimulation, and oocyte donors and recipients in the United States between 2008 and 2010.
Intervention(s): None.
Main Outcome Measure(s): Implantation, clinical pregnancy (CP), and live birth (LB) rates.
Result(s): Despite similar demographics, stimulation, and embryo parameters, donor oocyte recipients had significantly higher rates of implantation, CP, and LB compared to those undergoing fresh autologous cycles. Odds ratios for implantation, CP, and LB significantly favored the donor oocyte group in all comparisons, including those limited to intracytoplasmic sperm injection cycles, intracytoplasmic sperm injection with male factor, unexplained infertility, cleavage stage embryo transfer, blastocyst transfer, elective single blastocyst transfer, and autologous patients with prior tubal ligation.
Conclusion(s): Recent US data suggest that the hormonal environment resulting from autologous ovarian stimulation lowers IVF success rates. Further research is needed to determine when to avoid fresh embryo transfer in autologous patients. (Fertil Steril® 2014;■:■–■. ©2014 by American Society for Reproductive Medicine.)
Key Words: Ovarian, stimulation, endometrial, receptivity, detrimental

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Controlled ovarian stimulation (COS) during in vitro fertilization (IVF) cycles results in the development of multiple follicles; the aim of this process is to retrieve several oocytes. In most patients, this process generates supraphysiologic levels of estrogen at the time of fresh embryo transfer (ET), which may cause an unfavorable dyssynchrony between embryo and endometrium (1). Although the precise effect of COS on IVF outcomes remains unclear, many authors have suggested that the elevated hormone levels interfere with the uterine environment and cause derangements in gene activation, angiogenesis, and possibly even placentation (2–5).

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Not all fresh IVF cycles produce supraphysiologic hormone levels around the time of ET, however. In donor oocyte treatment cycles, egg donors undergo ovarian stimulation while the uterine lining of the recipient is simultaneously prepared with exogenous hormones. Because of this hormone addition, recipients undergoing programmed endometrial preparation have estradiol and progesterone levels that are more similar to those in a natural conception cycle. This important difference between autologous and donor oocyte cycles results in very different uterine environments at the time of implantation and provides a way to evaluate the effect of the supraphysiologic hormonal milieu on IVF cycle outcomes.

More commonly, investigators who aim to study the effect of COS compare outcomes between fresh and frozen ET (FET). Although the findings are mixed, recent studies using this methodology have found that success rates and outcomes after FET cycles are superior to those after fresh transfers (1, 6–11). These studies, however, are limited by the possibility that the process of cryopreservation and subsequent thaw may cull out embryos of lower quality and itself be the cause of benefit (12). Therefore, in order to examine the effect of COS on IVF success rates, a large national database was used to compare pregnancy outcomes in donor oocyte recipients undergoing programmed endometrial preparation with a comparable group of autologous patients undergoing COS. This study design benefits from not having FET outcomes included in the analysis, thus limiting the role of cryopreservation as a potential confounder.

MATERIALS AND METHODS

The Institutional Review Board at Duke University approved this study. This was a retrospective analysis comparing fresh autologous to fresh donor oocyte IVF cycles reported to the Society for Assisted Reproductive Technology (SART) registry between 2008 and 2010. Collected through voluntary submission, the SART registry is de-identified and represents approximately 90% of Assisted Reproductive Technology clinics in the United States. In the years analyzed, 436, 441, and 443 clinics reported cycle data to SART in 2008, 2009, and 2010, respectively (13–16).

Collected data used in this study included patient age, infertility diagnosis, use of intracytoplasmic sperm injection (ICSI), cycle type (autologous or donor oocyte), number of oocytes retrieved, embryo stage, number of embryos transferred, and pregnancy outcomes. Cycles with missing data for any of these parameters were excluded from analysis. The main outcomes evaluated in this study were implantation, clinical pregnancy (CP), and live birth (LB) rates; these are reported as percentages. Implantation rates were calculated by dividing the number of fetal heartbeats seen on the first trimester ultrasound by the number of embryos transferred. Clinical pregnancy was defined as visualization of an intrauterine gestational sac by ultrasound, coincident with a positive serum β-human chorionic gonadotropin. Live birth was defined as delivery of a live-born infant at $\geq$24 weeks' gestation.

The independent *t* test was used to compare patient age (autologous versus oocyte donors) and number of oocytes retrieved. Multivariate logistic regression was used to compare outcomes between the two groups. Adjustments were made for the age of the patient providing the oocyte (donors and autologous women), as well as the number of eggs retrieved and number of embryos transferred—factors the authors believed could influence egg quality and/or success rates. Adjusted odds ratios (ORs) and their 95% confidence intervals (CIs) are reported. Data were analyzed using STATA Version 11.0 (StataCorp).

Exclusion criteria were chosen to prevent analysis of patients with diminished ovarian reserve and therefore decreased egg quality (Table 1). Therefore, autologous cycles were limited to women age 20–30 years, inclusive, with $\geq$10 oocytes retrieved. Additionally, cycles were also excluded if autologous patients were coded with any diagnoses that could affect the uterine environment or interfere with implantation, such as polycystic ovary syndrome, uterine factor, endometriosis, or hydrosalpinx. Cycles from the recipient cohort were selected for similar characteristics: donors were limited to those age 20–30 years, inclusive, who had $\geq$10 oocytes retrieved. Diminished ovarian reserve was not exclusionary for oocyte recipients, as the majority of women in this group carried this diagnosis as the primary indication for their treatment. Because of existing evidence that pregnancy outcomes decline in older recipients, age in this group was limited to $\leq$45 years (17). Infertility factors that could interfere with implantation in the recipient were excluded in a similar manner as in autologous cycles (Table 1). Therefore, cycles analyzed in this study involved oocytes from autologous women and oocyte donors between age 20–30 years with $\geq$10 eggs retrieved.

Secondary analyses were also performed to identify and compare subgroups. Separate regression analyses were performed on cycles reporting use of ICSI alone and those reporting both ICSI use and male factor. No cases using testicular sperm extraction were included in either group. Cycles performed for unexplained fertility were also subanalyzed. Next, cycles reporting cleavage stage and blastocyst stage ETs were compared separately as a means to account for known differences in success rates associated with embryos at various developmental stages. Additionally, a comparison was performed of cycles reporting elective single blastocyst transfer. Finally, fresh donor oocyte cycles were compared to fresh autologous cycles performed for an indication of tubal factor infertility due to prior elective tubal ligation.

TABLE 1

Exclusion criteria for donor oocyte and autologous cycle cohorts.

Donor oocyte cycles	Autologous cycles
Donor age <20 or >30 y	Age <20 or >30 y
<10 oocytes retrieved	<10 oocytes retrieved
Recipient age ≥46 y	Diminished ovarian reserve
Uterine factor (recipient)	Uterine factor
Endometriosis (recipient)	Endometriosis
Polycystic ovary syndrome (recipient)	Polycystic ovary syndrome
Hydrosalpinx (recipient)	Hydrosalpinx

Yeh. Donor oocyte versus autologous cycles. Fertil Steril 2014.