



SUSTAINED IMPLANTATION RATE IS NOT IMPACTED BY INCREASING FRAGILE X PREMUTATION ALLELE SIZE

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OBJECTIVE: Fragile X (FX) premutation carrier patients are at risk for premature ovarian insufficiency (POI), which hinder the effects of IVF. Recent work demonstrated that FX associated embryology is comparable to controls. The questions that remain are 1) how many patients that present for FX PGD have at least one embryo suitable for transfer, and 2) is the sustained implantation rate (SIR) lower for embryos created from a FX premutation carrier?

DESIGN: Retrospective Observational Study

MATERIALS AND METHODS: Patients from March 2011 to April 2017 from a single IVF center who underwent PGD for FX (with concurrent qPCR-based aneuploidy screening) were included. PGD was performed by a single laboratory that utilized qPCR-based SNP genotyping for linkage analysis. This method determines which embryos inherited the FX-positive maternal chromosome, but cannot determine the size of the CGG repeat in the embryo. Patient characteristics, PGD results, and clinical outcomes including SIR (defined as presence of fetal cardiac activity at 8 weeks of pregnancy/ the number of embryos transferred) were analyzed. Embryos were considered available for transfer if they were euploid and negative for the FX affected haplotype.

RESULTS: 28 patients had probes developed for FX PGD and underwent a total of 49 attempted IVF cycles were included. The mean patient age was 31.7±4.8 years. The average CGG repeat size was 100.3 repeats, including 1 full mutation. Due to poor response, 1 patient did not proceed; resulting in 27 patients undergoing a retrieval. 24 patients produced viable blastocysts to undergo PGD. 21 patients had 68 embryos available for transfer, with only 3 patients not producing normal blastocysts. While 4 patients are awaiting their transfer cycles, 17 patients underwent a single embryo transfer. A total of 21 embryos were transferred. 15 patients experienced a successful implantation, yielding 18 ongoing pregnancies. The median number of cycles that a patient underwent was 1.7 cycles. 12 patients only needed 1 cycle to have a successful transfer. The euploid rate per cycle was 68.9%, as expected in this young patient cohort. The SIR for a patient's first transfer was 88.2%, and overall the SIR was 85.7%. These numbers also suggest that the SIR does not negatively correlate with an increasing maternal premutation allele size, although more patients are needed to fully investigate.

CONCLUSIONS: Nearly all patients presenting for PGD for FX were successful in achieving at least one sustained pregnancy. To our knowledge these data are the largest cohort to date of patients undergoing PGD for FX that includes clinical outcomes.

Maternal CGG Repeat Size	45-55	56-79	80-99	≥100
Number of patients who started at least one IVF cycle	2	12	8	6
% Patients with at least one usable embryo	100% (2/2)	82%(9/11)	100%(5/5)	83% (5/6)
Average sustained implantation rate (%)	100% (1/1)	63% (5/8)	100% (4/4)	100% (4/4)
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