

### BACKGROUND AND AIM

IVM preceded by a prematuration step (CAPA-IVM) improves the acquisition of oocyte developmental competence and can enhance embryo quality. CAPA-IVM has been applied first in Vietnam since 2016 and resulted in live births. There is no data reporting the long term follow-up of babies born from CAPA-IVM. We conducted this study to answer the question: "What are the longer-term development outcomes in children born after CAPA-IVM versus natural conception?"

### METHODS

A prospective cohort study was conducted at IVFMD, My Duc Hospital, HCMC, Viet Nam from August 2019 to September 2019. Twenty-three parents of all CAPA-IVM babies born alive were contacted via postal mail and email and asked to bring their children to the hospital for check-up. Another 23 parents of natural conception babies were chosen by propensity score matching method as controls. At the hospital, parents received training and under the supervision of a pediatrician, the parents were asked to complete the Developmental Red Flags and Ages & Stages Third Edition (ASQ-3) Questionnaires.

### RESULTS

A total of 46 parents (23 each group) of 55 babies were included in the study, of whom, 31 were CAPA-IVM children and 24 were natural conception children. Baseline characteristics, including mother's age, mother's BMI, gestational age at delivery, and birth weight were comparable. The mean age of children at the end of follow-up was 15 months. Weight was similar in the CAPA-IVM and natural pregnancy groups (9.9±1.4 vs 10.3±1.3 kg; p=0.26). The composite of abnormal ASQ-3 rate was 2/31 (6.5%) in CAPA-IVM group which is lower than the natural pregnancy group 5/24 (20.8%) but no statistically significant difference (p=0.24). The abnormal Red flag rate was comparable between two groups (3/31 (9.7%) vs 1/23 (4.2%), p=0.80).

Table 2. Abnormal scores per problem area compared between groups.

ASQ - 3	IVM (N = 31)	Natural (N = 24)	P-value
Age of completion of follow-up, months	15.03 ± 4.13	15.00 ± 4.57	0.978
- Singleton	15.87 ± 4.44	15.09 ± 4.77	0.621
- Twin	14.25 ± 3.79	14.00 ± 0.0	0.929
Weight of completion of follow-up, kgs	9.86 ± 1.35	10.26 ± 1.28	0.263
- Singleton	10.46 ± 1.45	10.29 ± 1.33	0.716
- Twin	9.29 ± 0.98	9.95 ± 0.21	0.372
Communication, n (%)	0 (0.0)	2 (8.3)	0.362
- Singleton	0/15 (0.0)	2/22 (9.1)	0.645
- Twin	0/16 (0.0)	0/2 (0.0)	-
Gross motor, n (%)	0 (0.0)	1 (4.2)	0.897
- Singleton	0/15 (0.0)	1/22 (4.5)	0.999
- Twin	0/16 (0.0)	0/22 (0.0)	-
Fine motor, n (%)	2 (6.5)	1 (4.2)	0.999
- Singleton	2/15 (13.3)	1/22 (4.5)	0.728
- Twin	0/16 (0.0)	0/2 (0.0)	-
Problem solving, n (%)	1 (3.2)	0 (0.0)	0.999
- Singleton	1/15 (6.7)	0/22 (0.0)	0.845
- Twin	0/16 (0.0)	0/2 (0.0)	-
Personal Social, n (%)	0 (0.0)	2 (8.3)	0.362
- Singleton	0/15 (0.0)	2/22 (9.1)	0.645
- Twin	0/16 (0.0)	0/2 (0.0)	-
Composite of abnormal ASQ-3, n (%)	2 (6.5)	5 (20.8)	0.238
- Singleton	2/15 (13.3)	5/22 (22.7)	0.773
- Twin	0/16 (0.0)	0/2 (0.0)	-
Redflag, n (%)	3 (9.7)	1 (4.2)	0.797
- Singleton	3/15 (20.0)	1/22 (4.5)	0.344
- Twin	0/16 (0.0)	0/2 (0.0)	-

Table 3. Joint effects of factors of influence on abnormal ASQ.

