SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS TO IDENTIFY TIME-LAPSE BIOMARKERS ASSOCIATED WITH LIVE BIRTH OUTCOME

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Background: Time-lapse imaging has enabled embryos to be continuously monitored without removing them from their incubators and has improved the accuracy of identifying established biomarkers and new non-invasive biomarkers. It is important to assess if these biomarkers can support embryo assessment in terms of live birth (LB) potential. Assessing the amount of time embryologists spend analyzing these biomarkers during an IVF cycle and exploring how technology can be used to lean processes to improve standards of care.
Objective: To identify which time-lapse derived biomarkers are associated with live birth outcome.

Materials and methods: PRISMA method and Ovid Medline were used to conduct the literature search to identify studies that investigated the clinical value of biomarkers in predicting live birth outcomes. Only studies written in English were included, where the sample size and live birth data were stated. Data presented as Odds ratio (OR) and 95% confidence interval (CI). Each factor associated with live birth outcome was assessed for the time required to annotate manually. A lean assessment was performed to quantify the value of using Artificial Intelligence (CHLOE-EQ) to assess these factors automatically.

Results:
The following biomarkers are predictors of positive live birth: 1PN [0.6(0.5-0.7),n=9040, 6 papers], morphokinetics (tPNf, t2, t3, t4, t5, t8) [OR=16.6 (14.6-18.9 CI), n=22,938, 5 papers], 8 or more cells on day 3 [OR=1.3 (1.1-1.5 CI), n=6468, 3 papers], ICM quality: A vs B[1.3(1.2-1.4),n=6267], A vs B&C[1.4(1.2-1.6),n=4568], A vs C [2.8(1.7-4.7),n=2581], A&B vs C[2.5(1.5-4.1),n=4568], B vs C [2.1(1.3-3.5),n=2076], TE quality: A vs B[1.4(1.3-1.6),n=6059], A vs B&C[1.6(1.4-1.8),n=4568], A vs C[2.5(1.9-3.3),n=2119], A&B vs C [2(1.5-2.6),n=4568] and B vs C[1.7(1.3-2.2),n=2746], 7 papers.

Biomarkers with a significant negative effect on LB were zona pellucida abnormalities [OR=0.6 (0.5-0.8CI), n=8287, 5 papers], DUC embryos [OR=0.2 (0.1-0.3 CI), n=3244, 4 papers], moderate fragmentation [20-50% vs 0-20%: OR=0.3 (0.2-0.5 CI), n=9744, 3 papers].

Smooth endoplasmic reticulum [OR=1 (0.8-1.3 CI), n=7175, 7 papers], multinucleation at the 2-cell stage [OR=0.9 (0.7-1.1 CI), n=1734, 3 papers] or reverse cleavage [OR=0.9 (0.8-1.1 CI), n=22,148, 4 papers] were not associated with live birth.

The embryologist time required to assess the factors associated with live birth manually was 1.1 hours per cycle (Morphokinetics, DUC, cell number, fragmentation, ICM and TE). This timing is reduced to 0 when using CHLOE-EQ.

Conclusion:
Zona pellucida abnormalities, morphokinetics, 1PN, DUC, degree of fragmentation, day 3 cell number, ICM quality, TE quality were biomarkers associated with LB. There is a need to extend the studies on other biomarkers with association to implantation to quantify their value in prediction to live

birth. Given the time-consuming nature of quantifying these biomarkers in time-lapse, as the list of biomarkers with evidence of live birth prediction increases, AI tools, can become critical in making it logistically feasible to ensure embryologists are aware of these important insights when assessing embryo development.