TITLE: TROPHECTODERM (TE) GRADE IS NOT ASSOCIATED WITH PLACENTAL PATHOLOGY AMONG IN-VITRO FERTILIZATION (IVF) CONCEIVED SINGLETONS.

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BACKGROUND: IVF pregnancies are at increased risk for placental-mediated adverse perinatal outcomes. Factors implicated include embryo manipulation and culture conditions, as well as treatment-induced hormonal changes altering the endometrial milieu all of which may negatively impact implantation, decidualization, and trophoblast invasion processes. Nevertheless, whether the quality of the TE also impacts placental pathology remains unclear.

OBJECTIVE: To evaluate the impact of TE grade on placental pathology among IVF conceived singletons.

MATERIALS AND METHODS:

Design: Retrospective cohort.

Setting: Academic fertility center.

Patients: 292 IVF conceived singleton livebirths with available placental pathology. Trophectoderm grade classified using Gardner's system [Grades: A (n=120), B (n=142), and C (n=30)].

Outcomes: Placental pathology reviewed and classified by an expert pathologist (using Amsterdam Consensus definitions), as *anatomic, vascular*, *inflammatory*, and *infectious*. Placental weight (grs) was a secondary outcome.

Statistical analysis: Parametric and non-parametric tests were used as appropriate. Logistic or linear regression models were utilized to calculate either odds ratios (OR) or beta coefficients (β) with 95% confidence intervals (95%CI), adjusting for maternal age, BMI, race, hypertensive disorders, IVF stimulation protocol, fertilization method, , inner cell mass grade, # of transferred embryos, fresh vs. frozen embryo transfer (ET), day 5 vs. 6 blastocyst, preimplantation genetic testing, and gestational age at birth. Subgroup analysis limited to fresh ETs only (n=235) was also performed.

RESULTS: AdjOR (95%CI) showed no differences in placental abnormalities between TE quality groups A-C, using grade A as *ref*. [**Grade B**: 1.05 (0.91-1.21), p: 0.54; 0.90 (0.78-1.04), p: 0.15; 0.98 (0.87-1.10), p: 0.73; 1.11 (0.96-1.30), p: 0.16; and **Grade C**: 0.97 (0.77-1.21), p: 0.79; 0.91 (0.74-1.12), p: 0.38; 0.95 (0.79-1.15), p: 0.61; 1.13 (0.90-1.44), p: 0.29; for *anatomic*, *vascular*, *inflammatory*, and *infectious* abnormalities, respectively].
Similarly, when further limiting the analysis to fresh ETs only, adjOR (95%CI) revealed any difference between TE quality groups A-C, using grade A as *ref*. [**Grade B**: 1.04 (0.90-1.20), p: 0.61; 0.88 (0.76-1.03), p: 0.11; 0.99 (0.87-1.12), p: 0.85; 1.07 (0.92-1.26), p: 0.37; **Grade C**: 0.99 (0.78-1.25), p: 0.95; 1.12 (0.89-1.39), p: 0.34; 0.99 (0.79-1.23), p: 0.92; 0.96 (0.73-1.27), p: 0.37; for *anatomic*, *vascular*, *inflammatory*, and *infectious* abnormalities, respectively].
Adjβ (95%CI) showed no differences in placental weight between TE groups A-C, using grade A as *ref*. [**Grade B**: 1.49 (-28.29, 31.27), p: 0.92; **Grade C**: 1.83 (-41.93, 45.58), p: 0.94], nor when limiting the analysis to fresh ETs only [adjβ (95%CI), **Grade B**: -0.29 (-34.13, 33.54), p: 0.99; **Grade C**: -21.22 (-85.14, 42.71), p: 0.52, grade A as *ref*.]

CONCLUSIONS: TE grade does not appear to impact placental pathology among IVF conceived singletons. These results limit the clinical utility of TE grading only in embryo selection processes indicating that it cannot serve as indicator of placental abnormalities.

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