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Title:

THE INCIDENCE OF MOSAICISM IS NOT ASSOCIATED WITH ADVANCED MATERNAL AGE OR DIMINISHED OVARIAN RESERVE

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Objective:

Targeted next generation sequencing (NGS) is now routinely utilized to screen embryos for aneuploidy. The increased resolution achievable using NGS presents the opportunity to detect embryo mosacism. While a direct relationship between advanced maternal age and embryonic aneuploidy is well established, the data linking ovarian aging and embryonic mosaicism is limited. Although mosaicism results from mitotic errors, advanced ovarian age could theoretically hinder the proper segregation of chromosomes via defects in cohesion molecules and microtubules. The study aimed to evaluate whether there is an association between the incidence of mosaicism and either advanced maternal age or diminished ovarian reserve.

Design:

Retrospective, observational study

Materials and Methods:

The study included all patients undergoing freeze-all autologous IVF cycles with targeted NGS for preimplantation genetic testing (PGT) from September 2016 to February 2017. Trophectoderm cells underwent biopsy and comprehensive chromosomal screening via targeted NGS. Patients cohorts were stratified by age as suggested by the Society for Assisted

Reproductive Technology (SART). Chi-square test and binary and linear logistic regression analysis were used.

Results:

A total of 315 patients had 1809 blastocysts screened for aneuploidy using targeted NGS, with a 9.4% (n=170) rate of mosaicism. There was no significant difference in the rate of mosaicism according to patient age (x^2=8.58, p=0.072) (Table 1). The odds of mosaicism was not modified by maternal age (OR 0.98 [95% CI 0.9-1.1], p=0.63), AMH (OR 1.0 [95% CI 0.99-1.02], p=0.7, basal antral follicle count (BAFC) (OR 1.01 [95% CI 0.9-1.06], p=0.6) or BMI (OR 0.96 [95% CI 0.9-1.04], p=0.3. The likelihood of mosaicism increased with the number of blastocysts biopsied (OR 1.4 [95% CI 1.2-1.6], p<0.0001).

Conclusion:

This study showed no correlation between the incidence of embryonic mosaicism and patient age or ovarian reserve. Unlike meiotically derived aneuploidy, mosaicism arises from impaired mitotic chromosome segregation which does not appear to increase with ovarian aging. While mosaicism has been long-acknowledged to be a pathological phenomenon arising during preimplantation embryonic development, until recently, predisposing factors and the precise frequency with which it occurs could not be studied. With increasing utilization of NGS for PGT, future studies will allow deeper investigation into clinical, treatment or patient-related factors that are correlated with the occurrence of mosaicism.

Support:

None

Table 1:

Mosaicism rate according to SART Age Groups:

NGS (N=315)	A: <35 N=114	B: 35-37 N=82	C: 38-40 N=83	D: 41-42 N=29	E: >42 N=7	P-value
Embryos Biopsied (N=1809)	9.7% (79/818)	12.3% (57/460)	6.1% (24/395)	8.7% (10/115)	0.0% (0/21)	0.0723