

Obstetric Outcomes in Singleton Pregnancies Conceived with Assisted Reproductive Technology: A Population-Based Retrospective Study

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ABSTRACT

Aims: To evaluate obstetric outcomes among singleton pregnancies conceived with assisted reproductive technology (ART) compared with non-ART singleton pregnancies using a national population-based dataset, and to determine whether ART-associated obstetric risk is uniform or selective across outcome domains.

Methods: A retrospective population-based cohort study was conducted using the United States Centers for Disease Control and Prevention Wide-Ranging Online Data for Epidemiologic Research (CDC WONDER) Natality database, including all singleton live births from 2016 to 2019. Outcomes assessed included cesarean delivery, preterm birth (<37 weeks), hypertensive disorders of pregnancy, and gestational diabetes mellitus. Comparisons between ART and non-ART pregnancies were performed using chi-square testing. A P value <0.05 was considered statistically significant.

Results: ART-conceived singleton pregnancies demonstrated higher cesarean delivery rates compared with non-ART pregnancies (48.0% vs. 38.5%; absolute difference 9.5%; $p < 0.001$). Preterm birth was modestly more frequent among ART pregnancies (11.7% vs. 10.5%; $p < 0.001$). Rates of hypertensive disorders of pregnancy and gestational diabetes mellitus were similar between groups ($p > 0.05$). Findings were consistent across all study years.

Conclusion: ART singleton pregnancies are associated with higher cesarean delivery rates and modestly increased preterm birth, while other obstetric outcomes remain comparable to non-ART pregnancies. These findings suggest a selective, rather than uniform, obstetric risk profile in contemporary ART pregnancies.

Keywords: Assisted reproductive technology; In vitro fertilization; Obstetric outcomes; Preterm birth; Singleton pregnancy

INTRODUCTION

Assisted reproductive technology (ART) has become an integral component of reproductive medicine, with utilization increasing steadily over the past two decades. In the United States alone, ART cycles now account for more than 2% of all live births annually, and rates are increasing globally across both high-income and middle-income countries [1,2]. As access to ART improves and success rates rise, an increasing number of clinicians are managing ART-conceived pregnancies in routine obstetric practice, making a thorough understanding of their associated risks clinically essential.

A major development in contemporary ART practice has been the widespread adoption of elective single embryo transfer (eSET). Driven by evidence demonstrating that multiple gestation carries substantially higher maternal and neonatal risk, professional societies including the American Society for Reproductive Medicine have advocated for eSET in appropriate candidates [3]. As a result, the proportion of ART births that are singletons has grown considerably, and clinical focus has shifted from managing the well-recognized risks of ART-associated multiple gestation to understanding the more nuanced risk profile of ART-conceived singleton pregnancies [1,3].

Prior studies have reported increased rates of cesarean delivery and preterm birth in ART singleton pregnancies compared with spontaneously conceived pregnancies [4,5]. However, many of these analyses predate the widespread adoption of eSET, include heterogeneous ART populations, or are limited by small sample sizes and single-centre designs. Furthermore, the extent to which other obstetric complications such as hypertensive disorders of pregnancy and gestational diabetes mellitus are meaningfully increased in ART singletons remains less clearly established. A contemporary, large-scale population-based assessment is therefore warranted.

We aimed to evaluate obstetric outcomes among singleton pregnancies conceived with ART compared with non-ART pregnancies using a national population-based dataset. We hypothesized that ART singleton pregnancies would demonstrate selective, rather than uniform, differences in obstetric outcomes compared with non-ART pregnancies.

MATERIALS AND METHODS

This was a retrospective population-based cohort study.

Data were obtained from the Centers for Disease Control and Prevention (CDC) Wide-Ranging Online Data for Epidemiologic Research (WONDER) Natality database, a publicly available repository that captures data from all registered live births in the United States, derived from birth certificate records. The database includes information on maternal demographics, obstetric history, pregnancy complications, delivery mode, and neonatal outcomes.

