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Title

Comparison of the incidence of perinatal complications among fresh embryo transfer, natural ovulation cycle and hormone-replacement-cycle frozen-thawed embryo transfer in 8,467 cycles of live birth

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Study question:
Are there differences in the incidence of perinatal complications depending on the embryo transfer method?

Summary answer:
The incidence of placenta accreta, atonic bleeding, and pregnancy-induced hypertension was higher in hormone-replacement-cycle frozen ET (HRC-FET) than Fresh-ET and natural-cycle frozen ET (NC-FET).

What is known already:
Women who conceived by ART have a higher risk of maternal/perinatal complications necessitating advanced obstetric care. An association between freeze-thaw embryo transfer and PIH, pre-eclampsia, placenta accreta, and large for gestational age (LGA) has been suggested.

Study design, size, duration:
We performed a retrospective analysis of 8,467 cycles of patients who underwent embryo transfer and resulted in live births between January 2015 and June 2022 (1,076 cycles of Fresh ET, 2,223 cycles of NC-FET, and 5,168 cycles of HRC-FET, respectively).

Participants/materials, setting, methods:
The incidence of placenta accreta, placenta previa, low-lying placenta, placental abruption,

atonic bleeding, uterine rupture, amniotic fluid embolism, maternal blood transfusion, gestational diabetes mellitus, and pregnancy-induced hypertension was examined among the three groups. A multivariate analysis was performed to investigate the influence of transfer methods including factors suggested to be associated with the occurrence of each complication (parturition history, age, gestational age, mode of delivery, endometrial thickness, and BMI) as covariates.

Main results and the role of chance:

The incidence of placenta accreta was 1.1% in Fresh ET, 1.6% in NC-FET, and 5.1% in HRC-FET, atonic bleeding was 3.2% in Fresh ET, 3.7% in NC-FET, and 9.0% in HRC-FET, and pregnancy-induced hypertension was 6.2% in Fresh ET, 5.6% in the NC-FET, and 10.8% in HRC-FET ($p<0.0001$). Multivariate analyses also showed a significantly higher odds of occurrence in HRC-FET compared with Fresh ET and NC-FET. On the other hand, there were no significant differences in the incidence of placenta previa, low-lying placenta, placental abruption, uterine rupture, amniotic fluid embolism, maternal blood transfusion, or gestational diabetes mellitus among the three groups. Multivariate analyses also showed no significant increase or decrease in the odds of occurrence of placenta previa or gestational diabetes mellitus in the HRC-FET compared with the Fresh ET and NC-FET.

Limitations, reasons for caution:

The data were retrospectively analyzed, which could be subject to bias. The number of cases of low-lying placenta, abruptio placenta, uterine rupture, amniotic fluid embolism, and maternal blood transfusion was small, so multivariate analyses could not be performed.

Wider implications of the findings:

To mitigate perinatal complications in ART pregnancies, it is advisable to opt for frozen-thawed embryo transfer during a natural ovulation cycle. Furthermore, from the perspective of reducing the time to pregnancy, fresh embryo transfer may be preferable, if feasible.