Perinatal and postnatal outcomes up to the third year of life after the transfer of mosaic embryos compared with euploid embryos

OBJECTIVE

To date, data after the transfer of blastocysts diagnosed as mosaic remain limited, especially regarding neonatal and early childhood outcomes (1–5). This study aimed to compare perinatal and postnatal outcomes of children born from mosaic embryo transfer (ET) with those born from euploid ET.

STUDY DESIGN

In this retrospective cohort study, cycles of vitrified-warmed ET after preimplantation genetic testing for aneuploidy (PGT-A) leading to the live birth of a newborn were assessed between October 2017 and August 2022.

Newborns included were categorized into two groups based on their classification as either euploid (n = 115) or mosaic embryos (n = 57) after PGT-A. The mosaicism threshold was 25%–50% of aneuploidy.

The clinical outcomes analyzed and compared in both groups were prenatal screening and testing as well as pregnancy complications, maternal age at birth, gestational age, type of delivery and delivery complications, newborn measures, neonatal admission, congenital anomalies, hospital admission, chronic diseases and chronic use of medication, and other health problems not involving hospital admission. Postnatal karyotyping was performed in six children from the mosaic group, by parental choice.

RESULTS

The analysis included a total of 172 singleton live births resulting from a single ET after PGT-A analysis (euploid group, n = 115; mosaic group, n = 57). Variables related to prenatal and perinatal periods, such as pregnancy and delivery complications, type of delivery, and gestational age, were comparable in both groups. Only maternal age was higher in the mosaic group (Table 1). Regarding newborn measures, there were no significant differences between the groups in birth weight, length, head circumference, and the Apgar score (Table 2). Table 2 shows no differences in the following additional postnatal outcomes: neonatal admissions, congenital anomalies, hospital admissions, and chronic diseases.

The main reasons for neonatal admission were prematurity and pulmonary maladaptation in both groups. With regard to congenital anomalies, all anomalies were minor, except for a single case of a major anomaly (hypospadias) in the euploid group. The most common minor defects in the euploid group included hip dysplasia (in 3 [2.6%] children) and mild facial dysmorphia (in 2 [1.7%] children). Other

TABLE 1

Prenatal and perinatal outcomes.

Outcome	Total children (n = 172)	Euploid group (n = 115)	Mosaic group (n = 57)	*P*
Pregnancy complications events, n (%)	42 (24.4)	30 (26.1)	12 (21.1)	.469[a]
Diabetes gravidaris, n (%)	11 (6.4)	7 (6.1)	4 (7.0)	1.000[a]
Hypertension, n (%)	11 (6.4)	7 (6.1)	4 (7.0)	1.000[a]
Hypothyroidism, n (%)	13 (7.5)	11 (9.6)	2 (3.5)	.224[a]
Premature rupture of membranes, n (%)	5 (2.9)	4 (3.5)	1 (1.8)	1.000[a]
Other, n (%)	2 (1.2)	1 (0.9)	1 (1.8)	.552[a]
Delivery complications events, n (%)	34 (19.8)	23 (20.0)	11 (19.3)	.913[a]
Instrumentalized childbirth, n (%)	10 (5.8)	6 (5.2)	4 (7.0)	.732[a]
Umbilical cord problems, n (%)	4 (2.3)	2 (1.7)	2 (3.5)	.600[a]
Placental abnormalities, n (%)	4 (2.3)	3 (2.6)	1 (1.8)	1.000[a]
Meconium aspiration syndrome, n (%)	2 (1.2)	2 (1.7)	0 (0.0)	—
Abnormal fetal monitoring, n (%)	5 (2.9)	4 (3.5)	1 (1.8)	1.000[a]
Other, n (%)	9 (5.2)	6 (5.2)	3 (5.3)	1.000[a]
Cesarean section, n (%)	78 (45.3)	53 (46.1)	25 (43.9)	.782[a]
Gestational age (wk), (mean ± SD)	39.15 ± 1.87	39.22 ± 1.92	39.00 ± 1.78	.332[b]
Preterm births (<37 wk), n (%)	12 (7.0)	7 (6.1)	5 (8.8)	.535[a]
Very preterm births (<32 wk), n (%)	3 (1.7)	2 (1.7)	1 (1.8)	1.000[a]
Maternal age at birth (y), (mean ± SD)	38.87 ± 3.25	38.27 ± 3.06	40.07 ± 3.32	<.001[b]

Note: Statistical significance is defined as $P < .05$.
[a] Fisher's exact test.
[b] Wilcoxon rank-sum test.

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Data regarding any of the subjects in the study have not been previously published unless specified. Data will be made available to the editors of the journal for review or query upon request.

TABLE 2

Postnatal outcomes.