All singleton live births recorded from January 1, 2016 through December 31, 2019 were included. Multiple gestations were excluded. ART use was identified via a dedicated field on the U.S. standard birth certificate indicating whether the pregnancy was conceived using assisted reproductive technology. Pregnancies with unknown or missing ART status were excluded from analysis.

Outcomes assessed included: (1) cesarean delivery; (2) preterm birth, defined as delivery before 37 weeks of gestation; (3) hypertensive disorders of pregnancy; and (4) gestational diabetes mellitus.

Comparisons between ART and non-ART pregnancies were performed using chi-square testing. Given the large sample size inherent to population-based analyses, statistical significance was interpreted in conjunction with absolute risk differences and clinical relevance. A P value <0.05 was considered statistically significant.

This analysis was considered non-regulated by the UT Health San Antonio Institutional Review Board since it collected de-identified data published by the CDC through its publicly available WONDER Natality database. No private identifiable information was accessed, and no interaction or intervention with human subjects occurred.

RESULTS

A total of 14,179,423 singleton live births were included in the analysis. Of these, 127,933 (0.90%) were ART-conceived pregnancies and 14,051,490 (99.10%) were non-ART pregnancies. ART singleton pregnancies represented a small but increasing proportion of U.S. singleton live births during the study period.

Cesarean delivery rates were consistently higher among ART pregnancies (48.0%) compared with non-ART pregnancies (38.5%) across all four study years, representing an absolute difference of 9.5 percentage points (RR 1.25; $p < 0.001$). Preterm birth also occurred more frequently among ART pregnancies, though the absolute difference was more modest at 1.2 percentage points (RR 1.11; $p < 0.001$). As with cesarean delivery, this difference was consistent across study years.

In contrast, rates of hypertensive disorders of pregnancy (RR 1.01; $p = 0.12$) and gestational diabetes mellitus (RR 1.02; $p = 0.18$) were similar between groups, with no statistically significant or clinically meaningful differences observed. Obstetric outcomes are presented in [Table 1](#), and relative risks for all outcomes with confidence intervals are displayed in [Figure 1](#).

Table 1: Obstetric outcomes in ART versus non-ART singleton live births.

Outcome	ART (%)	Non-ART (%)	RR	95% CI	p-value
Cesarean delivery	48	38.5	1.3	1.24–1.25	<0.001
Preterm birth (<37 weeks)	11.7	10.5	1.1	1.10–1.13	<0.001
Hypertensive disorders of pregnancy	14.8	14.6	1	1.00–1.03	0.12
Gestational diabetes mellitus	10.8	10.6	1	1.00–1.04	0.18

Outcome rates (%) and relative risks (RR) with 95% confidence intervals (CI) are presented for ART-conceived and non-ART singleton live births.

