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**EFFECT OF TROPHECTODERM REBIOPSY ON SERUM B-HUMAN CHORIONIC GONADOTROPIN LEVELS IN PREGNANCIES RESULTING IN LIVE BIRTHS**

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**OBJECTIVE:**

Approximately 5 to 7 cells are removed from the trophectoderm (TE) during embryo biopsy for preimplantation genetic testing for aneuploidy (PGT-A). Rebiopsy is performed in 1-3% of cases due to inconclusive results. The TE gives rise to the placenta which produces  $\beta$  human chorionic gonadotropin ( $\beta$ -hCG), an important diagnostic and prognostic marker in early pregnancy (1). Whether rebiopsy depletes TE cell count to a degree that could affect  $\beta$ -hCG levels is yet to be established. This study aimed to assess if rebiopsy is associated with lower  $\beta$ -hCG in early pregnancy compared to once-biopsied or untested embryos.

**MATERIALS AND METHODS:**

This retrospective study included patients who underwent euploid single frozen embryo transfer (sFET) following rebiopsy and achieved a live birth from 2015 to 2022. Patients were matched by age, body mass index, and anti-Müllerian hormone to those who underwent single-biopsy euploid sFET and untested sFET. Multiple gestations were excluded. The primary outcome was serum  $\beta$ -hCG on days 8-12 after embryo transfer. Secondary outcomes were rates of preterm birth and small for gestational age (SGA) infants. Statistics were performed using chi square, Student's t-test, ANOVA, and Kruskal-Wallis, with  $p < 0.05$  as significant.

**RESULTS:**

308 patients undergoing sFET were included: 44 rebiopsy, 132 single-biopsy, and 132 untested. Demographics and cycle characteristics were similar.  $\beta$ -hCG was significantly lower in the rebiopsy group compared to single-biopsy and untested groups on days 9-12 and days 8-9, 11-12, respectively (Table 1).  $\beta$ -hCG was similar between single-biopsy and untested groups. There were no significant differences in rates of preterm birth or SGA among all groups.

| Mean $\beta$ -hCG(mUI/mL) | Untested (0)  | Single-Biopsy(1) | Rebiopsy (2)  | p-value0 vs 1 | p-value0 vs 2 | p-value1 vs 2 |
|---------------------------|---------------|------------------|---------------|---------------|---------------|---------------|
| <b>Day 8</b>              | 111.2 + 67.7  | 96.2 + 45.3      | 65.4 + 36.9   | 0.35          | <b>0.04*</b>  | 0.16          |
| <b>Day 9</b>              | 152.5 + 80.3  | 149.6 + 67.2     | 110.4 + 69.0  | 0.34          | <b>0.03*</b>  | <b>0.04*</b>  |
| <b>Day 10</b>             | 285.4 + 210.8 | 226.7 + 144.8    | 130.8 + 91.4  | 0.28          | 0.06          | <b>0.002*</b> |
| <b>Day 11</b>             | 443.6 + 230.0 | 433.6 + 246.0    | 219.9 + 203.7 | 0.81          | <b>0.007*</b> | <b>0.001*</b> |
| <b>Day 12</b>             | 648.3 + 428.0 | 614.4 + 344.7    | 398.3 + 241.8 | 0.68          | <b>0.03*</b>  | <b>0.02*</b>  |

**CONCLUSIONS:**

$\beta$ -hCG was significantly lower in patients who underwent sFET with a rebiopsied embryo, yet no differences were observed in preterm birth or SGA.  $\beta$ -hCG was similar between single-biopsy and untested groups, suggesting an impact only when 10 or more TE cells are removed in rebiopsy. Understanding the relationship between rebiopsy and  $\beta$ -hCG can help guide management of these pregnancies as lower levels may not be indicative of poor pregnancy outcomes.

**IMPACT STATEMENT:**

Rebiopsy is associated with significantly lower  $\beta$ -hCG in pregnancies resulting in live births. The number of biopsies per embryo is an additional factor to be integrated in developing personalized prognostic information for patients.

**REFERENCES:**

1. Homan G, Brown S, Moran J, Homan S, Kerin J. Human chorionic gonadotropin as a predictor of outcome in assisted reproductive technology pregnancies. Fertil Steril. 2000 Feb;73(2):270-4. doi:10.1016/s0015-0282(99)00512-9. PMID: 10685527.