

ANEUPLOIDY RATES OF IVF CYCLES UTILIZING PGT-A AND PGT-M COMPARED TO IVF CYCLES UTILIZING PGT-A ALONE

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Background:

Patients utilizing PGT-M are less likely to be undergoing IVF for infertility than patients undergoing IVF with PGT-A alone. Statistically, patients undergoing PGT-M may require more embryos for testing to obtain an embryo suitable for transfer compared to patients undergoing PGT-A alone, as 25% to 50% of embryos will be affected by the pathogenic single gene variant. However, it is unknown whether aneuploidy rates differ among IVF cycles performed for the purpose of monogenic disease testing compared to IVF cycles utilizing with PGT-A alone.

Objective:

To compare aneuploidy rates among IVF cycles utilizing PGT-A and PGT-M testing for monogenic disorders compared to IVF cycles utilizing PGT-A alone.

Materials and Methods:

All IVF cycles from November 2019 through March 2023 for patients aged 18-45 undergoing PGT-A using next generation sequencing from trophoctoderm biopsies with or without concurrent PGT-M at a single genetics laboratory were analyzed. Cycles were stratified by SART age categories: <35, 35-37, 38-40, 41-42, and >42. Embryos were classified as euploid, mosaic (40-80% mosaicism), or aneuploid. Comparative analyses were performed using Chi-square and median tests.

Result(s): A total of 72,799 IVF cycles were included in the analysis, with 4,532 cycles (6.2%) utilizing PGT-A + PGT-M and 68,267 cycles (93.8%) utilizing PGT-A alone. Patients were significantly younger in the PGT-A + PGT-M group ($p < 0.001$), with 56.1% of cycles in patients <35 and only 2.4% of cycles in patients 43-45, compared to the PGT-A only group, with 30.5% of cycles in patients <35 and 12.4% of cycles in patients 43-45. The median number of embryos biopsied in the PGT-A + PGT-M group was slightly lower in patients <35 compared to PGT-A alone (4 v. 5 embryos, $p < 0.001$), but was equivalent for the other SART age groups: 35-37 (4), 38-40 (3), 41-42 (3), and 43-45 (2) (all $p = \text{NS}$). In cycles utilizing PGT-M testing, the five most frequently tested diseases were *FMR1* ($n=470$, 10.4%), *CFTR* ($n=355$, 7.8%), *BRCA1* ($n=197$, 4.4%), *HTT* ($n=184$, 4.1%), and *HBB* ($n=154$, 3.4%). Aneuploidy rates were not significantly different between PGT-A + PGT-M compared with PGT-A alone groups after stratifying by age. Similarly, there were no significant differences in mosaicism between the two groups (Table 1).

Conclusions: This is an important counseling tool for patients undergoing IVF for single gene testing. Despite the lower likelihood of an infertility diagnosis in PGT-M cases, these data demonstrate that IVF cycles with PGT-A and PGT-M testing have similar age-specific aneuploidy rates as IVF cycles with PGT-A alone.

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Table 1. Aneuploidy rate stratified by SART age for PGT-M + PGT-A versus PGT-A alone

	n (number of cycles) Mean (95% CI)		Median test P-value
	PGT-A + PGT-M (n = 4,532)	PGT-A alone (n = 68,267)	
<35	n = 2,542	n = 20,823	
<i>Aneuploid</i>	28.1% (0.270 – 0.292)	27.7% (0.279 – 0.287)	0.798
<i>Mosaic</i>	8.3% (0.076 – 0.090)	7.5% (0.073 – 0.077)	0.691
35-37	n = 812	n = 10,679	
<i>Aneuploid</i>	34.7% (0.325 – 0.368)	36.0% (0.355 – 0.366)	0.418
<i>Mosaic</i>	9.5% (0.081 – 0.108)	7.8% (0.075 – 0.081)	0.274
38-40	n = 833	n = 16,947	
<i>Aneuploid</i>	46.7% (0.443 – 0.491)	48.0% (0.475 – 0.485)	0.306
<i>Mosaic</i>	7.9% (0.066 – 0.091)	6.9% (0.067 – 0.072)	0.184
41-42	n = 238	n = 10,680	
<i>Aneuploid</i>	61.1% (0.565 – 0.657)	62.9% (0.623 – 0.6360)	0.414
<i>Mosaic</i>	5.4% (0.036 – 0.072)	6.2% (0.059 – 0.066)	0.578
43-45	n = 107	n = 9,138	
<i>Aneuploid</i>	76.4% (0.699 – 0.829)	74.2% (0.735 – 0.750)	0.998
<i>Mosaic</i>	5.1% (0.019 – 0.084)	4.8% (0.045 – 0.052)	0.951