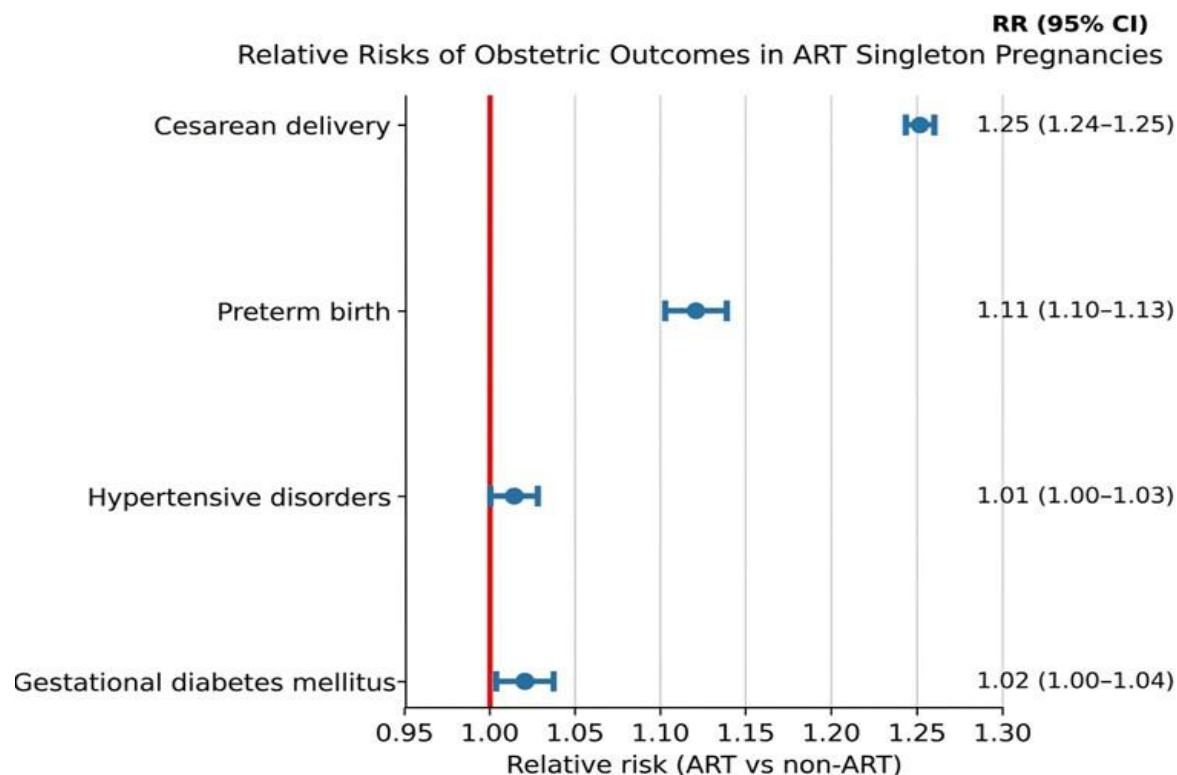


Figure 1: Relative risks of obstetric outcomes in ART versus non-ART singleton pregnancies.

Forest plot displaying relative risks (RR) with 95% confidence intervals for cesarean delivery, preterm birth, hypertensive disorders of pregnancy, and gestational diabetes mellitus in ART-conceived compared with non-ART singleton live births. The vertical line at RR = 1.0 represents no difference between groups.

DISCUSSION AND CONCLUSION

In this large population-based study of singleton live births in the United States from 2016 to 2019, ART singleton pregnancies were associated with substantially higher rates of cesarean delivery and a modest increase in preterm birth, while rates of hypertensive disorders of pregnancy and gestational diabetes mellitus were comparable to those of non-ART singleton pregnancies. Taken together, the results indicate that the obstetric risk conferred by ART in singleton pregnancies is selective rather than uniform, a distinction with meaningful implications for patient counseling and clinical management.

The elevated cesarean delivery rate observed in ART pregnancies in this study is consistent with prior systematic reviews and meta-analyses [5]. Reported higher cesarean rates in IVF/ICSI singleton pregnancies compared with spontaneous conceptions, a finding corroborated by [4] in a broader meta-analysis encompassing multiple ART modalities. Our findings support these observations that elevated cesarean rates persist in the current era of predominantly single embryo transfer.

Multiple mechanisms likely contribute to the higher cesarean delivery rate in ART pregnancies. Patients who conceive via ART are on average older than those who conceive spontaneously, and advanced maternal age is an independent risk factor for cesarean delivery [6]. Underlying infertility diagnoses, including uterine anomalies, prior uterine

surgery, and conditions such as endometriosis, may directly increase the likelihood of operative delivery. Additionally, the phenomenon of “precious pregnancy,” where both patients and clinicians perceive ART-conceived pregnancies as higher risk and of heightened value, may lower the threshold for cesarean delivery in the absence of a clear obstetric indication. [7] demonstrated that IVF/ICSI pregnancies in older nulliparous women ended in prelabor cesarean section significantly more often than spontaneously conceived pregnancies and found that one in five gynaecologists agreed with performing cesarean section on maternal request alone in ART pregnancies, indicating that both patient and provider attitudes contribute to elevated operative delivery rates.

