Preimplantation Genetic Screening Markedly Improves Live Birth Rates and Lowers Miscarriage and Twin Rates For All Age Groups Undergoing Frozen Embryo Transfer

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BACKGROUND

- Preimplantation genetic testing for aneuploidy (PGT-A), utilizing Next Generation Sequencing, improves reproductive outcomes by selecting for euploid embryos, deemed "euploid" or "mosaic".
- Studies show PGT-A with frozen embryo transfer (FET) of euploid embryos; increases live birth rate (LBR), decreases miscarriage rate (MR), and decreases twin rate (TR).
- However, benefits observed primarily in patients >35 years old.

OBJECTIVE

- Evaluate the impact of PGT-A on reproductive outcomes by age group and embryo classification (euploid vs. mosaic).
- Assess whether PGT-A increases live birth rate (LBR) and lowers miscarriage rate (MR) and twin rate (TR) in frozen embryo transfer (FET) cycles.
- Compare reproductive outcomes among untested, mosaic, and euploid embryos.

MATERIALS & METHODS

- Single-institution study including all embryos from FET cycles transferred between 3/2015 and 11/2023; no cycles were excluded and no aneuploid embryos were transferred.
- Assessed the effect of PGT-A on clinical intrauterine pregnancy (CIUP), miscarriage rate (MR), twin rate (TR), live birth rate per cycle (LBR/c), and live birth rate per embryo (LBR/e), with LBR/e as the primary outcome.
- Outcomes compared between PGT-A-tested and untested groups, stratified by age (<35, 35-37, 38-40, and >40 years). "Tested" group includes all biopsied embryos, whether labeled euploid, mosaic, or no result.
- Embryos classified as: (1) Euploid: All whole or partial chromosomal segments with less than a 20% risk of monosomy or trisomy. (2) Mosaic: Partial or whole chromosome monosomy or trisomy ranging from 20% to 60%.
- The tested group is larger than the combined mosaic and euploid groups, as SART did not collect mosaic data prior to 2020.
- Chi-square analysis with Yate's correction (as needed) was used to compare per-cycle data between the tested versus untested groups and between the mosaic, euploid, and untested groups.

RESULTS

Among patients ≥35, PGT-A testing lowered the MR from 21% (12/67) to 9% (36/408), p=0.005; improved the LBR/c from 34% (45/134) to 51% (371/727) p<0.001; and improved our primary outcome of LBR/e from 32% (109/342) to 52% (408/802), p<0.001. CIUP was significantly increased from 43% (58/134) for untested to 56% (408/727) in tested, p=0.006.

Tested (T) vs. Untested (UT)

Age Groups	MR (T)	MR (UT)	MR P	LB/c (T)	LB/c (UT)	LB/c P	TR (T)	TR (UT)	TR P	LB/e (T)	LB/e (UT)	LB/e P
< 35	23/252 (9%)	8/64 (13%)	NS	229/396 (58%)	52/109 (48%)	NS	6/229 (3%)	9/52 (17%)	< 0.001	235/413 (57%)	61/141 (43%)	0.005
35 - 37	14/180 (8%)	6/31 (19%)	0.042	166/324 (51%)	24/52 (46%)	NS	5/166 (3%)	2/24 (8%)	NS	171/349 (49%)	26/78 (33%)	0.012
38 - 40	15/159 (9%)	4/17 (24%)	0.17 (NS)	144/280 (51%)	13/42 (31%)	0.013	7/144 (5%)	0/13 (0%)	NS	151/301 (50%)	13/65 (20%)	<0.001
>40	7/69 (10%)	2/10 (20%)	NS	62/123 (50%)	8/40 (20%)	0.001	2/62 (3%)	1/8 (13%)	NS	64/131 (49%)	9/58 (16%)	<0.001
Total	**59/660 (9%)**	**20/122 (16%)**	**0.012**	**601/1123 (54%)**	**97/243 (40%)**	**< 0.001**	**20/601 (3%)**	**12/97 (12%)**	**< 0.001**	**621/1194 (52%)**	**109/342 (32%)**	**< 0.001**

Biochemical rate was 180/840 (21%) in the tested group and 29/151 (19%) in the untested group.

Mosaic (M) vs. Euploid (E) vs. Untested (UT)

Age Groups	MR (M)	MR (E)	MR (UT)	MR P	LB/c (M)	LB/c (E)	LB/c (UT)	LB/c P	TR (M)	TR (E)	TR (UT)	TR P	LB/e (M)	LB/e (E)	LB/e (UT)	LB/e P
< 35	0/8 (0%)	12/163 (7%)	8/64 (13%)	NS	8/12 (67%)	150/269 (56%)	52/109 (48%)	NS	1/8 (13%)	3/150 (2%)	9/52 (17%)	<0.001	9/15 (60%)	153/278 (55%)	61/141 (43%)	0.059 NS
35 - 37	0/6 (0%)	7/118 (6%)	6/31 (19%)	0.013	6/11 (55%)	108/220 (49%)	24/52 (46%)	0.007	0/6 (0%)	3/108 (3%)	2/24 (8%)	NS	6/12 (50%)	111/228 (49%)	26/78 (33%)	0.017
38 - 40	2/10 (20%)	10/109 (9%)	4/17 (24%)	0.020	6/19 (32%)	99/207 (48%)	13/42 (31%)	0.021	1/6 (17%)	2/99 (2%)	0/13 (0%)	0.021	7/20 (35%)	101/214 (47%)	13/65 (20%)	<0.001
>40	0/5 (0%)	5/49 (10%)	2/10 (20%)	0.22 NS	4/10 (40%)	43/82 (52%)	8/40 (20%)	<0.001	1/4 (25%)	0/43 (0%)	1/8 (13%)	0.003	5/12 (42%)	43/82 (52%)	9/58 (16%)	<0.001
Total	**2/29 (7%)**	**34/439 (8%)**	**20/122 (16%)**	**0.013**	**24/52 (46%)**	**400/778 (51%)**	**97/243 (40%)**	**0.007**	**3/24 (13%)**	**8/400 (2%)**	**12/97 (12%)**	**<0.001**	**27/59 (46%)**	**408/802 (51%)**	**109/342 (32%)**	**<0.001**

Biochemical rate was 12/41 29% in the mosaic group, 134/573 23% in the euploid group, and 29/151 (19%) in the untested group.

CONCLUSION

- PGT-A, whether utilizing euploid, mosaic, or undiagnosed embryos, significantly improves LBR, while reducing miscarriages and nearly eliminating twin pregnancies when compared to FET with unbiopsied embryos.
- For patients <35 undergoing PGT-A, the LBR/e was significantly increased from 43% to 57%, a 25% increase; while the risk of a twin birth was reduced by over by over 82.4%, from 17% to 3%.
- For patients ≥35 our data reconfirms that PGT-A vastly improves the LBR and significantly reduces miscarriages.
- Our data suggests that mosaic embryos yield comparable reproductive outcomes to euploid embryos in all age groups, however the higher utilization of DET among mosaics led to TR equivalent to untested embryos.
- Combining PGT-A with eSET in all age groups would markedly improve LBR, allow for minimal MR and nearly eliminate the TR.