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Mini Review

The Possibility of Avoidance of Euploid Pregnancy Loss- Is it Feasible with the Utilization of Time Lapse Microscopy Only-A Short Communication

Kulvinder Kochar Kaur[1]*, Gautam Allahbadia[2] and Mandeep Singh[3]

[1]*Scientific Director, Centre for Human Reproduction, Jalandhar, Punjab, India*

[2]*Scientific Director, Ex-Rotunda-A Centre for Human Reproduction, Mumbai, India*

[3]*Neurology Consultant Neurologist, Swami Satyanand Hospital, Jalandhar, Punjab, India*

***Corresponding Author:** Kulvinder Kochar Kaur, Scientific Director, Centre for Human Reproduction, Jalandhar, Punjab, India.

Received: August 25, 2021; **Published:** September 21, 2021

Abstract

Despite the utilization of preimplantation genetic testing (PGT) for aneuploidy (PGT-A), to rule out the chromosomal aberrations during an *in vitro* fertilization (IVF) that result in pregnancy losses along with Time lapse microscopy (TLM) for the avoidance of pregnancy loss following single euploid embryo transfer (ET) has still not become feasible. Thus, to further study the details of morphokinetic characteristics with the utilization of TLM, McQueen., *et al*. attempted a more detailed evaluation of the morphokinetic characteristics from time to syngamy to time to morula in addition to time to blastocyst generation. Subsequent to a single euploid embryo transfer with their studies of embryos which ended in an euploid abortion did not reveal any aberrant morphokinetic on the utilization of time lapse imaging. Hence as per their conclusions the etiology of euploid pregnancy loss is secondary to lot of factors that is inclusive of both embryo in addition to endometrial factors, with greater research required for finding the factors that can cause anticipation of as well as prevention of euploid loss. Apparently, the only answer lies in the use of Artificial Intelligence (AI), for this anticipation once available.

Keywords: *Embryo Morphokinetic; In Vitro Fertilization (IVF); Time Lapse Imaging; Euploid Pregnancy Loss*

Introduction

Following an *in vitro* fertilization (IVF), roughly 60% of the pregnancy losses occur due to numerical chromosomal imbalances [1]. In case of pregnancies which got conceived following the utilization of *in vitro* fertilization (IVF), the advancements in the preimplantation genetic testing (PGT) for aneuploidy (PGT-A), have escalated the capacity to pick up chromosomal aberrations, in case of most of the advanced centres. Nevertheless, aneuploidy can't explain all the losses in pregnancy subsequent to IVF with the causes of euploid pregnancy losses being mostly uncertain. Time lapse microscopy (TLM) aids in the continuous evaluation of the embryos existing in culture in addition to giving an aid for a noninvasive strategy for the isolation of the embryos that possess the maximum capacity for implantation. Since TLM has the ability of capturing images every 15', it has been posited an observer possesses the chances of recording unique embryo morpho kinetic factors, like the time to cell cleavage, which are correlated with the pregnancy results [2,3]. In 2019, Rienzl., *et al.* [4], documented that time to morulation, in addition to quality of trophectoderm were the significant anticipators of live birth subsequent to an euploid embryo transfer [4]. Practically a decade earlier the first publication of evaluation of lot of embryos with the utilization of time lapse monitoring system (TLM) occurred. Following these studies our familiarity with the new terminology like "morpho kinetic", morphology "dynamics" in addition to "algorithms" escalated besides their utilization got initiated with regards to embryo selection [5]. Subsequently,

a lot of scientific literature has evaluated how much probability this particular knowledge that we get from time lapse monitoring (TLM) might possess over the anticipation of the reproductive results, that is a travel from blastulation forecast right via Implantation capacity to the euploidy anticipation. With the common absence of replication potential amongst these studies, one can say that the possible compounding factors (like age, controlled ovarian stimulation method, fertilization strategies utilized etc.) might have interference with the utilization of the present "algorithms" with regards to choice of embryo for the embryo transfer [6].

