Chromosomal, gestational, and neonatal outcomes of embryos classified as a mosaic by preimplantation genetic testing for aneuploidy

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Objective: To understand the clinical risks associated with the transfer of embryos classified as a mosaic using preimplantation genetic testing for aneuploidy.

Design: Analysis of multicenter data collected between 2017 and 2023.

Setting: ■■■

Patients: Patients of infertility treatment.

Intervention: Comparison of pregnancies resulting from embryos classified as euploid or mosaic using the 20%–80% interval in chromosomal intermediate copy numbers to define a mosaic result.

Main Outcome Measures: Rates of spontaneous abortion, birth weight, length of gestation, incidence of birth defects, and chromosomal status during gestation.

Results: Implanted euploid embryos had a significantly lower risk of spontaneous abortion compared with mosaic embryos (8.9% [n = 8,672; 95% confidence interval {CI95} 8.3, 9.5] vs. 22.2% [n = 914; CI95 19.6, 25.0]). Embryos with mosaicism affecting whole chromosomes (not segmental) had the highest risk of spontaneous abortion (27.6% [n = 395; CI95 23.2, 32.3]). Infants born from euploid, mosaic, and whole chromosome mosaic embryos had average birth weights and lengths of gestation that were not statistically different (3,118 g and 267 days [n = 488; CI95 3,067, 3,169, and 266, 268], 3052 g and 265 days [n = 488; CI95 2,993, 3,112, and 264,267], 3,159 g and 268 days [n = 194; CI95 3,070, 3,249, and 266,270], respectively). Out of 488 infants from mosaic embryo transfers (ETs), one had overt gross abnormalities as defined by the Centers for Disease Control and Prevention. Most prenatal tests performed on pregnancies from mosaic ETs had normal results, and only three pregnancies produced prenatal test results reflecting the mosaicism detected at the embryonic stage (3 out of 250, 1.2%; CI95 0.25, 3.5).

Conclusion: Although embryos classified as mosaic experience higher rates of miscarriage than euploid embryos (with a particularly high frequency shortly after implantation), infants born of mosaic ETs are similar to infants of euploid ETs. Prenatal testing indicates

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that mosaicism resolves during most pregnancies, although this process is not perfectly efficient. In a small percentage of cases, the mosaicism persists through gestation. These findings can serve as risk-benefit considerations for mosaic ETs in the fertility clinic. (Fertil Steril® 2023;■:■–■. ©2023 by American Society for Reproductive Medicine.)

Key Words: Mosaic, embryo, PGT-A, chromosome, IVF

Embryonic mosaicism is the coexistence of cells with different chromosomal copy numbers within a single embryo. This phenomenon is the consequence of chromosome segregation errors during mitosis that take place postfertilization. In contrast to meiotic errors occurring in the germline, which are destined to give rise to uniformly abnormal embryos, mosaicism can result in a mix of euploid and aneuploid cells. Although mosaicism in embryos has been documented for over 30 years (1), the question of its appropriate clinical management has only recently become relevant, thanks to ever-improving methods of preimplantation genetic testing for aneuploidy (PGT-A) with superior resolution. State-of-the-art in vitro fertilization involves isolating a multicellular biopsy of the trophectoderm layer of blastocyst-stage embryos and testing the cells in that sample collectively. Preimplantation genetic testing for aneuploidy results denoting a copy number of two for a chromosome indicates uniform disomy within the tested cells, whereas copy numbers one or three indicate uniform monosomy or trisomy, respectively. However, results from multicellular biopsies can produce intermediate copy numbers (ICNs), which can reflect the capture of euploid-aneuploid cell mixes within the biopsy. For example, copy number 2.5 suggests that half of the probed cells are disomic and half are trisomic, and the source embryo is said to be a "mosaic." Studies have evaluated the performance of various PGT-A platforms to accurately identify such ICNs (2–6).

