Clinical outcomes following implementation of a non-invasive PGT-A program: results from 217 single embryo transfers in ovum donation, good prognosis and advanced maternal age patients

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PURPOSE & OBJECTIVES

Evidence indicates that, as embryos develop *in vitro*, they release cell-free DNA (cfDNA) into the surrounding media; providing an alternative source of genetic material for non-invasive preimplantation genetic testing for aneuploidy (niPGT-A).

The aim of this study was to investigate the reproductive outcomes following niPGT-A implementation in three patient groups: ovum donation, good prognosis patients (<38 years; no clinical indication for testing) and advanced maternal age patients (38-42 years; AMA).

MATERIAL & METHODS

Retrospective, multicentre, international data analysis from five IVF centres following clinical application of niPGT-A. Between July 2020-June 2024, 695 embryos from 263 cycles were cultured following a niPGT-A embryo culture protocol for fresh or previously vitrified blastocysts.

Following thorough denudation and post-denudation washes, fresh embryos were cultured in standard conditions until day 4, then washed and transferred to a 10µl drop. On day 6/7, blastocyst media samples were collected and frozen at -20°C. Previously vitrified blastocysts were thawed on day 5/6, washed and cultured for 24/8 hours, respectively, before media collection. All blastocysts were (re-)vitrified (Fig. 1).

Samples were sent to the same genetics laboratory for analysis using next generation sequencing (Ion ReproSeq PGS kit, ThermoFisher Scientific). Results were processed using a custom algorithm. Embryo prioritisation reports were provided to clinics, and 217 single embryo transfers (SET) were performed according to the niPGT-A results (Tables 1 and 2).

RESULTS

Clinical outcomes were reviewed for 203 euploid SETs. The ovum donation group included 12 transfers (mean age = 42.8±4.2), with clinical pregnancy rate (positive fetal heartbeat; CPR) of 58.3% (7/12) and no clinical miscarriages (Fig.2).

The good prognosis group had 75 transfers (mean age = 34.2±2.6): CPR of 45.3% (34/75) and miscarriage rate of 8.8% (3/34) (Fig.2).

The AMA group comprised 116 transfers (mean age = 39.7±1.4): CPR was 41.4% (48/116) and miscarriage rate was 18.8% (9/48) (Fig.2).

Miscarriage rate was significantly higher in the AMA versus good prognosis patient group (Chi-Squared: p=0.03).

Sub-analysis compared outcomes for AMA patients based on embryo quality: CPR was significantly higher in the good (AA/AB/BA/BB; 41.0%) versus poor (AC/CA/BC/CB/CC; 12.5%) embryo quality group (Chi-Squared: p<0.01). Sub-analysis was not possible in good prognosis patients (all embryos were good quality) or donors (low sample size).

Additionally, 12 SETs of embryos with non-informative media results were performed, resulting in three clinical pregnancies (25%). Two non-euploid blastocysts were transferred, with one healthy livebirth resulting from a blastocyst with a segmental aneuploidy.

Prenatal follow-up in 58 pregnancies revealed low risk results for all cases.

Figure 1. Non-invasive PGT-A embryo culture protocol.

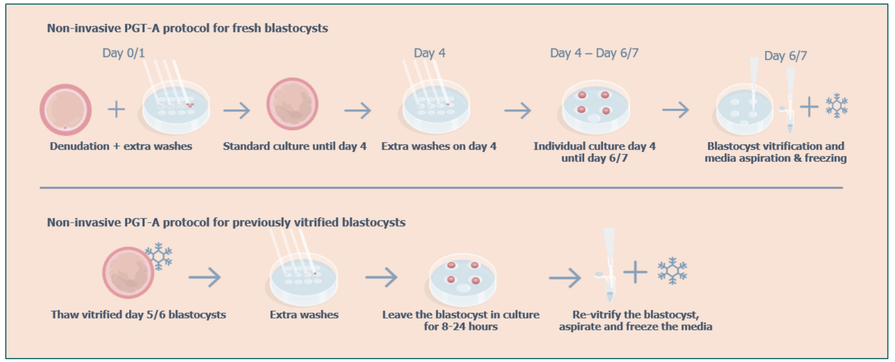


Table 1. Patient and cycle characteristics.

Characteristics	Overall
Number of transfers, n	217
Fresh, % (n/N)	97.7% (212/217)
Frozen, % (n/N)	2.3% (5/217)
Female age, mean ±SD, y*	37.04, ±4.24
Expansion grade	
2 (blastocyst), % (n/N)	0.9% (2/217)
3 (full blastocyst), % (n/N)	6.9% (15/217)
4 (expanded blastocyst), % (n/N)	57.1% (124/217)
5 (hatching blastocyst), % (n/N)	20.4% (44/217)
6 (fully hatched blastocyst), % (n/N)	14.7% (32/217)
Embryo quality	
Good (AA/AB/BA/BB), % (n/N)	95.9% (208/217)
Poor (AC/CA/BC/CB/CC) % (n/N)	4.1% (9/217)
Egg origin	
Autologous, % (n/N)	94.5% (205/217)
Donor, % (n/N)	5.5% (12/217)

** Female age does not include ovum donation cases*

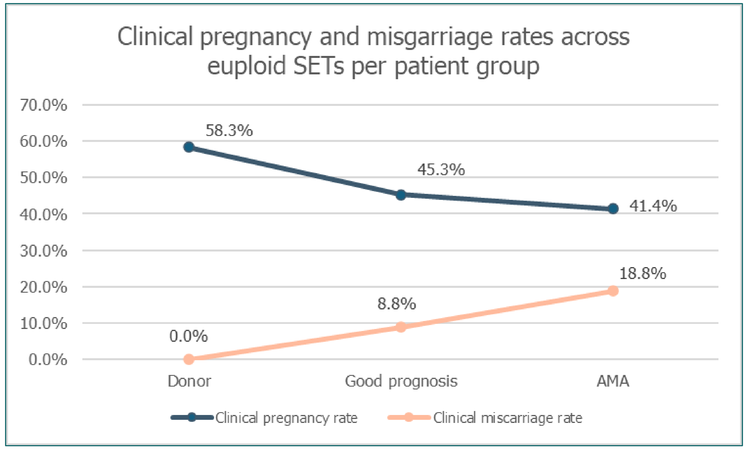
Table 2. Non-invasive PGT-A results for transferred embryos.

Result	Overall
Number of samples, N	217
Informative, % (n/N)	94.5% (205/217)
Euploid, % (n/N)	99.0% (203/205)
Aneuploid, % (n/N)	1.0% (2/205)
Uniform aneuploid, % (n/N)	50% (1/2)
Segmental aneuploid only, % (n/N)	50% (1/2)
No DNA detected, % (n/N)	-
Non-informative, % (n/N)	5.5% (12/217)

CONCLUSIONS

Our results show that both good prognosis and AMA patients could benefit from non-invasive PGT-A, with significantly better results in AMA patients when using good quality embryos.

Figure 2. Clinical pregnancy and miscarriage rates across the three patient groups for euploid SETs.



Analysis of embryonic cell-free DNA could provide objective and helpful information in prioritising the best embryo for transfer, potentially improving IVF outcomes.

REFERENCES

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2. Bakalova D, Navarro-Sánchez L, Rubio C. Non-invasive preimplantation genetic testing. *Genes*. 2025. *16*, 552. https://doi.org/10.3390/genes16050552.

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CONTACT INFORMATION