Mc Queen., *et al.* [7], attempted to carry out a retrospective cohort study of embryo morpho kinetic estimation in their recent article in case of all single embryo transfers (ET) conducted in their single academic fertility centre from oct 2015 to January 2018 with the utilization of time lapse imaging. In context with the anticipation of a morpho kinetic algorithm with the utilization of a euploidy single embryo transfer, in contrast with the embryo morpho kinetic factors amidst the euploid embryo that caused a pregnancy loss from those that caused a live birth rates (LBR) with time to fusion/alias syngamy, time to 2 cells, time to 3 cells, time to 4 cells, time to 8 cells, time to morula generation (tM) in addition to time to blastocyst generation (tB). They documented that in case of 192 euploid single embryo transfers, there was a pregnancy rate of 78% (150 /192) in addition to live birth rates (LBR) of 63% (121/192). Thus 43 ETs did not cause a pregnancy, 15 biochemical pregnancy losses, 13 abortions in addition to 121 live births occurred. McQueen., *et al.* [7], accumulated in addition to evaluation of all the bbaseline properties, cycle details, besides results that were inclusive of, embryo morpho kinetic estimation, which got evaluated with the utilization of time lapse imaging (time to syngamy, till, time to morula generation (tM) in addition to time to blastocyst generation (tB). No significant variations got in the observation of McQueen., *et al.* [7], in case of unadjusted along with adjusted models of embryo which resulted in a miscarriage in contrast to those which resulted in a live birth, thus concluding further that loss of a euploid pregnancy is possibly secondary to a lot of factors that were inclusive of both endometrium as well as embryonic factors. As per Mc Queen., *et al*. [7], this represented the biggest datasets with regards to miscarriage secondary to euploid embryos, which one might not agree upon, despite that one has to agree that it is so tough to lay hands on embryos, which end up in miscarriage from a preimplantation genetic testing (PGT) for aneuploidy (PGT-A) program. Despite the relevance of their results, as validated by the present literature, to get embryo to decipher this conclusion from just 13 miscarriage is very difficult. Meticulous time has to be given to late processes like tM in addition to tB that get delayed 3 - 4h in the miscarriage embryos, in contrast to the live birth positive embryos as it has already got documented in a lot of publications [4,8]. The major variation from these articles is the greater sample size documented, in addition to contrasting of live birth vs miscarriage in contrast to pregnancy vs no pregnancy, the times of tM in addition to tB in the cohort of clinical loss were 2.53h as well as 3.25 hours slower in cohort of live birth, although this variation did not attain statistical significance at the tM time point. Existence of the probability is that absence of statistical significance is secondary to small sample size. Actually McQueen., *et al.* [7] documented that rather than find a significant variation at the tM time point with 80% power as well as on alpha of 0.05, 99 clinical losses along with 851 live birth subsequent to single euploid embryo transfer would be required. Intriguingly, the biochemical pregnancy loss cohort revealed a reverse pattern, with the times to tM in addition to tB happen to be faster in contrast to the live birth cohort.

Meticulous emphasis are required to get drawn to the linear mixed models whose utilization in this article, besides inclusion of blastocyst morphology in the evaluation of possible confounding factors in addition to harmful factors. that were correlated with a miscarriage. McQueen., *et al.* [7], illustrated those significant variations in morphology amidst groups in addition to embryo morphology got recruited in the adjusted models as a possible confounding factor. Embryo scoring was done morphologically on the day of embryo transfer in addition to morphologic evaluation of the inner cell mass (ICM), along with trophectoderm (TE), possessed significant correlation with the pregnancy results. Embryos that caused a live birth possessed a greater probability of possessing advantageous score for ICM along with TE in contrast to the embryos that resulted in a pregnancy loss clinically. No significant variation amongst the morphological scores where embryos that resulted in a live birth vis a vis biochemical pregnancy loss. What is significant is just 3 /13 pregnancy losses underwent genetic evaluation of the products of conception (POC). Thus no proof exists that the embryos were actually euploid. Nevertheless, all the specimens undergoing testing were validated to be euploid on evaluation of the POC [9].

Conclusion

Still there exists need for enhancement in the anticipation value of embryos generation for pregnancy loss. This might in future we might be able to get through use of Artificial Intelligence (AI), although the application of Artificial neural networks over all morpho kinetics data, that is inclusive of computer morphology evaluation, that might give higher consistencies to the evaluation done by embryologist [9-11].

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Volume 10 Issue 10 October 2021