The first report of transferred embryos with prior knowledge of their mosaic status described 16 embryos resulting in the birth of eight infants that, by routine obstetrical inspection, displayed signs of good health (7). Numerous reports from different groups have followed, generally showing that, although mosaic embryos have lower rates of implantation and are more likely to miscarry (5, 8–10), pregnancies going to term result in seemingly healthy neonates (10–13). Such observations agree with the studies showing that mosaicism is often limited to the trophectoderm and not throughout the inner cell mass (14–16), as well as the model that chromosomal mosaicism can resolve itself (self-correct) during gestation through elevated selective fitness of euploid cells compared with aneuploid cells (17, 18).

The potential transfer of mosaic embryos represents new opportunities for prospective parents who, alternatively, would take measures such as undergoing additional rounds of infertility treatment, procuring donor gametes or embryos, or giving up altogether on assisted reproductive technology (ART). However, systematic large-scale analyses of chromosomal, obstetrical, and neonate outcomes from mosaic embryo transfers (ETs) have not been performed. To facilitate an appropriate risk-benefit assessment of the prospective transfer of mosaic embryos, we assembled multicenter data on prenatal chromosomal testing, pregnancy information, obstetrical metrics, and neonate health data from transfers of embryos classified as a mosaic.

MATERIALS AND METHODS

Data Collection

The analyses presented here were approved by the Institutional Review Board of the Zouves Foundation (OHRP IRB00011505, Protocol #0002). A subset of euploid and mosaic ET outcome data analyzed in this study has been previously published by the International Registry of Mosaic Embryo Transfers (10), a consortium of centers contributing embryology data, PGT-A results, and clinical outcome information to a central database. Additional unpublished clinical outcome data, as well as chromosomal testing and neonate information from 2017 to 2023, was assembled from the following participating centers:

- Zouves Fertility Center, Foster City, California, USA
- Villa Mafalda, Center For Reproductive Medicine, Rome, Italy
- New York University Langone Fertility Center, New York, New York, USA
- CReATe Fertility Centre, Toronto, Canada
- Lee Women's Hospital, Taichung, Taiwan
- Centre for Reproductive Medicine, Co.Ltd. "Next Generation Clinic," Moscow and St. Petersburg, Russia
- IRCCS San Raffaele Scientific Institute, Milan, Italy
- Eurofins Genoma Group, Molecular Genetics Laboratories, Rome, Italy
- Istanbul Memorial Hospital, Istanbul, Turkey

Neonate metrics and health information about pregnancies and deliveries were obtained by written communication from the patient, attending obstetrician, and/or pediatrician. Detailed information on two cases of mosaicism persisting through gestation included in this analysis has been published elsewhere (19).

Patient Counseling

The attending clinician and/or genetic counselor provided comprehensive guidance to all patients contemplating the transfer of mosaic embryos. The discussion included the potential risks associated with pregnancy and birth, the option of undergoing prenatal testing, and the possibility of performing postnatal chromosomal testing upon birth. The advantages and disadvantages of procedures such as chorionic villus sampling (CVS), noninvasive prenatal testing (NIPT), and amniocentesis were thoroughly addressed.

Preimplantation Genetic Testing for Aneuploidy

Embryos in the study underwent PGT-A using the Veriseq Next Generation Sequencing (NGS) platform (Illumina/Vitrolife), sequencing either on a MiSeq or NextSeq instrument. All participating centers used the same criteria to define a mosaic result. An embryo with a result containing ICN values for one or more whole chromosomes or subchromosomal (segmental) regions was classified as "mosaic," unless that sample contained additional uniform aneuploidies in other chromosomal regions, in which case the embryo was deemed "aneuploid." The ICN range was defined as the interval between chromosomal copy numbers 1.2 and 1.8 for a mosaic loss, and 2.2 and 2.8 for a mosaic gain (also known as the 20%–80% threshold).