Variables	Abnormal ASQ-3 N = 7	Normal ASQ-3 N = 48	OR (95%CI), P-values	OR* (95%CI), P-values*
Group, n (%)				
- Natural	5 (71.4)	19 (39.6)	Ref	Ref
- IVM	2 (28.6)	29 (60.4)	0.26 (0.03-1.35), 0.131	0.22 (0.03-1.24), 0.105
Maternal age, years	27.83 ± 5.15	29.77 ± 3.40	0.86 (0.67-1.09), 0.226	
Maternal BMI, kg/m <sup>2</sup>	21.17 ± 0.84	20.98 ± 0.79	1.37 (0.46-4.05), 0.569	
Twins, n (%)	0 (0.0)	18 (37.5)	-	
Gestational age at delivery, wks	37.08 ± 0.97	37.41 ± 1.30	0.81 (0.40-1.53), 0.521	
Group of Gestational age at delivery, n (%)				
- >37wks	1 (14.3)	23 (47.9)	Ref	Ref
- 34 - 37wks	6 (85.7)	25 (52.1)	5.52 (0.85-108.46), 0.126	6.03 (0.76-131.37), 0.136
LB weight, 100 grams				
- Singleton	3171.43 ± 546.85	3086.67 ± 364.58	1.06 (0.85-1.32), 0.608	
- Twin	0	2504.44 ± 370.85	-	
NICU admission, n (%)	3 (42.9)	10 (20.8)	2.85 (0.50-15.10), 0.214	1.58 (0.22-10.19), 0.633

### CONCLUSIONS

No difference was found in the development of CAPA-IVM children compared to natural conception children.

### KEYWORDS

In vitro fertilization, in-vitro maturation, CAPA-IVM, development outcomes.

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Characteristics	IVM (N = 23)	Natural (N = 23)	P-value
Age, yr	29.48 ± 3.89	29.39 ± 3.75	0.939
BMI, kg/m <sup>2</sup>	21.13 ± 0.94	20.99 ± 0.41	0.534
Anti-Müllerian hormone, ng/mL	12.16 ± 4.42	-	
Duration of infertility, yrs	3.00 ± 2.00	-	
No of previous IVF attempts, n (%)			
- 1	22 (95.7)	-	
- ≥ 2	1 (4.3)	-	
Type of infertility, n (%)			
- Primary	13 (56.5)	-	
- Secondary	10 (43.5)	-	
IVF indication, n (%)			
- Male factor	1 (4.3)	-	
- PCOS	21 (91.3)	-	
- Low OR	1 (4.3)	-	
- Tubal factor	0 (0.0)	-	
- Unexplained	0 (0.0)	-	
Type of delivery, n (%)			
- Cesarean	20 (87.0)	23 (100.0)	0.232
- Spontaneous	3 (13.0)	0 (0.0)	
Gestational age at delivery, wks	37.20 ± 1.24	37.91 ± 1.17	0.055
- > 37wks	11 (47.8)	12 (52.2)	0.987
- 34 - 37wks	12 (52.2)	11 (47.8)	0.899
- < 34wks	0 (0.0)	0 (0.0)	-
Twins, n (%)	8 (34.8)	1 (4.3)	0.026
Birth weights, gram			
- Singleton	3206.67 ± 435.02	3031.82 ± 363.04	0.193
- Twin	2536.25 ± 378.36	2250.00 ± 212.13	0.318
NICU admission, n (%)	7 (22.6)	6 (25.0)	0.999
- Singleton	5/15 (33.3)	4/22 (18.2)	0.506
- Twin	2/16 (12.5)	2/2 (100.0)	0.057
Neonatal composite, n (%)	6 (26.1)	4 (16.7)	0.994
- Singleton	4/15 (26.7)	4/22 (18.2)	0.999
- Twin	2/16 (12.5)	0/2 (100)	0.989