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**Title:**

# THE EFFECT OF ADVANCING PATERNAL AGE ON PREGNANCY AND NEONATAL OUTCOMES FOLLOWING A SINGLE EUPLOID FROZEN EMBRYO TRANSFER IN A DONOR OOCYTE MODEL

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**Objective:**

Advanced maternal age is a significant determinant of oocyte quality and a risk factor for adverse obstetrical outcome. Less is known about the effect of paternal age on in vitro fertilization (IVF) and neonatal outcomes. Population-based studies have suggested that advanced paternal age may be associated with preterm birth and low birth weight. Previously, our center demonstrated no association between paternal age and impaired fertilization, blastulation, or increased embryonic aneuploidy. While chromosomal copy number variants are largely derived from errors in oocyte meiosis, there is evidence showing a positive correlation between paternal age and de novo germline mutation rates. We hypothesize that a higher prevalence of de novo mutations in embryos derived from men with advancing paternal age could be associated with early pregnancy loss (EPL), lower ongoing pregnancy/live birth (OP/LB) rates, and adverse perinatal outcomes. Using a donor oocyte derived euploid embryo, in a frozen embryo transfer (FET) model, this study sought to elucidate the relationship between paternal age and pregnancy/perinatal outcomes.

**Design:**

Retrospective cohort analysis

## Materials and Methods:

The study included patients undergoing a single euploid FET of donor oocyte-derived embryos from 2012 to 2019. Oocyte donors were ≤35 years of age. Paternal age was treated as a continuous variable. The primary outcome of the study was OP/LB rate. Secondary outcomes included clinical pregnancy (CP) rate, EPL rate, gestational age (GA) at delivery, and neonatal birth weight. Data were evaluated using multivariate linear regressions with generalized estimating equations.

## Results:

A total of 303 single euploid FET cycles from 187 patients were included in this study. Paternal age ranged from 27.6 to 66.7 years (44.5 ± 6.5). There was no statistically significant association between paternal age, CP rate (OR 1.01 [95% CI 0.96-1.07], p=0.62), OP/LB rate (OR 0.99 [95% CI 0.94-1.05], p=0.75), or EPL rate (OR 1.00 [95% CI 0.96-1.07], p=0.96) after controlling for oocyte age, BMI, endometrial thickness at transfer, embryo morphology grade, and days required for blastulation. No association between paternal age and birth weight (β= 8.17, p= 0.91) was observed after controlling for GA, fetal sex, and BMI. Paternal age was not associated with GA at delivery (β= -0.02, p= 0.83).

## Conclusion:

In a large, homogeneous cohort of single, euploid FETs derived from donor oocytes, paternal age was not associated with pregnancy or perinatal outcomes. Our results are encouraging, as they did not demonstrate a link between paternal age and preterm delivery or birth weight. While reassuring, this does not address other multifactorial diseases such as schizophrenia and autism that have been associated with advanced paternal age.1 As the diagnostic capabilities of preimplantation genetic testing expand to include the detection of de novo mutations and higher resolution detection of copy number variants, future studies might investigate the impact of paternal age on the embryonic genome, pregnancy outcomes, and newborn health and development.