Case Matching Criteria

To appropriately compare the birth metrics of infants born from mosaic and euploid ETs, each mosaic embryo with a birth outcome was matched to a euploid embryo with a birth outcome considering the following criteria: sex of the embryo, maternal age at oocyte retrieval, morphology graded using the Gardner and Schoolcraft system (20), single or double pregnancy (because of embryo splitting or double embryo transfer), and indication for PGT-A (advanced maternal age, repeat implantation failure, repeat miscarriage, or male factor). In cases of twin pregnancies after a double embryo transfer, the two embryos and resulting infants were distinguishable because of their opposite sexes (male and female). Cases of double ET with equal-sex embryos or cases of vanishing twin syndrome were not included in the study. For matching purposes, each twin pregnancy from mosaic ETs was matched to a twin pregnancy from euploid ETs. Out of 488 infants included in the study resulting from mosaic embryos, 68 were from twin pregnancies, whereas 420 were from single pregnancies. By our matching method, each infant born from a twin pregnancy was matched with an infant born from a euploid ET, resulting in a twin pregnancy.

Statistics and Data Preparation

Statistical analyses were performed in Prism (GraphPad). Graphs were assembled in Illustrator (Adobe). Comparisons between groups with categorical outcome variables were performed according to sample size with a two-tailed chi-square test with Yate's correction or a two-tailed Fisher's exact test. Comparisons with quantitative outcome variables were performed with an unpaired, two-tailed *t*-test. For categorical or numerical values, 95% confidence intervals (CI95) of proportion or mean were determined, respectively. For all analyses: *, $P<.05$; **, $P<.01$; ***, $P<.001$; ****, $P<.0001$; ns (not significant), $P\geq.05$.

RESULTS

Rates of Spontaneous Abortions

At the time of manuscript preparation, the International Registry of Mosaic Embryo Transfers included the transfer of 2,031 embryos designated as "mosaic" using PGT-A. Out of these, 914 (accounting for 45.0%; CI95 42.8, 47.2) were successfully implanted (Fig. 1 for a study flow chart). The criterion for "implantation" was the observation of the gestational sac using ultrasound. Out of the 914 mosaic embryos that implanted, a total of 203 pregnancies were not carried to term (representing 22.2%; CI95 19.6, 25.0) (Fig. 2A). Among them, 195 resulted in miscarriages, whereas 8 were terminated because of various clinical considerations. In contrast, for a control group composed of transferred embryos classified as euploid (n = 14,673), 8,672 embryos resulted in implantation (59.1%; CI95 58.3, 59.9), of which 771 (representing 8.9%; CI95 8.3, 9.5) spontaneously aborted (Fig. 2A).

Differences between mosaic and euploid groups were more pronounced when only considering mosaic embryos in which the chromosomal aberration affected whole chromosomes (excluding segmental losses or gains). Out of a total of 1,013 transfers within this group, 395 (39.0%; CI95 36.0, 42.1) resulted in successful implantations (Fig. 2A). Out of these successful implantations, 109 (27.6%; CI95 23.2, 32.3) did not progress to full term. A total of 79 (71.4%; CI95 63.1, 80.6) of the losses occurred very early in the pregnancy, as evidenced by the failure to observe fetal heartbeat, whereas the remaining 30 (27.6%; CI95 19.4, 36.9) occurred between positive detection of fetal heartbeat and week 20 of gestation (Fig. 2A).

