MORPHOKINETIC BEHAVIOR IN EMBRYOS LEADING TO BIOCHEMICAL PREGNANCY

Assumpto Iaconelli Jr.[1,2], Amanda Setti[2,3], Daniela Braga[2,3], Patricia Guilherme[1], Vinicius Medina Lopes[4], Edson Borges Jr.[1,2]

[1] Fertility Medical Group/FERTGROUP Medicina Reprodutiva [2] Instituto Sapientiae - Centro de Estudos e Pesquisa em Reprodução Assistida, [3] Fertility Medical Group, [4] Instituto Verhum/FERTGROUP Medicina Reprodutiva

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INTRODUCTION

One of the possible outcomes of the pregnancy test is a biochemical pregnancy; where the pregnancy test is positive but does not progress into a clinical pregnancy. Despite its unknown etiology, several associated factors have been suggested such as embryo aneuploidy, abnormal uterine lining, sperm DNA damage and so on. Embryo monitoring with timelapse imaging (TLI) may be a valuable approach to evaluate whether embryonic morphokinetics can predict the occurrence of a biochemical pregnancy. The aim of this study was to investigate whether embryos leading to biochemical pregnancy behave morphokinetically different than those leading to positive or negative pregnancy result.

METHODS

Cohort study performed in a private university–affiliated IVF center between March/2019 and April/22

Women undergoing ICSI cycles → n=753

Split into groups according to pregnancy outcome:
- Biochemical group (n=30 cycles / 54 transferred embryos)
- Positive Group (n=255 cycles / 444 transferred embryos)
- Negative Group (n=468 cycles / 750 transferred embryos)

Embryo culture until D5 with TLI

Kinetic markers were recorded

tPNa	t6	cc2
tPNf	t7	cc3
t2	t8	s1
t3	tM	s2
t4	tSB	s3
t5	tB	

11 focal planes

Every 10 min

Generalized mixed models followed by Bonferroni post-hoc test were used to compare morphokinetics among the groups
(post hoc achieved power > 90%)

RESULTS

ICSI outcomes	Biochemical Group	Negative Group	Positive Group	p-value
n	30	468	255	
Maternal age (years)	**38.2 ± 0.6 ab**	38.0 ± 0.15 [a]	37.2 ± 0.2 [b]	0.016
Paternal age (years)	**43.2 ± 1.3 a**	38.5 ± 0.4 [b]	38.6 ± 0.5 [b]	0.003
Female BMI (kg/m2)	**23.6 ± 1.4**	24.2 ± 0.4	24.2 ± 0.5	0.916
Total dose of FSH (IU)	**2200.0 ± 349.9**	2375.4 ± 92.8	2455.5 ± 121.2	0.739
Aspirated follicles (n)	**8.0 ± 1.4**	8.1 ± 0.4	9.8 ± 0.5	0.687
Retrieved oocytes (n)	**7.0 ± 1.1**	6.9 ± 0.3	7.5 ± 0.4	0.412
Mature oocytes rate (%)	**77.4**	76.7	74.3	0.795
Fertilization rate (%)	**86.7**	76.1	78.4	0.176
Blastocyst development (%)	**43.0**	41.0	44.7	0.599
Transferred embryos (n)	**1.8**	1.7	1.7	0.696

Table 1. Comparison of demographic data and ICSI cycles' characteristics between Biochemical, Positive and Negative groups (n=753 cycles)

Table 2. Comparison of embryo morphokinetic parameters between Biochemical, Positive and Negative groups (n=1248 embryos)

Morphokinetics	Biochemical Group	Negative Group	Positive group (Reference group)	
n	54	750	444	p-value
tPNa	5.53 ± 0.65 [a] B: -0.865 (CI: -2.227 – 0.496)	7.54 ± 0.18 [b] B: 1.144 (CI: 0.562 –1.726)	6.40 ± 0.23 [a]	<0.001
tPNf	23.47 ± 0.81 [a] B: -0.597 (CI: -2.284 – 1.089)	25.60 ± 0.22 [b] B: 1.528 (CI: 0.824 – 2.232)	24.07 ± 0.28 [a]	<0.001
t2	25.99 ± 0.85 [a] B: -0.584 (CI: -2.352 – 1.184)	28.38 ± 0.23 [b] B: 1.805 (CI: 1.067 – 2.542)	26.58 ± 0.30 [a]	<0.001
t3	36.70 ± 0.93 [a] B: -1.356 (CI: -3.283 – 0.571)	39.00 ± 0.25 [b] B: 0.953 (CI: 0.149 – 1.758)	38.05 ± 0.32 [a]	0.008
t4	39.00 ± 1.03 [a] B: -0.061 (CI: -2.201 – 2.079)	41.57 ± 0.28 [b] B: 2.514 (CI: 1.621 – 3.407)	39.06 ± 0.36 [a]	<0.001
t6	52.68 ± 1.34 [ab] B: -0.100 (CI: -2.880 – 2.680)	54.87 ± 0.36 [b] B: 2.098 (CI: 0.950 – 3.246)	52.78 ± 0.46 [a]	0.001
t7	55.53 ± 1.30 [ab] B: 0.412 (CI: -2.282 – 3.106)	57.45 ± 0.36 [b] B: 2.327 (CI: 1.209 – 3.445)	55.12 ± 0.44 [a]	<0.001
t8	58.58 ± 1.44 [ab] B: 0.839 (CI: -2.149 – 3.828)	61.28 ± 0.40 [b] B: 3.550 (CI: 2.294 – 4.806)	57.74 ± 0.50 [a]	<0.001
cc2	10.63 ± 0.14 [a] B: -0.842 (CI: -1.279 – -0.405)	11.47 ± 0.18 [b] B: 1.172 (CI: 0.811 – 2.275)	10.70 ± 0.50 [a]	0.001
s1	2.52 ± 0.12 [ab] B: 0.014 (CI: -0.238 – 0.266)	2.66 ± 0.03 [b] B: 0.156 (CI: 0.051 – 0.261)	2.51 ± 0.04 [a]	0.012
s2	2.30 ± 0.56 [ab] B: 1.295 (CI: 0.139 – 2.451)	2.57 ± 0.15 [b] B: 1.561 (CI: 1.078 – 2.043)	1.01 ± 0.19 [a]	<0.001
s3	8.12 ± 1.16 [ab] B: 0.654 (CI: -1.752 – 3.060)	10.55 ± 0.33 [b] B: 3.090 (CI: 2.079 – 4.101)	7.46 ± 0.40 [a]	<0.001
KIDScore	5.59 ± 0.35 [a] B: -0.397 (CI: -1.133 – 0.340)	4.73 ± 0.11 [b] B: -1.257 (CI: -1.583 – -0.932)	5.99 ± 0.13 [a]	<0.001

CONCLUSIONS

Embryos that resulted in a biochemical pregnancy did not display evidence of abnormal morphokinetics on time-lapse imaging. Biochemical pregnancy is likely multifactorial, including both embryo and endometrial factors. Further research is needed to identify factors that can predict and prevent biochemical pregnancy.