Endometriosis and Cumulative Live Birth Rate After Fresh and Frozen IVF Cycles With Single Embryo Transfer in Young Women: No Impact Beyond Reduced Ovarian Sensitivity—A Case Control Study

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ABSTRACT

Although endometriosis affects approximately 10% of women of reproductive age and 40% of infertile women, the physiological mechanism of how this chronic inflammatory disease affects fertility remains unclear. There is little consensus in the literature that IVF/ICSI outcomes are impacted by endometriosis. One previous meta-analysis indicated a decrease in oocyte yield and reduced clinical pregnancy rate in patients with endometriosis undergoing IVF; however, multiple embryos had been replaced in most included studies, and the live birth rate (LBR) was similar. It is unclear if endometriosis does negatively influence pregnancy rates; this impact may be due to adverse effects on endometrial or ovarian factors.

This cross-sectional case-control study aimed to test the hypothesis that endometriosis would mainly affect ovarian reserve and to a lesser extent would impair implantation. This was done by comparing outcomes of fresh and frozen embryo transfer in women with endometriosis with a control cohort of infertile women with no signs of endometriosis. Perspective subjects were recruited at the Reproductive Medicine Clinic of Karolinska University Hospital from January 2009 until December 2013. Inclusion criteria required subjects to be younger than 40 and nulliparous before IVF/ICSI as a study procedure. Subjects were classified in the endometriosis cohort as either a minimal to mild or moderate to advanced endometriosis case. The primary outcome measured was LBR by oocyte pickup including consecutive frozen-thawed cycles and OSI (Ovarian Sensitivity Index). Secondary measures included pregnancy rate by embryo transfer, miscarriage rate, and number of retrieved oocytes.

The study cohort included 2757 infertile couples treated by IVF/ICSI. Of these, 172 had histopathologically confirmed endometriosis and 2585 comprised the control population. Women in the endometriosis cohort underwent 297 fresh and 220 frozen-thawed cycles, whereas women in the control cohort underwent 4301 and 3405, respectively. Women with endometriosis showed lower OSI ($P < 0.001$) and smaller oocyte yields (8.47 vs 9.54, $P = 0.015$) after FSH stimulation compared with controls, indicating a 35.3% proportion of low responders in endometriosis compared with 22.2% of controls. Both cohorts had greater than 60% of subjects who had consecutive frozen-embryo transfers after fresh ET ($P = 0.49$), and the total number of ETs performed did not differ between the groups ($P = 0.32$). The adjusted pregnancy rates per LBR/oocyte pickup and per ET were not significantly different between women with endometriosis compared with controls after fresh cycles (32.4% vs 31.1%, $P = 0.73$ and 35.8% vs 34.6%, $P = 0.81$, respectively). Pregnancy rates were similar between the endometriosis and control groups when restricted to frozen-thawed cycles (26.2% vs 31.6%, respectively, $P = 0.37$). Cumulative LBR including both fresh and frozen cycles did not differ significantly between the endometriosis and control cohorts (35.6% vs 34.7%, respectively, $P = 0.83$). No significant difference was found in LBR or OSI between the mild endometriosis and moderate to advanced endometriosis cohorts.

These results show that although decreased ovarian response is found in women with endometriosis, the likelihood of pregnancy and live-birth after IVF/ICSI are maintained and do not differ significantly from those without endometriosis.

EDITORIAL COMMENT

(Whether endometriosis has an impact on IVF outcome, and if so, via what mechanism, remains controversial. This cross-sectional case-control study tested the hypothesis that endometriosis...
affects ovarian reserve and implantation. It compared outcomes of fresh and frozen embryo transfer in women with endometriosis to infertile women without endometriosis. Perspective subjects had minimal to mild or moderate to advanced endometriosis. Outcomes included LBR by oocyte pickup and OSI, a marker of ovarian reserve, pregnancy rate by embryo transfer, miscarriage rate, and number of retrieved oocytes. Women with endometriosis showed lower OSI and smaller oocyte yields compared with controls. Thirty-five percent of endometriosis patients compared with 22% of controls had low response. The number of ETs performed and the pregnancy rate per LBR/oocyte pickup did not differ between the groups. Pregnancy rates after frozen-thawed cycles, cumulative LBR, LBR, and OSI did not differ between the endometriosis and control groups. Thus, despite decreased ovarian response occurring more frequently in women with endometriosis, pregnancy outcomes of endometriosis patients do not differ appreciably from those of infertile women without endometriosis.—DK

What Is the Clinical Impact of the Endometrial Receptivity Array in PGT-A and Oocyte Donation Cycles?

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ABSTRACT

Endometrial receptivity is a critical factor to likelihood of implantation after embryonic transfer (ET), yet potential biomarkers for receptivity have thus far failed at reliably predicting clinical pregnancy. Recent evidence has suggested that the Endometrial Receptivity Analysis (ERA), a microarray-based test to evaluate endometrial gene expression, may be valuable in prediction of endometrial receptivity and recommendation of endometrial preparation before ET.

This retrospective cohort study aimed to evaluate the influence of the ERA test on the reproductive outcomes in patients with previously documented implantation failure (IF) in IVF with preimplantation testing for embryonic aneuploidy (PGT-A) or oocyte donation cycles. Patients in the intervention group had previous IF and underwent an ERA test before March 2018 and a post-ERA ET between October 2012 and December 2018. The intervention group was stratified into the Euploid-ET group if the patient had ≥1 prior failed euploid embryo transfer and the Donor-ET group if the patient had ≥2 prior failed ET from reception cycles without PGT-A. The control cohort included patients with prior IF who underwent ET without a prior ERA test during the same study period. Only blastocyst stage transfers were included in this analysis. The ERA test was performed in a hormone replacement therapy mock cycle. ERA test results were divided to receptive, prereceptive, or postreceptive, and recommendations regarding endometrial receptivity and recommendation of endometrial preparation before ET.

A total of 333 patients were included in this study, and the proportion of ERA tests performed was equal in the Euploid-ET group (16.8%; 24/143) and in the Donor-ET group (16.8%; 32/190). The total pregnancy rate was 68.5% (98/143) and 60.0% (114/190) in the Euploid-ET group and Donor-ET group, respectively. A lower implantation rate (IR) (26.8% [12.3%–41.4%] vs 57.2% [50.1%–64.3%]) and clinical pregnancy rate (CPR) (34.4% vs 65.2%; P = 0.001) were found in the Donor-ET ERA group compared with the control. Similarly, a lower IR and CPR was found in the Euploid-ET ERA group compared with the control, although this difference was not statistically significant. Multivariate analysis revealed that transferring top quality embryos...