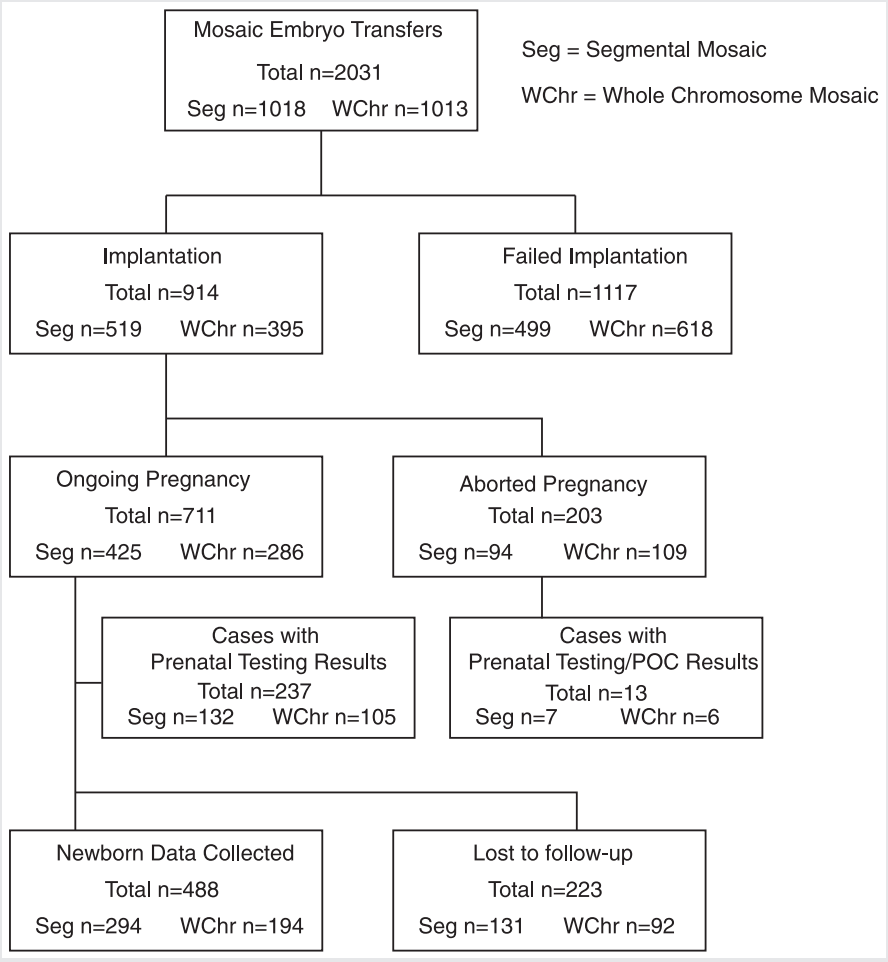
Newborn Weight, Length of Gestation, and Birth Defects

We obtained birth data from a total of 488 infants born through mosaic ETs, along with 488 infants born through case-matched euploid ETs (Supplemental Table 1, available online) (see Materials and Methods for Matching Criteria). When assessing birth weight or length of gestation, there was no statistical difference between groups (Fig. 2B). This similarity remained consistent even when considering only mosaic embryos with whole chromosome aneuploidies (Fig. 2B). Absolute instances of low birth weight and very low birth weight, as well as preterm and very preterm births, were similar for the different groups (summarized in Supplemental Table 2, available online). Of the 488 neonates born from mosaic embryos, one was reported to have a major congenital anomaly at birth (as defined by the Centers for Disease Control and Prevention), accounting for 0.2% (CI95 0.01, 11.4). That case had a heart defect involving aortic dysplasia. We were able to collect the results of eight postnatal chromosomal tests performed on blood samples of neonates (three conventional karyotype analyses and five microarrays), all of which were normal.

Chromosomal Analysis of Pregnancies from Mosaic ETs

To gauge whether the embryonic mosaicism detected with PGT-A persisted through the pregnancy, we collected prenatal testing data from 250 pregnancies. Some patients underwent more than one test type, resulting in a total of 365 test results, which included NIPT, CVS, and amniocentesis (Fig. 3). We also collected data from eight products of conception (POC)

FIGURE 1



Study flow chart. POC = products of conception; Seg = segmental mosaic; WChr = whole chromosome mosaic.

