REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY

Impact of monozygotic twinning on multiple births resulting from in vitro fertilization in the United States, 2006–2010

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OBJECTIVE: To determine the contribution of monozygotic twining to in vitro fertilization multiple births.

STUDY DESIGN: We performed a retrospective analysis of the incidence of monozygotic twining in multiple births resulting from fresh embryo transfers using 2006-2010 data from the Society for Reproductive Technology Clinic Outcome Reporting System.

RESULTS: The number of embryos transferred were fewer than the number of births in 0.5% (223/40950) of twin, 29% (659/2289) of triplet, and 64% (43/67) of quadruplet births resulting from transfer of fresh embryos from 2006 to 2010. In 2010, 37% of triplets and 100% of quadruplet births occurred when fewer than 3 and fewer than 4 embryos respectively were transferred.

CONCLUSION: Monozygotic twinning plays a key role in the development of triplet and quadruplet pregnancies achieved through in vitro fertilization.

Key words: IVF, monozygotic twining, quadruplet birth, singleton birth, triplet birth, twin birth

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Monozygotic twins (MZT) carry a significantly higher risk of perinatal morbidity and mortality than singleton and dizygotic twins.[1-5] They are associated with a greater risk of prematurity and increased risk of anomalies as well as complications from placental sharing such as twin-twin transfusion syndrome, selective intrauterine growth restriction, and reversed arterial perfusion sequence. These complications can progress to severe morbidity and fetal death. Complications because of placental sharing are not limited to twins and are higher in dichorionic triamniotic triplet pregnancies compared with trichorionic triplet pregnancies.[6-8]

Dichorionic/diamniotic twins occur with embryo division between fertilization and morula stage, 4 days postfertilization. Monochorionic/diamniotic twins occur with embryo division between days 4 and 8 postfertilization. Monochorionic/monoamniotic twins occur when embryo division happens between postfertilization days 8 and 12 and carry additional pregnancy risks because of shared placental mass and fetoplacental circulation. After day 13, embryo division results in conjoined twins. In natural conceptions, two-thirds of monozygotic twins are monochorionic.[9] In spontaneous pregnancies, MZT are an infrequent event with an incidence of 1 in 240 (0.41%) naturally conceived births.[10-13] Monozygotic twining has been found in 24% to 44% of spontaneous triplet pregnancies.[6-7,14] Monozygotic rates following assisted reproductive technology (ART) procedures are reported to be between 2 and 12 times higher than the natural occurrence of 0.4%.[8,10,12,15-19]

The number of quadruplet and higher births resulting from ART reached a peak of 316 in 1997 when they contributed to 54% of quadruplet and higher order births in the United States.[20] The number of triplet births resulting from ART peaked at 3498 in 1998, when they accounted for more than 50% of all triplet births in the United States.[20] In response to these high numbers, the American Society of Reproductive Medicine and the Society for Assisted Reproductive Technology (SART) in 1998 and 1999 respectively published national guidelines limiting the number of fresh embryos transferred to 2 for patients age <35 and one for patients with the best prognosis and additional embryos to cryopreserve.[22-23] Because of these recommendations, the number of triplet and quadruplet births because of ART has decreased markedly; however, the number of twins has not.[21] We hypothesize that the failure of twin rates to decrease following in vitro fertilization (IVF), and triplet and higher order multiple rates to decrease further may in part be because of increased MZT twinning rates in the IVF population.

To define the role of MZT in multiple births resulting from IVF, we conducted a retrospective analysis of the number of embryos transferred for all singleton and multiple births resulting from transfer of fresh nondonor embryos in the United States during the years

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2006-2010 using the SART Clinic Online Reporting System (CORS). To remain consistent with the majority of past studies of MZT following assisted conception,[12] we assumed MZT to have occurred when initial heart rates were greater than the number of embryos transferred.

Materials and Methods

Study population

The records from the SART CORS dataset included 141,030 live births resulting from fresh nondonor embryo transfers for the years 2006-2010 (Figure). Data from more than 90% of clinics performing ART in the United States has been collected, verified by SART and reported to the Centers for Disease Control and Prevention since 1992 in compliance with the Fertility Clinic Success Rate and Certification Act of 1992 (Public Law 102-493, 24 October 1992). Institutional review board approval for our study was obtained from SART, Louisiana State University School of Medicine, and Tulane University School of Medicine.

Determination of zygosity

Zygosity was determined by ultrasound during the first 6-7 weeks of gestation. Monozygotic twining was determined to have occurred when the maximum number of fetal heart rates exceeded the number of embryos transferred.

