P-776 Singleton pregnancies conceived with infertility treatments and the risk of neonatal and infant mortality

G. Farley[1], M. Sauer[2], J. Brandt[2], C. Ananth[2]

[1]Rutgers Robert Wood Johnson Medical School, MD Candidate, New Brunswick, U.S.A. ;
[2]Rutgers Robert Wood Johnson Medical School, Department of Obstetrics Gynecology and Reproductive Sciences, New Brunswick, U.S.A.

Study question: Is maternal infertility treatment associated with an increased risk of neonatal and infant mortality when compared to natural conception?
Summary answer: Infertility treatment is associated with a 70% increased adjusted risk of neonatal mortality. This association is strongly mediated by preterm delivery.
What is known already: The number of assisted reproduction technology (ART) cycles performed in the United States (US) increased by 39% from 142,435 cycles in 2007 to 197,737 in 2016. Within this growing experience, several studies described an increased risk of preterm delivery, low birth weight, congenital malformations, neonatal intensive care unit admission, stillbirth, and perinatal mortality among singletons conceived through ART compared to those conceived naturally. Experts have called for ART patients to be advised of potential increased risk for adverse perinatal outcomes and for obstetricians to manage these pregnancies as high risk.
Study design, size, duration: This is a cross-sectional study of 11,289,466 pregnancies in the United States (US) from 2015-2017 that resulted in a non-malformed singleton live birth. The exposure group includes births resulting from any infertility treatment method, including ART and fertility-enhancing drugs. The control group includes births resulting from natural conceptions. The primary outcomes measured were neonatal (within 1 month), post-neonatal (1 month to a year), and infant (up to 1 year) mortality.
Participants/materials, setting, methods: Pregnancies (n=11,289,466) resulting in a non-malformed singleton live birth in the US from 2015-2017. Associations were estimated from log-linear Poisson regression models with robust variance. Risk ratio (RR) and 95% confidence interval (CI) were derived as the effect measure with adjustments for confounders. The impact of exposure misclassification and unmeasured confounding biases were assessed. A causal mediation analysis of the infertility treatment-mortality association with preterm delivery (<37 weeks) was performed.

Main results and the role of chance: Any infertility treatment was documented in 1.3% (n=142,215) of singleton live births during the study period. Any infertility treatment was associated with a 70% increased adjusted risk of neonatal mortality (RR 1.70, 95% CI 1.54-1.88), with an even higher risk for early neonatal (RR 1.82, 95% CI 1.63-2.05) than late neonatal (RR 1.37, 95% CI 1.11-1.69) mortality. These risks were similar among pregnancies conceived through ART and treatment with fertility-enhancing drugs. The mediation analysis showed that 68% (95% CI 59-81) of the total effect of infertility treatment on neonatal mortality was mediated through preterm delivery. In a sensitivity analysis, following corrections for exposure misclassification and unmeasured confounding biases, these risks were higher for early neonatal (bias-corrected RR [RRbc] 2.94 95% CIbc 2.16-4.01), but not for late neonatal (RRbc 1.04, 95% CIbc 0.68-1.59) mortality.
Limitations, reasons for caution: Limitations of the study include the potential underreporting of infertility treatment on birth certificates and potential confounding from sociodemographic characteristics that were not accounted for in this study.
Wider implications of the findings: Pregnancies conceived with infertility treatment are associated with increased neonatal mortality and this association is mediated by the increased risk of preterm delivery. Knowledge of this risk should be shared with prospective couples consulting for fertility care in order to best provide adequate informed consent.
Trial registration number: not applicable