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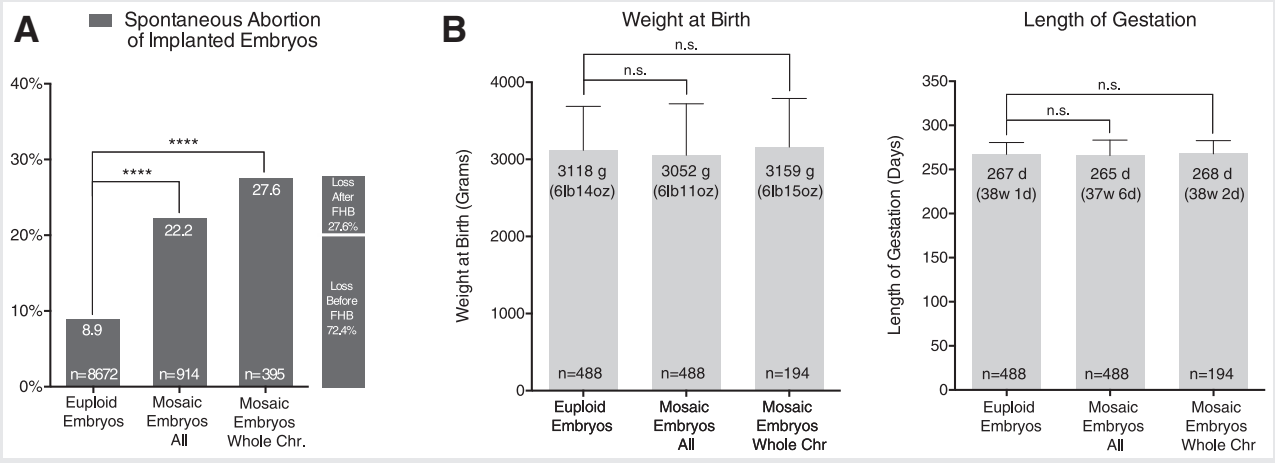
analyses of miscarried or terminated pregnancies. Collectively, 347 out of 365 (95.1%; CI95 92.3, 97.1) test results were normal, and 236 out of 250 (94.4%; CI95 90.8, 96.9) pregnancies had normal prenatal testing results. The remaining 14 pregnancies with abnormal prenatal test results (accounting for 5.6%, CI95 3.1, 9.2) are subdivided into three categories (summarized in Table 1):

- A total of nine cases with uniform abnormalities. Eight cases resulted in infants with no abnormalities, with prenatal tests detecting small losses and gains under the 10 Mb resolution of PGT-A and/or located in a chromosome other than the originally detected mosaicism. Such abnormalities are presumably unrelated to the mosaicism detected at PGT-A, are clinically benign or of unknown clinical significance, and are likely to be found at similar rates in pregnancies from euploid ETs. One case spontaneously aborted, and the POC test indicated tetraploidy, which is therefore unrelated to the original mosaicism detected with PGT-A.
- Two cases had mosaic results in the prenatal or POC test with a different mosaicism than the original one detected with PGT-A. Such cases suggest a separate mitotic error occurred during gestation, giving rise to a new chromosomal mosaic conformation (unrelated to the original one detected with PGT-A).
- Three cases had mosaic results in the prenatal or POC test, with the same mosaicism as the original one detected using PGT-A. In the first case, a low-level complex mosaic embryo that involved several chromosomes (including mosaic trisomy 21) produced CVS results (using karyotype and array) and amniocentesis results (using karyotype and fluorescence in situ hybridization [FISH]) detecting mosaic trisomy 21. The patient opted to terminate after a week 19 ultrasound showed severe anomalies in the fetus and placenta. The second case was the transfer of an embryo with a low-level mosaic segmental deletion in the p arm of Chromosome (Chr) 1 (1p36.33-p31.1), which was detected with PGT-A and again in amniocentesis using FISH. The patient decided to terminate the pregnancy after

FIGURE 2



Rates of spontaneous abortions and birth metrics after euploid or mosaic embryo transfers. (A) Embryos classified as mosaic are significantly more likely to miscarry than euploid embryos. (B) Birth weight and length of gestation are similar between the groups. Error bars represent standard deviation, and numbers in brackets indicate the CI95. CI95 = 95% confidence interval; FHB = fetal heartbeat; n.s. = nonsignificant; Whole Chr = Whole chromosome.

