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Embryonic Aneuploidy – Morphokinetic Behaviors as a Potential Diagnostic Biomarker

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Abstract : The number of people who receive in vitro fertilization (IVF) treatment has increased on a startling trajectory over the past two decades. Despite advances in this field, particularly the introduction of intracytoplasmic sperm injection (ICSI) and the preimplantation genetic screening (PGS), the IVF success remains low. A major factor contributing to IVF failure is embryonic aneuploidy (abnormal chromosome content), which often results in miscarriage and birth defects. Although PGS is often used as the standard diagnostic tool to identify aneuploid embryos, it is an invasive approach that could affect the embryo development, and yet inaccessible to many patients due its high costs. As such, there is a clear need for a non-invasive cost-effective approach to identify euploid embryos for single embryo transfer (SET). The reported differences between morphokinetic behaviors of aneuploid and euploid embryos has shown promise to address this need. However, current literature is inconclusive and further research is urgently needed to translate current findings into clinical diagnostics. In this ongoing study, we found significant differences between morphokinetic behaviors of euploid and aneuploid embryos that provides important insights and reaffirms the promise of such behaviors for developing non-invasive methodologies. Methodology—A total of 242 embryos (euploid: 149, aneuploid: 93) from 74 patients who underwent IVF treatment in Carolinas Fertility Clinics in Winston-Salem, NC, were analyzed. All embryos were incubated in an EmbryoScope incubator. The patients were randomly selected from January 2019 to June 2021 with most patients having both euploid and aneuploid embryos. All embryos reached the blastocyst stage and had known PGS outcomes. The ploidy assessment was done by a third-party testing laboratory on day 5-7 embryo biopsies. The morphokinetic variables of each embryo were measured by the EmbryoViewer software (Uniesense FertiliTech) on time-lapse images using 7 focal depths. We compared the time to: pronuclei fading (tPNf), division to 2,3,...,9 cells (t2, t3,...,t9), start of embryo compaction (tSC), Morula formation (tM), start of blastocyst formation (tSC), blastocyst formation (tB), and blastocyst expansion (tEB), as well as intervals between them (e.g., c23 = t3 – t2). We used a mixed regression method for our statistical analyses to account for the correlation between multiple embryos per patient. Major Findings— The average age of the patients was 35.04 yrs. The average patient age associated with euploid and aneuploid embryos was not different (P = 0.6454). We found a significant difference in c45 = t5-t4 (P = 0.0298). Our results indicated this interval on average lasts significantly longer for aneuploid embryos - c45(aneuploid) = 11.93hr vs c45(euploid) = 7.97hr. In a separate analysis limited to embryos from the same patients (patients = 47, total embryos=200, euploid=112, aneuploid=88), we obtained the same results (P = 0.0316). The statistical power for this analysis exceeded 87%. No other variable was different between the two groups. Conclusion— Our results demonstrate the importance of morphokinetic variables as potential biomarkers that could aid in non-invasively characterizing euploid and aneuploid embryos. We seek to study a larger population of embryos and incorporate the embryo quality in future studies.

Keywords : IVF, embryo, euploidy, aneuploidy, morphokinteic
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