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**Title:**

**Perinatal outcomes in live births from fresh versus frozen single embryo transfers**

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**Objective:**

Single embryo transfer (SET) has revolutionized IVF treatment, driving down the rate of major obstetrical complications, often seen with multiple gestations. One potential risk factor for adverse outcomes in IVF singleton pregnancies appears to be the hormonal environment of the endometrium at the time of implantation, which could influence placentation, fetal development and growth. Singleton births from frozen-thawed ET (FET) have been widely reported to have significantly greater birthweight than those resulting after a fresh ET. Some studies have reported that FET singletons are at increased risk of macrosomia and morbidly adherent placentation. However, many of the existing studies to date are based on large registries which may be biased due to missing records and differential obstetrical classification and management. We sought to compare the perinatal outcomes of patients who underwent fresh versus frozen SETs resulting in live singleton s.

**Design:**

Retrospective cohort analysis

**Materials and Methods:**

Patients who had a live singleton birth after a fresh or frozen blastocyst SET from 2002 to 2015 were included. Monozygotic twins were excluded. Demographic, SET cycle characteristics and prenatal and obstetrical data was collected and analyzed with respect to cycle type. Student's t-test, chi square, linear and binary logistic regression analysis were used.

**Results:**

Two hundred fifty-one patients underwent SET, in a fresh (n=127) or frozen (n=124) cycle. Patient demographics, ET cycle characteristics and obstetrical outcomes are shown in Table 1. Patients were significantly older in the FET group (35.9 vs. 34.4, p<0.05). The incidence of



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adverse perinatal outcomes was similar among groups. Birthweight was significantly increased in the FET group (3385.5 vs. 3154.1g,  $p < 0.0005$ ), with equal infant sex ratios and similar gestational age at delivery in both groups. Fresh ET patients were deemed small for gestational age (SGA) more often than FET patients, based growth sonograms at 24 and 32 weeks gestation. Endometrial thickness at transfer was significantly increased in the Fresh ET group (9.7 vs. 9.0mm,  $< 0.005$ ). Controlling for cycle type, each 1mm increase in endometrial thickness was correlated with -53.8g in birthweight ( $p = 0.06$ ). A significantly higher proportion of blastocysts underwent preimplantation genetic screening (PGS) in the FET group (52.4% vs. 20.4%,  $p < 0.05$ ). Controlling for cycle type, there was a trend towards increased birthweight (+189.5g) in the biopsied cycles ( $p = 0.08$ ). There was no significant difference in the rate of cesarean section and operative delivery.

**Conclusions:**

Our findings are consistent with the majority of studies which report increased neonatal following FET. Overall, the rates of adverse perinatal outcomes, including decreased growth, were reassuringly low in both groups. The use of SET continues to drive down the risks of IVF pregnancy. SET cycle characteristics, such as endometrial thickness and the use of PGS did not have a significant impact on birthweight. The increase in birthweight in the FET group was not pathologic; there was not an increased incidence of macrosomia or need for cesarean or operative delivery in the FET group. Although the incidence of low birthweight was shown to be rare in both cohorts, further research is needed to understand pathophysiology behind the lower birthweight in fresh cycles.

**Support:**

None

**Table 1:**

	Fresh SET	Frozen SET	P value
Live births	127	124	
Age	34.4 ± 4.7	35.9 ± 4.6	<0.05
BMI	22.9 ± 3.6	22.8 ± 3.8	NS
Parity	0.4 ± 0.6	0.6 ± 0.6	<0.05
Prior uterine scar	0.3 ± 0.4	0.3 ± 0.6	NS
Pregnancy weight gain (lbs)	45.8 ± 47.7	49.7 ± 51.2	NS
Endometrial thickness at ET (mm)	9.7 ± 2.4	9.0 ± 1.8	<0.005
Trophectoderm biopsied	20.4% (26/127)	52.4% (65/124)	<0.05



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Gestational hypertension	10.2% (13/127)	6.5% (8/124)	NS
Severe preeclampsia	3.9% (5/127)	4.8% (6/124)	NS
1 hour glucose tolerance test	110.2 ± 29.0	110.8 ± 30.6	NS
Gestational diabetes	6.3% (8/127)	4.8% (6/124)	NS
Anatomy scan cervical length (cm)	4.6 ± 0.9	4.9 ± 0.9	NS
Small for gestational age (<10%) (SGA) at 24 weeks	2.4% (3/127)	0.8% (1/124)	NS
SGA at 32 weeks	2.4% (3/127)	0% (0/124)	NS
Head to abdominal circumference ratio	1.2 ± 0.1	1.1 ± 0.1	NS
Placenta previa	3.1% (4/127)	0.8% (1/124)	NS
Gestational age at delivery (weeks)	38.7 ± 2.4	38.2 ± 5.3	NS
Preterm delivery (<37 weeks)	11.0% (14/127)	6.5% (8/124)	NS
Infant gender ratio (M:F)	1.4 (74:53)	1.0 (63:61)	NS
Birthweight (g)	3154.1 ± 590.1	3385.5 ± 570.7	<0.005
Low Birthweight (<2500g)	5.5% (7/127)	5.6% (7/124)	NS
Macrosomia (>4500g)	0.8% (1/127)	1.6% (2/124)	NS
Labor Induction	26.0% (33/127)	19.4% (24/124)	NS
Cesarean section delivery	48.0% (61/127)	54.8% (68/124)	NS
Operative delivery	3.9% (5/127)	5.6% (7/124)	NS



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