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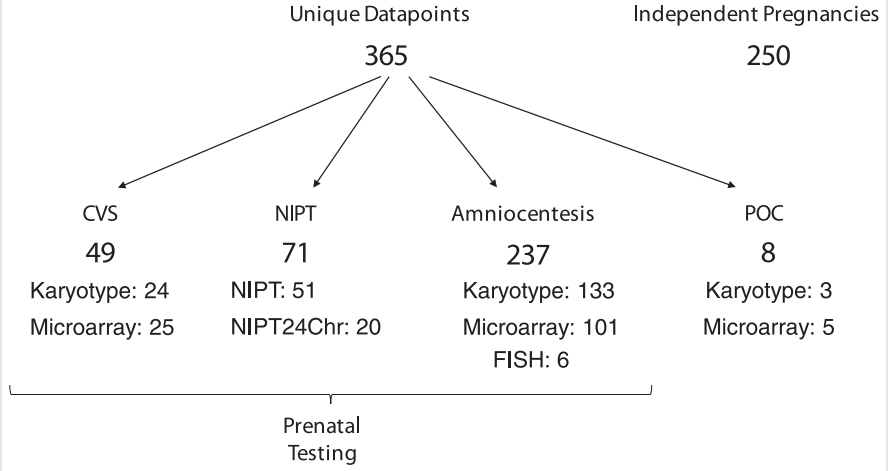
counseling and considering that the specific deletion is associated with severe intellectual disability and other health problems. Analysis of the donated POC using FISH revealed the presence of the segmental deletion in a subset of brain cells. The third case was the transfer of an embryo with two low-level mosaic segmental regions using PGT-A (+4q32.2q34.3, -Xq27.3-q28), of which one resolved but the other persisted during gestation. Chorionic villus sampling using a microarray confirmed the presence of mosaic gain in +4q32.2q34.3. The pregnancy went to term, resulting in an infant without any gross birth defects.

In summary, persistence of mosaicism detected with PGT-A at the blastocyst stage was confirmed during gestation in 3 out of 250 pregnancies, or 1.2% (CI95 0.25, 3.5) of cases.

DISCUSSION

Multicenter analysis of pregnancies and newborns resulting from the transfers of embryos classified as mosaic by PGT-A indicates a higher likelihood of spontaneous abortion compared with euploid embryos but the potential to result in neonates that are on average similar to newborns of

FIGURE 3



Breakdown of prenatal tests and POC analyses performed in pregnancies from mosaic embryo transfers. CVS = chorionic villus sample; FISH = and fluorescence in situ hybridization; NIPT = noninvasive prenatal testing, typically quantifying Chr 13, 18, 21, X, and Y; NIPT24Chr = noninvasive prenatal testing quantifying all chromosomes; POC = products of conception.

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TABLE 1

Details of abnormal results of prenatal tests performed in pregnancies from mosaic embryo transfers.

PGT-A result	Abnormal prenatal and POC test	Clinical outcome
mos(-10p) [20%]	Amnio microarray (1 Mb duplication of unknown significance in a different chromosome)	Birth
mos(+13q) [31%]	Amnio microarray (duplication of unknown significance in a different chromosome below the resolution of NGS PGT-A, maternally inherited)	Birth
mos(+5p) [36%]	Amnio microarray (likely benign duplication in different chromosomes below the resolution of NGS PGT-A, maternally inherited)	Birth
mos(-5p) [37%]	Amnio microarray (likely benign unrelated deletion in a different chromosome below the resolution of NGS PGT-A, maternally inherited)	Birth
mos (-2, -8) [30%]	Amnio microarray (interstitial microdeletion Chr2q13, 84.11 Kb)	Birth
mos(-17) [30%]	Amnio microarray (translocation; 46, XY, t (1:16) (p32-p13.3)	Birth
mos(+16p) [30%]	Amnio microarray (unrelated microdeletion in XX fetus, below the resolution of NGS PGT-A)	Birth
mos(+1p) [20%–40%]	Amnio microarray (likely benign CNV, below the resolution of NGS PGT-A)	Birth
mos(+18p) [40%]	POC cytogenetic karyotype (tetraploidy 92, XXXX) approximately 8 wk into pregnancy)	Spontaneous abortion
mos(-2) [22%]	POC Microarray (mos[+2, +14,+X]), confirmed no maternal contamination	Spontaneous abortion
mos(-14q) [29%]	Amnio microarray (mosaicism and UPD of a different chromosome)	Terminated
mos (+1q, -7, -8,+9,-19, -20, +21) [40%]	CVS karyotype G-banding (mos+21, 80%), CVS array (mos+21), Amnio karyotype and FISH (mos+21, 16%)	Terminated
mos(-1p36.33p31.1) [40%]	Amnio FISH: 15% of cells with a deletion in 1p36 POC FISH: 1.5% of analyzed brain cells with a deletion in 1p36, no abnormal cells found in villous tissue, or myocardium	Terminated
mos(+4q32.2q34.3, -Xq27.3-q28) [40%]	CVS microarray (mos+4q32.2q34.3, 60%)	Birth

