הכינוס השנתי ה-66 של
האגודה הישראלית לחקר הפוריות (אי"ה)
7 במאי 2024, מלון דיוויד אינטרקונטיננטל, תל אביב
האגודה הישראלית לחקר הפוריות (אי"ה)
THE ISRAEL FERTILITY ASSOCIATION (IFA)
الجمعية الإسرائيلية لأبحاث الخصوبة

Rescuing the undiagnosed blastocysts in preimplantation diagnosis for monogenic indications (PGT-M)

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INTRODUCTION

Preimplantation genetic testing for monogenic indications (PGT-M) is currently performed in our laboratory using haplotype analysis, to reduce misdiagnosis due to allelic dropout. Nevertheless, some blastocysts remain without diagnosis for several reasons. We evaluated the rate of non-diagnosed blastocysts in our unit, and examined the diagnostic success rate for repeat biopsies for cases with insufficient genetic material (IGM), defined as amplification success of less than three DNA markers.

METHODS

Day 5 trophectoderm biopsy was performed for PGT-M, on either fresh or thawed blastocysts. Fresh blastocysts were vitrified following the biopsy. For blastocysts with non-diagnosis due to IGM, a second biopsy was attempted contingent on the blastocyst morphology, either on day 6, or on the next thawing cycle. For six hatched blastocysts, zona pellucida was used for re-diagnosis instead. Genetic analysis was performed using in-house protocols for microsatellite haplotyping.

RESULTS

PGT-M for 861 blastocysts was performed between 2021 and 2023 for various monogenic conditions. Non-diagnosis rate was 18% (155 blastocysts). This resulted from IGM (83%), more than one same parent allele (10%) or recombination in the pathogenic variant interval (6%) (Figure 1). The majority of the non-diagnosable embryos were not fit for further verification or repeat biopsy. Repeat biopsy, or zona pellucida testing, was performed on 30 blastocysts of which 20 were diagnostic (67%) (Figure 2). Of those, 14 non-affected blastocysts were diagnosed (46.6%) and were of good morphological quality to be vitrified. Zona pellucida tests were diagnostic in 4/6 embryos, two were non affected. Nine blastocysts have been already transferred to date, but did not undergo implantation.

Figure 1: Results of undiagnosed blastocysts

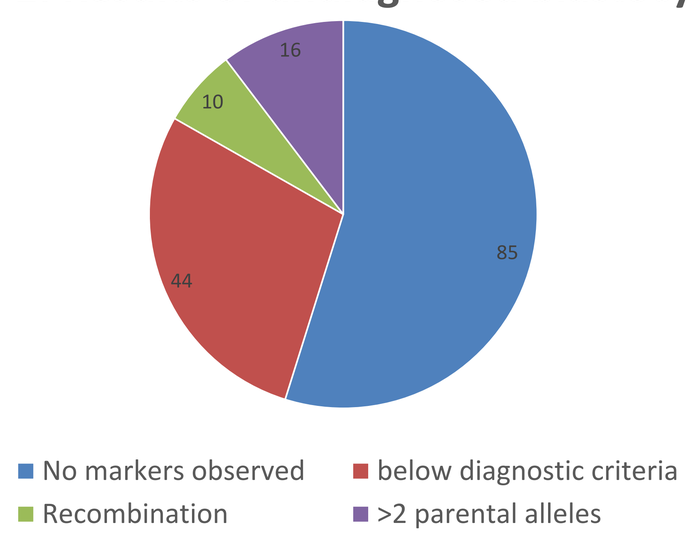
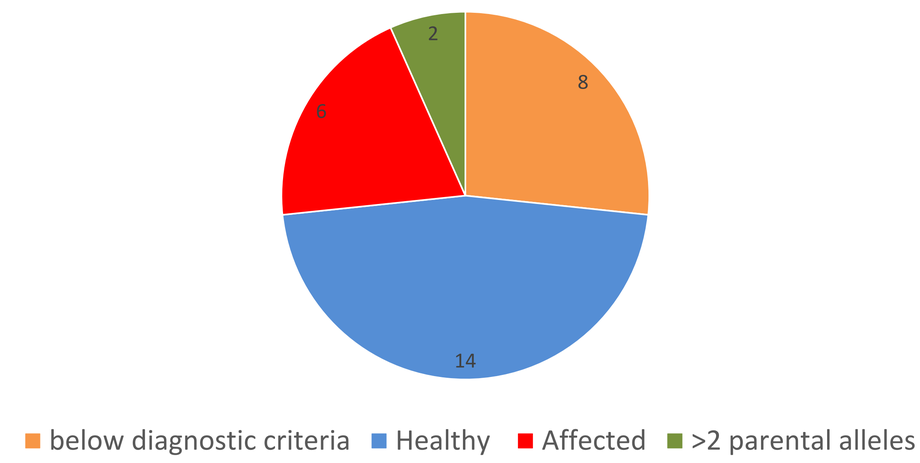


Figure 2: Results of second biopsy diagnosis



SUMMARY and CONCLUSIONS

Most PGT-M test failures in our laboratory are due to IGM, the majority of which are due to low blastocyst quality. A second biopsy will increase the diagnostic yield and number of blastocysts available for transfer. The rate of non-diagnosis is comparable to published data from other PGT laboratories (Spinella et al, 2023). The diagnosis success observed with direct zona pellucida testing merits further evaluation as a promising re-diagnosis option.

REFERENCE

Spinella F, Bronet F, Carvalho F, Coonen E, De Rycke M, Rubio C, Goossens V, Van Montfoort A

ESHRE PGT Consortium data collection XXI: PGT analyses in 2018 Hum Reprod Open. 2023 PMID: 3709122

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