



AMERICAN SOCIETY FOR
REPRODUCTIVE MEDICINE



77th ASRM Scientific Congress & Expo
October 16-20, 2021 // Baltimore, MD, USA

DO EARLY HCG DYNAMICS AFTER EMBRYO TRANSFER DIFFER BASED ON DAY OF EMBRYO BIOPSY?

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Title:

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OBJECTIVE:

Serum HCG threshold levels and rate of rise are established predictors of successful pregnancy in IVF embryo transfer cycles. While prior studies on HCG dynamics in early IVF pregnancies have accounted for factors such as stage of embryo development, these studies have not accounted for the speed of embryo development. Day 7 embryos have been shown to have reduced implantation potential.¹ However, no study has yet to review the relationship between day 7 embryo transfer and the level of HCG secretion when early pregnancy is achieved. The objective of this study is to compare initial HCG levels and the rate of HCG increase between day 5, 6, and 7 single, euploid frozen embryo transfers (FET).

MATERIALS AND METHODS:

The study included patients who underwent a single, euploid FET, from January 2012 to March 2021. Initial serum HCG levels were reviewed on day 9 post FET, and if positive, the rate of HCG rise, by day 11, was noted. FET cycles were stratified by day of embryo biopsy and cryopreservation (Group A: Day 5; Group B: Day 6; Group C: Day 7). Baseline demographics were compared and analyzed by ANOVA and Kruskal-Wallis. A logistic regression was then performed to evaluate the differences in HCG levels when controlling for Patient Age, Oocyte age, BMI, AMH, BAFC, day 3 FSH, and endometrial thickness at progesterone initiation.

RESULTS:

A total of 1,707 single euploid FETs were included and separated into three groups: Group A (n = 1,104), Group B (n = 577), and Group C (n = 26). The mean serum HCG value on day 9 after ET was 168.7 in Group A, 143.0 in Group B, and 94.8 in Group C. Initial HCG level and the percent of HCG rise was significantly different between the three groups ($p < 0.0001$). Day 5 embryos had a significantly higher absolute difference in HCG levels, from day 9 to day 11, compared with day 6 embryos (OR 1.41 [95% CI 1.23-1.75]) and day 7 embryos (OR 4.74 [95% CI 2.16-10.40]). The percent rise of HCG between days 9 and 11 in day 5 embryos was significantly lower than day 7 embryos (OR 2.36 [95% CI 1.079-5.16]), but was similar compared with day 6 embryos (OR 1.19 [95% CI 0.955-1.48]).

CONCLUSIONS:

The HCG dynamics of early pregnancies from a single, euploid FET, are significantly impacted by the day of embryo development. Our findings show that reproductively competent day 7 embryos have lower initial HCG levels, but then a higher rate of HCG rise compared with faster growing day



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5/6 embryos. The increased rate of HCG rise in day 7 embryos may reflect a mechanism such as compensation for a delayed activation of the embryonic transcriptome which these slower growing embryos are able to overcome to be able to successfully implant.

IMPACT STATEMENT:

The initial rate of HCG rise in early pregnancies from single, euploid FET cycles correlates with day of embryo development.

References:

1. Hernandez-Nieto C, Lee JA, Slifkin R, Sandler B, Copperman AB, Flisser E. What is the reproductive potential of day 7 euploid embryos? *Hum Reprod.* 2019 Sep 29;34(9):1697-1706. doi: 10.1093/humrep/dez129. PMID: 31398251.