Note: "PGT-A result" indicates the original call produced from PGT-A at the blastocyst stage. Square brackets indicate the level of mosaicism. "Abnormal test" indicates the nature of the prenatal test performed and details of the abnormality detected. "Clinical outcome" indicates the clinical outcome of the associated pregnancy. CNV = copy-number variation; CVS = chorionic villus sample; FISH = fluorescence in situ hybridization; NGS = next-generation sequencing; PGT-A preimplantation genetic testing for aneuploidy; POC = products of conception; UPD = uniparental disomy.

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euploid ETs. From a chromosomal normalcy point of view, mosaicism detected using PGT-A at the blastocyst stage persisted in 3 out of 250 pregnancies or 1.2% of cases.

Together with previous reports showing that embryos classified as mosaic have, on average, lower implantation rates than their euploid counterparts (10, 13, 21), the findings presented here suggest that mosaicism has a pronounced clinical effect early on (higher rates of implantation failure and early miscarriage), but the impact subsides during the pregnancy, as evidenced by low retention of the mosaic chromosomal status and the birth of infants that displayed signs of good health without increased risk of gross birth defects.

Such observations are in line with the model of self-correction of mosaicism by differential proliferation, whereby aneuploid cells are gradually diluted out to the point of clinical irrelevance (17, 18, 22). Across species, euploid cells have higher competitive fitness than aneuploid cells (23). The notable exception is cancer, where malignant cells are often aneuploid and divide rapidly. This, however, is because of mutations in oncogenes, tumor suppressor genes, and other cell checkpoint-evading mutations, not the aneuploidy itself (24). In embryos, higher compensatory rates of cell division in euploid cells coupled with increased apoptosis in aneuploid cells can result in clonal depletion of the latter (17, 18). Various lines of experimental evidence support this model: profiling of aneuploid cells in human embryos reveals distinct programs of antiproliferation, proteotoxic stress, autophagy, and p53-mediated apoptosis (25–27); human embryos in extended culture to day 12 indicate frequent conversion from a mosaic state into a uniformly euploid state (28); immunofluorescent imaging in human embryos shows elevated levels of apoptotic and compensatory mitotic markers in mosaic embryos compared with euploid embryos (5); and mouse chimera mixes of euploid and aneuploid cells show a selective loss of the aneuploid cell compartment (29, 30).

It must also be considered that, because PGT-A relies on assessing a trophectoderm biopsy, a mosaic result indicates the presence of aneuploid cells specifically in that tissue lineage and not necessarily the inner cell mass. Therefore, any persisting aneuploid cells would more likely be found in the placenta than in the fetus proper. However, placentopathies were not overrepresented in our mosaic embryo transfer group compared with the euploid group, and in our amassed dataset of 49 CVS procedures and 20 NIPTs assessing all 24 chromosomes (both tests assess placenta-derived DNA), the mosaicism observed at the blastocyst stage was confirmed only in two (2.5%) instances. This is in line with the rate of confined placental mosaicism, or the presence of aneuploid cell clones in the placenta, reported to be approximately 1%–2% in pregnancies from natural conceptions and ART (31–34).

Indeed, although evidently providing a strong selection against aneuploidy, the self-correction process does not appear to be 100% efficient. A previous report described the transfer of an embryo with a detected Chr 2 mosaic monosomy, which at amniocentesis showed a reciprocal Chr 2 mosaic trisomy, and again at birth indicated the presence of Chr 2 mosaic trisomy in a blood sample (35). The pattern of mosaicism indicates a mitotic nondisjunction event where one daughter cell inherited an extra copy of Chr 2 and the other daughter cell lacked one copy of it. In that case report, both mother and infant were healthy at birth with no pathological findings.