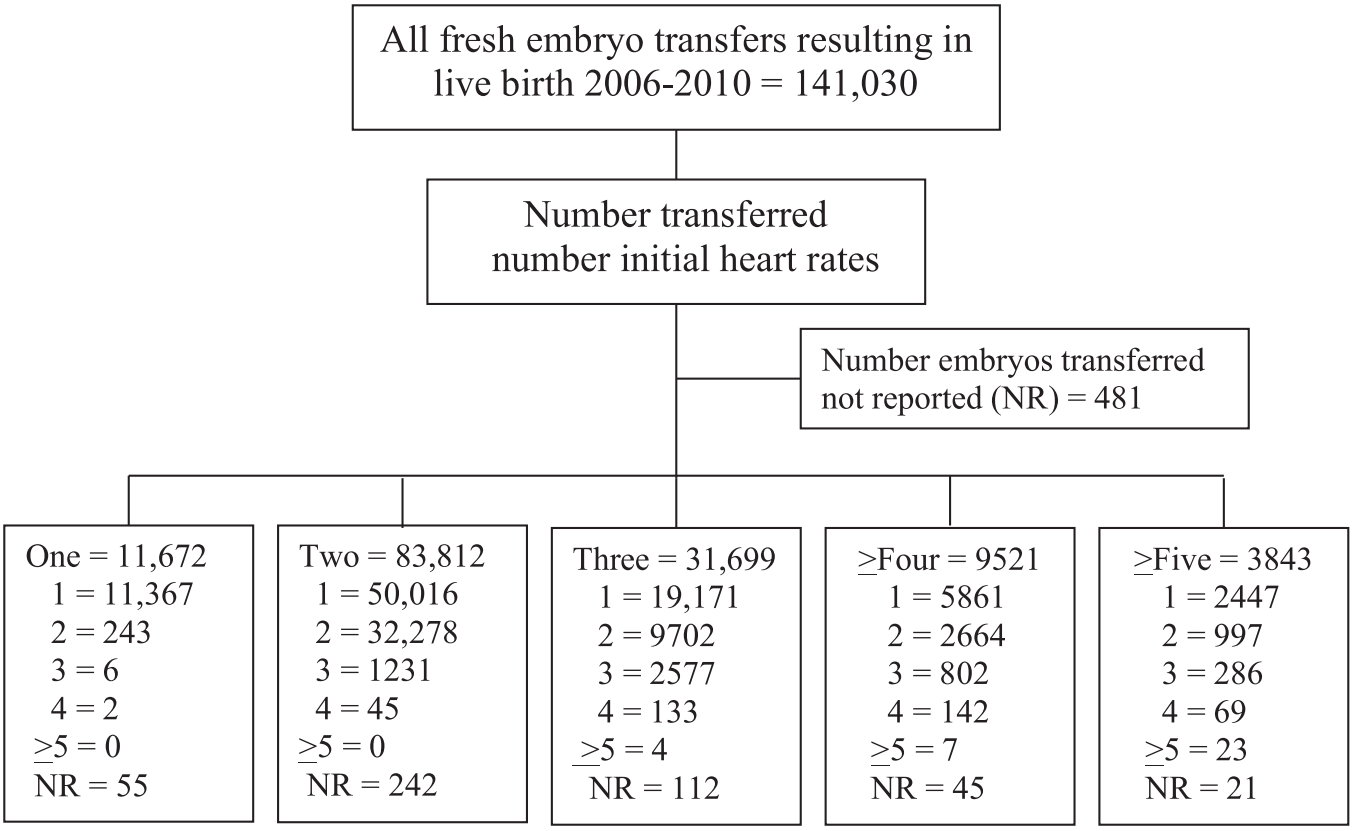
Inclusion and exclusion criteria

All records were included for which the number of embryos transferred was recorded. Records were excluded from analysis if numbers of initial heart rates or the number of infants born were. After exclusions there were 97,236 singleton, 40,950 twin, 2293 triplet births, and 68 quadruplet births, for a total of 140,547 births. This number included 4 triplet and 1 quadruplet birth reported following single embryo transfer.

Statistical analysis

χ^2 test and χ^2 test for trend were used to compare the percent of singleton and multiple births attributable to transfer of 1 to 5 or more embryos. Analysis was further stratified by year of birth. The proportion of births that were twin, triplet, and quadruplet following transfer of 1 to 5 or more embryos was calculated using WinPepi Describe version 2.51J. (available at: http://www.brixtonhealth.com/pepi4windows.html; accessed Feb. 13, 2014) with percent with 95% confidence interval. The Cochrane-Armitage test was used to determine trends. All *P* values were 2-tailed, at a significance of .05.

FIGURE
All live births resulting from IVF with fresh embryo transfer: 2006-2010



IVF, in vitro fertilization.

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