Outcome	Euploid group (n = 115)	Mosaic group (n = 57)	B[a] (95% CI)/OR[b] (95% CI)	*P*
Newborn measures				
Birth weight (g), (mean ± SD)	3,222.5 ± 581.2	3,227.5 ± 530.3	51.310[a] (-110.392; 13.013)	.532
Birth weight <2,500 g, n (%)	10 (8.7)	2 (3.5)	0.072[b] (0.004; 1.462)	.087
Birth weight <1,500 g, n (%)	2 (1.7)	1 (1.8)	0.136[b] (0.002; 11.324)	.377
Birth length (cm), (mean ± SD)	49.9 ± 2.7	50.1 ± 2.7	0.483[a] (-0.245; 1.212)	.192
Birth head circumference (cm), (mean ± SD)	34.5 ± 1.9	34.5 ± 1.9	0.147[a] (-0.525; 0.820)	.664
Apgar score, (mean ± SD)	8.6 ± 2.5	8.9 ± 1.8	0.702[a] (-0.334; 1.738)	.181
Neonatal admission, n (%)	10 (8.7)	5 (8.8)	1.727[b] (0.408; 7.306)	.458
Congenital anomalies, n (%)	10 (8.7)	4 (7.0)	0.836[b] (0.233; 3.005)	.784
Hospital admission, n (%)	6 (5.2)	0 (0.0)	0.000[b] (0.000; —)	.997
Surgical intervention, n (%)	2 (1.7)	0 (0.0)	—	—
Medical hospitalization, n (%)	4 (3.5)	0 (0.0)	—	—
Chronic diseases, n (%)	1 (0.9)	1 (1.8)	1.781[b] (0.079; 40.104)	.610
Age of the child (y), (mean ± SD)	3.48 ± 0.81	2.92 ± 1.32	—	.010[c]

Note: Statistical significance is defined as $P < .05$.
CI = confidence interval; OR = odds ratio.
[a] Coefficient of the multivariate linear regression.
[b] OR of the multivariate binary logistic regression. Both regression analyses were adjusted using pregnancy and delivery complications, cesarean section, gestational age, and maternal age at birth as confounding factors. Reference category: euploid embryos. Because of the low number of cases in these groups, it was not possible to calculate 95% CIs for the OR.
[c] Wilcoxon rank-sum test.

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anomalies such as hydrocele, strabismus, pyelectasis, and fossa sacra were reported in only 1 (0.9%) child each. In the mosaic group, there were 2 (3.5%) cases of skin anomalies (café-au-lait spots or hemangioma), 1 (1.8%) of ectopic kidney, and 1 (1.8%) of syndactyly. In the euploid group, surgical intervention was performed in two children, and medical hospitalization was required in four children. No hospital admission was reported in the mosaic group. Comparable rates of chronic diseases were reported in the two groups, and no other health problems were recorded. The average age of the children at the time of the study was 3.48 ± 0.81 years in the euploid group and 2.92 ± 1.32 years in the mosaic group. Prenatal screening and testing were performed in 50.9% of pregnancies in the mosaic group with a normal result. In addition, postnatal karyotyping in six children was also normal.

Finally, the analysis revealed that clinical outcomes did not differ on the basis of the classification of the transferred embryo (mosaic or euploid) until the child's average age of approximately 3 years. Detailed methods and results are included in the Supplemental Data (available online).

CONCLUSION

This study suggests that the transfer of low-level mosaic embryos results in apparently healthy children up to the age of 3 years, similar to the transfer of euploid embryos. It is the first study to analyze prenatal, perinatal, and postnatal outcomes beyond birth weight, gestational age, and congenital anomalies in children from mosaic embryos compared with those from euploid embryos, and it is also the first to report details of physical health during early infancy. Although these data are limited by the relatively small cohort size, which does not allow for the analysis of the impact of mosaicism type, and the shorter follow-up period for the mosaic group, it provides reassuring evidence that there are no health problems in children from this type of mosaic embryo. Further long-term follow-up studies are necessary to assess the safety of mosaic ET.

CRediT Authorship Contribution Statement

Ruth Morales: Writing – review & editing, Writing – original draft, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Belén Lledó:** Writing – review & editing, Visualization, Validation, Data curation, Conceptualization. **José A. Ortiz:** Writing – review & editing, Visualization, Validation, Methodology, Formal analysis, Data curation. **Laura Arenas:** Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Alba Cascales:** Writing – review & editing. **Jorge Ten:** Writing – review & editing, Visualization. **Andrea Bernabeu:** Writing – review & editing, Visualization. **Rafael Bernabeu:** Writing – review & editing, Visualization.

Declaration of Interests

R.M. has nothing to disclose. B.L. has nothing to disclose. J.A.O. has nothing to disclose. L.A. has nothing to disclose. A.C. has nothing to disclose. J.T. has nothing to disclose. A.B. has nothing to disclose. R.B. has nothing to disclose.

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