In our dataset, complete clonal depletion of aneuploidy failed in at least three cases for which prenatal testing reflected the same mosaicism that was detected at the blastocyst stage with PGT-A. One case involved a mosaic trisomy of Chr 21, which in newborns is responsible for an estimated 2%–4% of Down syndrome cases (36). An ultrasound at week 19 of the pregnancy revealed severe structural abnormalities in the placenta and fetus, prompting the couple to terminate the pregnancy. The second case comprised a mosaic loss in the p36 segment of Chr 1, which is the most common terminal microdeletion in humans (37). The 1p36 microdeletion syndrome comprises multiple anomalies (including severe intellectual disability and organ defects). After elective termination, POC analysis showed the mosaic presence of the segmental loss in brain cells. During the preparation of this manuscript, the two cases above were published as case reports (19). The third case was an embryo with two mosaic segmental abnormalities, of which one (mosaic gain in the q arm of Chr 4) persisted and was identified as a mosaic gain using microarray CVS. The pregnancy went to term, resulting in an infant without apparent gross abnormalities. Follow-up of this case is ongoing.

We also noted two instances where a mosaic ET resulted on a prenatal test, indicating mosaicism on a different chromosome. Because the mosaicism at the blastocyst stage and during gestation did not match, they were likely unrelated. Probably, the original embryonic mosaicism resolved itself (self-correction), although a later mitotic error established the mosaicism observed with the prenatal test. Such occurrences are to be expected, considering that 0.25%–0.4% of all amniocenteses indicate mosaicism (38–42). An alternative explanation is that, because of sampling bias, the mosaicism captured and detected in one test was missed in the other, and vice versa (an important limitation of mosaicism testing).

Besides sampling bias, a further caveat to mosaicism analysis is the variable performance of prenatal testing platforms in detecting mosaicism. For example, routine NIPT does not test for all chromosomes, meaning that there might be hidden instances of mosaicism persistence that are not identified because the NIPT test only evaluated chromosomes 13,18, 21, X, and Y and not the chromosome that was mosaic with PGT-A. In addition, although ICN results are consistent with chromosomal mosaicism, they might also represent true uniform euploid or aneuploid results with superimposed technical noise. However, if uniform aneuploidies were erroneously being classified as mosaics with PGT-A, one would expect instances of uniform aneuploidy after mosaic ETs. In our dataset of 256 prenatal tests and eight POC results, we never observed a uniform aneuploidy that matched the chromosome that was originally deemed mosaic with PGT-A. Furthermore, the findings presented here might not be applicable universally to PGT-A platforms other than the one used in the present study (see Materials and Methods), as different PGT-A methods are known to have different accuracies in detecting ICN and results consistent with mosaicism (2, 3, 43).

Among the 488 neonates from mosaic ETs, there was only one case of major congenital anomaly, presenting a heart defect. This is under the 2%–3% published incidence of major congenital anomalies in infants from ART (44), an inconsistency likely explained by the limited sample size of the group. Because some of this information was gathered by communication with patients, there is a chance the low incidence also reflects under-reporting. This, along with the subjects lost to follow-up, are caveats of this study.

Professional societies, including the Preimplantation Genetic Diagnosis International Society, the American College of Obstetricians and Gynecologists, and the American College of Medical Genetics and Genomics, recommend offering prenatal testing to all pregnant patients, including after in vitro fertilization with PGT-A (45). However, reports describe the frequent reticence of patients to undergo prenatal testing even after the transfer of an embryo classified as a mosaic (46). In our dataset, prenatal testing was able to uncover three cases of mosaicism persistence, similar to a previous case report where mosaicism endured to birth (35). Although the presence of mosaicism identified during prenatal testing does not necessarily indicate complications in pregnancy, it is important to note that adverse outcomes can occur in cases of confined placental mosaicism or true fetal mosaicism (19, 42). The rarity of such instances and ability to identify them should be factored into making evidence-based recommendations for prenatal testing for patients considering the transfer of embryos classified as mosaic (47).

CONCLUSION

In summary, the data presented here should aid in performing evidence-based risk-benefit analyses of transferring embryos designated as mosaics using PGT-A. Such embryos experience higher rates of early spontaneous abortions, and even though mosaicism can persist through gestation in rare instances, it is resolved in most cases, leading to infants that typically display signs of good health and are similar to those stemming from embryos designated as euploid.

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