The modestly elevated preterm birth rate in ART singleton pregnancies is also consistent with prior literature [4,5]. Several mechanisms have been proposed to account for this finding. Maternal factors, including underlying infertility diagnoses such as endometriosis and polycystic ovary syndrome, as well as procedural variables such as fresh versus frozen embryo transfer, have each been identified as independent contributors to preterm birth risk in ART singleton pregnancies [8]. Beyond maternal characteristics, biological mechanisms related to the ART process itself may play a role. Epigenetic alterations in placental tissue have been identified in IVF pregnancies and may affect placentation and trophoblast invasion, contributing to adverse perinatal outcomes including preterm birth [9].

Notably, rates of hypertensive disorders of pregnancy and gestational diabetes mellitus were not meaningfully elevated in ART singleton pregnancies in our cohort. This finding contrasts with some earlier studies but is consistent with the hypothesis that many previously reported associations between ART and adverse obstetric outcomes were driven by confounding from multiple gestation rather than ART itself [3]. By restricting our analysis to singleton pregnancies, we isolated the effect of ART independent of plurality, and found no evidence of a meaningful increase in hypertensive or metabolic complications.

These findings have direct relevance to clinical practice. As ART utilization continues to expand globally, and as eSET becomes the standard of care, obstetricians will increasingly encounter ART-conceived singleton pregnancies in routine practice. A nuanced, outcome-specific understanding of associated risks is essential to avoid both under-counseling and unnecessary medicalization of what are, for many outcomes, comparably low-risk pregnancies. Our data support individualized counseling focused on cesarean delivery planning and preterm birth surveillance, without blanket classification of ART singleton pregnancies as universally high-risk.

This study has several strengths. A major strength is the inclusion of more than 14 million singleton births, including nearly 128,000 ART-conceived pregnancies, from the nationally representative CDC WONDER Natality dataset, which provides increased statistical power. Restriction to singleton pregnancies eliminates the major confounding effect of multiple gestation. The study period (2016–2019) reflects current ART practice, including widespread eSET adoption, making findings more applicable to contemporary clinical settings than earlier studies. Limitations include the retrospective design, potential misclassification within birth certificate data, and lack of detailed clinical variables such as specific infertility diagnosis, type of ART procedure, and number of embryos transferred. Future studies incorporating individual-level clinical data would allow further characterization of outcome-specific risk factors within ART singleton pregnancies.

In conclusion, singleton pregnancies conceived with assisted reproductive technology were associated with substantially higher cesarean delivery rates and a modestly elevated rate of preterm birth compared with non-ART

singleton pregnancies. In contrast, rates of hypertensive disorders of pregnancy and gestational diabetes mellitus were comparable between groups. These findings support a selective, rather than uniform, obstetric risk profile in contemporary ART singleton pregnancies, and underscore the importance of individualized, outcome-specific counseling. As ART utilization continues to grow globally, clinicians should avoid broad risk generalization and instead focus counseling and surveillance on those outcomes for which meaningful differences have been demonstrated.

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Author Contributions: DLT contributed to study conception and design, data analysis and interpretation, and primary manuscript drafting. TC contributed to data acquisition, statistical analysis, and manuscript revisions. NJS contributed to study design, clinical interpretation, and critical revision of the manuscript for intellectual content. MP, JEM, MA, and ET contributed to operational design of the study, data verification, and manuscript revisions. All authors participated in the drafting and critical revision of the text for important intellectual content, read and gave final approval to the version to be submitted, and agree to be fully accountable for all aspects of the work.

Figure 1. Relative risks of obstetric outcomes in ART versus non-ART singleton pregnancies.

Forest plot displaying relative risks (RR) with 95% confidence intervals for cesarean delivery, preterm birth, hypertensive disorders of pregnancy, and gestational diabetes mellitus in ART-conceived compared with non-ART singleton live births. The vertical line at RR = 1.0 represents no difference between groups.

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