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Title:
Vitrification and Thawing of Preimplantation Embryos Does Not Affect Perinatal Outcome

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Objective:
The increased birthweight of infants conceived via frozen embryo transfer (FET) is often attributed to the absence of supraphysiologic estrogen levels from controlled ovarian hyperstimulation (COH), rather than an effect of the freeze-thaw process. However, FET singletons have been reported to have higher rates of macrosomia compared with non-IVF singletons, suggesting there could be an independent effect of cryopreservation on early embryo and placental development. Proposed mechanisms include subtle epigenetic modifications to non-imprinted loci in the preimplantation embryo which could modify embryo-endometrial signaling and implantation. This study compares singleton live births from fresh versus frozen ET in synthetic, donor oocyte (OD) cycles to evaluate the perinatal impact of embryo cryopreservation.

Design:
Retrospective cohort study

Materials and Methods:
OD recipients that underwent synthetic, hormonal endometrial preparation followed by a single, fresh or frozen ET resulting in live birth, from February 2003 to July 2015, were included. Monozygotic twins were excluded. All embryos were derived from fresh donor oocytes and transferred at the blastocyst stage. Main outcome measures included gestational age at delivery and birthweight. Student's t-test, chi-square, linear and binary logistic regression analysis were performed.

Results:
One hundred forty eight SETs (fresh ET: n=79; FET: n=69) were identified. Baseline demographics, cycle characteristics and perinatal outcome are shown in Table 1. There was no

significant difference in gestational age at delivery, infant birthweight or height in the fresh vs. frozen ET groups. After controlling for oocyte age, recipient age and BMI, the odds of preterm delivery (OR 1.3 [95% CI 0.6-2.8], p=0.56), low birthweight (OR 1.5 [95% CI 0.3-6.4], p=0.60), normal birthweight (OR 0.5 [95% CI 0.1-1.6], p=0.24) and macrosomia (OR 1.0 [95% CI 0.99-1.0], p=0.56) were similar among fresh vs. frozen ET.

Conclusions:

Singleton live births from OD cycles resulting from a single, fresh or frozen ET, demonstrated no difference in gestational age at delivery, infant size and birthweight. These finding reassure clinicians and patients that exposure of the screened blastocyst to the vitrification and thawing process has no effect on perinatal outcome.

Support:

None

Table 1:

	Fresh OD ET	Frozen-thawed OD ET	P value
Total live births	79	69	
Patient's age at ET	43.3 ± 4.9	44.0 ± 4.0	NS
Oocyte's age	27.2 ± 3.5	27.5 ± 3.5	NS
Recipient's BMI	24.0 ± 4.0	25.6 ± 5.6	NS
Endometrial Thickness at ET (mm)	9.8 ± 2.4	9.2 ± 2.2	NS
Peak E_2	682.6 ± 501.6	605.7 ± 450.1	NS
Gestational age at delivery	37.7 ± 2.8	37.9 ± 1.3	NS
Preterm delivery (<37 wks)	22.8% (18/79)	18.8% (13/69)	NS
Height	20.1 ± 1.0	20.3 ± 1.1	NS
Birthweight	3292.1 ± 589.8	3419.6 ± 498.4	NS
Low Birthweight (<2500g)	6.3% (5/79)	4.3% (3/69)	NS
Normal Birthweight (2500-4200g)	84.8% (67/79)	89.9% (62/69)	NS
Macrosomia (>4500g)	2.5% (2/79)	0% (0/69)	NS