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DOES THE INCIDENCE OF EMBRYONIC MOSAICISM VARY WITH GENETIC INDICATION FOR IN VITRO FERTILIZATION

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OBJECTIVE:

The prevalence of embryonic mosaicism does not seem to be determined by the same rules that govern embryo aneuploidy, as mosaicism is neither associated with meiotic errors nor maternal age. Recent research has identified specific subsets of patients experiencing a higher frequency of mosaic embryos compared to the broader population undergoing in vitro fertilization (IVF) with preimplantation genetic testing for aneuploidy (PGT-A). This study aimed to explore whether patients undergoing PGT for segmental rearrangements (PGT-SR) or monogenic diseases (PGT-M) exhibit similar rates of mosaic embryos within an IVF cycle incorporating PGT-A.

MATERIALS AND METHODS:

This retrospective, single center academic center study included all patients undergoing IVF with PGT from 2019 to 2024. Cohorts were separated based on the indication of PGT (A, A and SR, or A and M). PGT testing was performed using next generation sequencing (NGS) that reported for mosaicism. The primary outcome was embryonic mosaicism status. Patients undergoing IVF for PGT-A and SR or A and M with an additional infertility diagnosis were excluded from the analysis. Demographics, cycle, and laboratory characteristics were collected. ANOVA, Kruskall-Wallis, chi-square, and multivariate logistic regression fitted with a GEE model were used for data analysis. A sample size of 230 embryos per group was calculated to detect a difference of 15% in mosaicism rate with 80% power (alpha = 0.05).

RESULTS:

A total of 11538 cycles were analyzed: 10464 underwent PGT-A (48521 embryos), 134 PGT-A and SR (640 embryos), and 940 PGT-A and M (5695 embryos). Maternal age was significantly higher in patients undergoing PGT-A when compared to PGT- A and SR and PGT- A and M (37.2

±4.1 vs33.5±7 vs 33.1±32; p=0.0001; respectively). Patients undergoing IVF for PGT-A and M had more embryos for biopsy than patients undergoing PGT-A and PGT- A and SR respectively (6.1±2 vs4.6±1.3 vs 4.2±1.2; p=0.002). No other significant differences were found in demographic, cycle, and laboratory characteristics between cohorts. Embryonic mosaicism rates were comparable among groups: PGT-A 10% (n=4887 /48521), PGT-A and SR 9.3% (60/640), PGT-A and M (515/ 5695); p=0.69). After adjusting for maternal age and number of biopsied embryos, no association was found with the indication of PGT and higher odds of embryonic mosaicism (OR 0.70, CI95% 0.5-2.1).

CONCLUSIONS:

The advent of NGS has significantly broadened the understanding of early human genomics among reproductive specialists. Our analysis reveals that patients undergoing IVF with PGT for single gene mutations and structural rearrangements exhibit mosaic rates comparable to those of the infertile population.

IMPACT STATEMENT:

The incidence of mosaicism does not correlate with the indication for IVF with PGT.

REFERENCES:

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