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**OUTCOMES FOLLOWING TRANSFER OF EMBRYOS WHOSE PGT-A RESULTS WERE
INDETERMINATE AND THAT WERE NOT RE-BIOPSIED**

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OBJECTIVE:

PGT-A with NGS is broadly utilized by reproductive specialists at modern ART treatment centers to improve embryo transfer selection. However, there are technical limitations to PGT which might prevent formal designation of the embryo as euploid or aneuploid. While re-biopsy of the embryo is possible, some studies suggesting that the selection of twice biopsied embryos at time of transfer might compromise overall implantation¹. Hence, patients have been known to electively select embryos with indeterminate results for transfer. The aim of this study is to evaluate clinical outcomes following transfer of indeterminate embryos compared to re-biopsied euploid embryos.

DESIGN:

Retrospective analysis.

MATERIALS AND METHODS:

The study included patients who underwent a single FET of blastocysts that underwent a trophoctoderm biopsy from 2016 to 2020. Cohorts were separated into 2 groups: (Group 1: single biopsy embryos with an indeterminate result; Group 2: initial embryo biopsy with indeterminate result that underwent a secondary biopsy and was diagnosed as euploid). Patients whose PGT-A results were indeterminate had extensive clinical and genetic counseling and signed informed consent prior to re-biopsy and/or ET. Demographic characteristics,



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embryology parameters and clinical outcomes were compared. Comparative statistics and an adjusted multivariate regression were used for analysis.

RESULTS:

61 FET cases were included in the analysis: indeterminate PGT results embryos (n= 21); double biopsied euploid embryos (n=40). Patients that elected to transfer indeterminate result embryos had higher age at oocyte retrieval (39.0 vs 36.9, p=0.02) and at ET (39.3 vs 37.2, p=0.01) than patients in group 2. All other demographic variables, embryonic quality at ET, implantation, clinical pregnancy (CPR), ongoing pregnancy (OPR) and clinical pregnancy loss (CPL) rates were statistically comparable among groups. After adjusting for BMI, age, AMH, and embryo quality at FET, transfer of an indeterminate embryo was not associated with lower odds of implantation (OR 1.03 CI95% 0.2-4.3, p=0.96), CPR (OR 1.02 CI95% 0.2-3.8, p=0.40), OPR (OR 1.4 CI95% 0.3-4.9, p=0.60) when compared with double biopsied embryos. Also, there was no association with higher CPL rates (OR 0.4 CI95% 0.3-5.2, p=0.50).

CONCLUSIONS:

This is the first study to describe outcomes when embryos biopsied for PGT-A were indeterminate and selected for transfer without re-biopsy. Our study suggests that implantation and ongoing pregnancy rates are lower when indeterminate embryos are selected for transfer compared to the selection of embryos that underwent a second biopsy and were found to be euploid, albeit the differences were not statistically significant. We recommend re-biopsy of embryos upon an initial indeterminate result to allow for enhanced transfer selection and greatest reproductive potential. However, for patients that have frozen indeterminate embryos and are unable to undergo another IVF cycle, comparable reproductive outcomes are achievable, especially in younger patients who have a higher prevalence of embryonic euploidy.

REFERENCES:

1. Cimadomo D, Rienzi L, Romanelli V, Alviggi E, Levi-Setti PE, Albani E, et al. Inconclusive chromosomal assessment after blastocyst biopsy: prevalence, causative factors and outcomes after rebiopsy and re-vitrification. A multicenter experience. Hum Reprod. 2018;33(10):1839–46