



Maternal and perinatal risks in ART-conceived monozygotic twins: a need for tailored surveillance

Casati D^{1,2}, Lanna M^{1,2}, Laoreti A^{1,2}, Faiola S^{1,2}, Di Domenico F¹, Morelli R¹, Santapaola M¹, Lista G³, Savasi V¹

¹ Department of Woman, Mother and Neonate, V. Buzzi Children's Hospital, University of Milan, Milan, Italy; ² Fetal Therapy Unit "U. Nicolini", V. Buzzi Children's Hospital, University of Milan, Milan, Italy; ³ Division of Neonatology, V. Buzzi Children's Hospital -ASST-FBF-SACCO, Milan, Italy

Introduction

Monozygotic (MZ) twin pregnancies are associated with a heightened risk of severe maternal, fetal, and neonatal complications. Assisted Reproductive Technology (ART) has been associated with a higher and poorly controlled incidence of MZ twin pregnancies, yet the impact of ART on maternal and perinatal outcomes in this subgroup remains unclear.

Objectives

To investigate whether conception via ART is associated with increased maternal, fetal, and neonatal complications in MZ twin pregnancies, and to identify areas for improved clinical management and research.

Results

A retrospective cohort study was conducted on MZ twin pregnancies referred to a tertiary fetal medicine center from 2020 to 2023. A total of 100 ART-conceived MZ pregnancies (77 by homologous ART and 23 by egg donation) were compared to 343 spontaneously conceived MZ pregnancies. Maternal outcomes, fetal complications, and neonatal outcomes were analyzed. Logistic regression models were used to calculate Odds Ratios (OR) adjusted for maternal factors. Generalized Estimating Equations (GEE) were used to account for within-twin pair correlation. Women with ART-conceived MZ pregnancies were older, more frequently nulliparous, and predominantly Caucasian ($p < 0.01$). ART-conceived MZ pregnancies were associated with a significantly higher risk of pregnancy complications (aOR 3.14, 95% CI 1.76-5.60), particularly hypertensive disorders of pregnancy (aOR 3.43, 95% CI 1.23-9.53) and postpartum hemorrhage ($p < 0.05$). No significant differences concerning gestational age at delivery, birthweight, birthweight discordance and mode of delivery were found among groups. Intrauterine fetal demise was more frequent in ART pregnancies (aOR 2.09, 95% CI 1.09-4.05, $p = 0.02$), though significance was lost after adjusting for twin correlation (OR 1.77, 95% CI 0.89-3.55, $p = 0.10$). ART-conceived twins had lower rates of twin-to-twin transfusion syndrome but a significantly poorer survival after laser treatment ($p < 0.01$). Postnatal morbidity was higher in ART-conceived MZ twins (aOR 1.55, 95% CI 0.91-2.63). No differences in maternal or perinatal outcomes were observed between fresh and frozen embryo transfer cycles.

Conclusions

In the largest reported cohort of ART-conceived MZ twin pregnancies, we identified a significantly elevated risk of maternal, fetal, and neonatal complications. These findings raise important concerns given the global rise in ART usage. Further research is urgently needed to elucidate the underlying mechanisms—including ART-related biological factors, abnormal placental development, impaired fetoneonatal adaptation, and altered maternal cardiovascular regulation—in order to better prevent MZ twinning and reduce associated risks. Tailored surveillance protocols and centralized management in specialized referral centers with expertise in ART, fetal therapy, and neonatal intensive care should be considered essential to improve outcomes in this high-risk population.

Recommended reading

- American College of Obstetricians and Gynecologists' Committee on Obstetric Practice; Committee on Genetics; U.S. Food and Drug Administration. Committee Opinion No. 671: Perinatal Risks Associated with Assisted Reproductive Technology. *Obstet Gynecol.* 2016;128(3):e61-8.
- Aston KI, Peterson CM, Carrell DT. Monozygotic twinning associated with assisted reproductive technologies: a review. *Reproduction.* 2008;136(4):377-86.
- Lanna MM, Consonni D, Faiola S, et al. Incidence of cerebral injury in monozygotic twin survivors after spontaneous single demise: long-term outcome of a large cohort. *Diagn Ther.* 2020;47(1):66-73.
- Lewi L, Deprest J, Hecher K. The vascular anastomoses in monozygotic twin pregnancies and their clinical consequences. *Am J Obstet Gynecol.* 2013;208(1):19-30.
- Marleen S, Kodithuwakku W, Nandasena R, et al. Maternal and perinatal outcomes in twin pregnancies following assisted reproduction: a systematic review and meta-analysis involving 802 462 pregnancies. *Hum Reprod Update.* 2024;30(3):309-322.
- Parazzini F, Cipriani S, Bianchi S, et al. Risk of monozygotic twins after assisted reproduction: a population-based approach. *Twin Res Hum Genet.* 2016;19(1):72-6.
- Vitthala S, Gelbaya TA, Brison DR, et al. The risk of monozygotic twins after assisted reproductive technology: a systematic review and meta-analysis. *Hum Reprod Update.* 2009;15(1):45-55.