Clinical Comparative Analysis of Pregnancy Outcomes Between Embryos with Intermediate Copy Numbers and No Aneuploidy Found Embryos

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Abstract

Background and Aims: Preimplantation genetic testing for aneuploidy (PGT-A) using next-generation sequencing (NGS) enables embryos to be classified as aneuploid or no aneuploidy found (NAF). However, mitotic chromosomal segregation errors may cause mosaicism. In clinical reporting, these findings may appear as intermediate copy numbers (ICNs), characterized by copy-number deviations that do not meet established thresholds for monosomy or trisomy. The clinical significance of ICNs remains uncertain. This study aimed to compare pregnancy outcomes between NAF embryos exhibiting ICNs and NAF embryos without ICNs following embryo transfer.

Methods: This single-center retrospective study included 115 embryo transfers classified as NAF at the time of transfer. ICN status was not disclosed during clinical decision-making. Following transfer, chromosomal copy-number profiles were retrospectively reviewed to identify embryos with ICNs, which were further categorized as whole-chromosome ICNs (wICN) or segmental ICNs (sICN). Maternal age averaged 38 years in the NAF group without ICNs and 37 years in the ICN group. Clinical outcomes were assessed based on biochemical pregnancy, defined as serum β-hCG >7 mIU/mL in conjunction with progesterone III >11.0 ng/mL.

Results: ICNs were identified in 8.7% of embryo transfers (10/115), comprising five wICN and five sICN embryos. Among NAF embryos without ICNs, biochemical pregnancy was achieved in 92 of 105 transfers. In the ICN group, pregnancy occurred in 4 of 5 transfers involving wICN embryos and in all 5 transfers involving sICN embryos. Overall, no apparent reduction in pregnancy potential was observed in NAF embryos with ICNs compared with those without ICNs.

Conclusions: NAF embryos exhibiting intermediate copy-number profiles demonstrated pregnancy outcomes similar to NAF embryos without ICNs. These findings suggest that ICNs, which may reflect low-level mosaicism below conventional reporting thresholds, were not associated with an obvious reduction in pregnancy potential in this cohort. Careful interpretation of ICNs may support more informed embryo selection strategies in clinical PGT-A practice.

Keywords: Preimplantation genetic testing for aneuploidy (PGT-A), chromosomal mosaicism, intermediate copy number (ICN)