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Title:

IS THERE MORE TO THE STORY THAN ANEUPLOIDY: UNCOVERING FACTORS ASSOCIATED WITH EARLY PREGNANCY LOSS FOLLOWING EUPLOID EMBRYO TRANSFER

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Background:

Advances in preimplantation genetic screening (PGS) have revolutionized the field of personalized and genomic medicine. PGS enables the clinician to select a single euploid embryo for transfer, resulting in high pregnancy rates and nearly eliminating the risk of multiple gestations. Unfortunately, PGS of embryos has not eliminated the risk of early pregnancy loss (EPL) [1]. Published research has suggested links between the incidence of biochemical pregnancies and the presence of diminished ovarian reserve [2] and/or endometrial or immune factors [3], though the precise etiology and pathophysiology remain unclear.

Objective:

To evaluate possible factors contributing to spontaneous loss following transfer of euploid embryos

Materials and Methods:

Patients who underwent frozen embryo transfer (FET) cycles utilizing PGS from July 2011 to April 2016 were analyzed. Only trophectoderm biopsied, blastocyst-staged FETs were included. Monozygotic twins were excluded. Outcome measures were age, day 3 follicle stimulating hormone (FSH), anti-mullerian hormone (AMH), body mass index (BMI), endometrial thickness at transfer, number of eggs retrieved, and aneuploidy rates. Student's t-test, chi-square, linear and binary logistic regression analysis were performed.

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Result(s):
A total of 1048 FET cycles were included. Table 1 reveals baseline demographics and cycle characteristics. The overall rate of miscarriage was 21.3% (n=223). The rate of biochemical pregnancy was 8.8% (n=92), and the rate of implantation loss was 12.5% (n=131). There was no significant increase in the odds of early pregnancy loss with respect to oocyte age (OR 1.0 [95% CI 0.9-1.0]), day 3 FSH (OR 1.0 [95% CI 0.9-1.0]), AMH (OR 1.0 [95% CI 0.9-1.0]), BMI (OR 1.0 [95% CI 0.9-1.0]) number of eggs retrieved (OR 0.9 [95% CI 0.9-1.0), aneuploidy rate (OR 0.7 [95% CI 0.1-2.8]) or endometrial thickness at transfer (OR 0.8 [95% CI 0.7-1.0]).

Conclusion(s):
Patient age, ovarian reserve, endometrial thickness, and percentage of aneuploid embryos were not associated with increased likelihood of early pregnancy loss following PGS. The source of pregnancy loss after euploid embryo transfer has yet to be identified, as limitations in modern PGS technology persist. While the occurrence of microdeletions, microduplications, mosaicism, and embryo-endometrial asynchrony may all contribute to the incidence of EPL, our evaluation did not reveal a clear association with EPL given the parameters studied. Further research is needed to determine the possible causes and contributors in order to provide optimal patient care.

References:

1. Harton, G., et al. Diminished effect of maternal age on implantation after preimplantation genetic diagnosis with array comparative genomic hybridization. Fertil Steril, 2013. 100(6): p. 1695–1703.
2. Munne, S., et al. Embryo morphology, developmental rates, and maternal age are correlated with chromosome abnormalities. Fertil Steril 1995. 64(2): p. 382-391.
3. Kwak-Kim J., et al. Increased T helper 1 cytokine responses by circulating T cells are present in women with recurrent pregnancy losses and in infertile women with multiple implantation failures after IVF. Hum Reprod 2003. 18(4):767–773.

Table 1:

	Loss	No Loss	P Value
Average age	36.6 ± 4.0	36.4 ± 4.1	NS
Day 3 FSH	6.3 ± 3.1	6.1 ± 3.2	NS
BMI	23.5 ± 4.3	23.0 ± 4.0	NS
AMH	4.1 ± 5.4	3.7 ± 3.9	NS
Endometrial thickness	9.1 ± 2.0	9.2 ± 2.0	NS
Number of eggs retrieved	16.3 ± 10.2	17.1 ± 10.0	NS
Percent aneuploid embryos	36.3 % (458/1262)	36.8% (1183/3219)	NS