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Title:

FIRST TRIMESTER VAGINAL BLEEDING DOES NOT PREDICT SMALL FOR GESTATIONAL AGE NEWBORNS FOLLOWING SINGLE EUPLOID FROZEN EMBRYO TRANSFER

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Objective:

Newborns that are small for gestational age (SGA) have birth weights below the 10th percentile. Uterine/placental factors associated with SGA neonates include decreased blood flow the uterus and placenta, placental abruption, placenta previa, and uterine infection. A secondary analysis of data from the NICHD Fetal Growth Studies suggests that more than one day of vaginal bleeding (VB) in the first trimester is associated with lower infant birth weight. However, it is unclear whether this holds true in pregnancies achieved with the use of assisted reproductive technology treatment. The objective of this study was to determine in an infertile population undergoing in vitro fertilization (IVF) whether first-trimester VB is associated with the likelihood of having an SGA infant.

Design:

Retrospective cohort analysis

Materials and Methods:

The study included patients at an academic ART center who underwent a single euploid FET and experienced a live birth from 2012 to 2019. Natural language processing was performed to

identify pregnancies complicated by VB prior to 10 weeks of gestation. Blind review of the database was conducted by two independent reviewers to verify data quality. Incidents of 'spotting' or 'staining' were excluded from the analysis. Primary outcome was the presence of a SGA infant, which was determined using the sex-specific weights for the 10th percentile of neonatal birth weight. Data were evaluated using T-tests, chi-square tests, and multivariate logistic regression models.

Results:

A total of 1611 FET cycles with a live birth outcome from 1528 patients were included in the study. The overall incidence of VB was 17.69% (n= 285). Pregnancies were divided into two groups: (1) pregnancies with VB prior to the 10th week of gestation and (2) pregnancies with no VB. Univariate analysis demonstrated significant differences in BMI, gravidity, and route of progesterone administration between groups. There was no difference in aspirin use, average birth weight, or gestational age at delivery between groups. There were a total of 18 (6.32%) SGA infants in the VB group, and 115 (8.67%) SGA infants in the no VB group. Controlling for BMI, gravidity, and route of progesterone administration, multivariate regression analysis did not demonstrate any significant association between VB and the incidence of SGA newborns (OR 0.53 [95% CI 0.24-1.20], p=1.23).

Conclusion:

In contrast to the study published by Bever et al., 1 patients who experienced first trimester VB did not demonstrate a higher incidence of SGA newborns. Use of natural language processing of electronic medical records enabled us to re-construct first trimester incidents not otherwise easily obtainable, limiting potential recall bias as a confounding variable. A limitation of our study design was the lack of a quantitative method to track quantity and duration of VB. Nevertheless, patients undergoing single euploid FET can be reassured that first trimester VB is not associated with a higher incidence of SGA infants.