

Use of assisted reproductive technologies for male and female infertility and perinatal outcomes

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Objective: To compare adverse perinatal outcomes between naturally conceived and pregnancies conceived by assisted reproductive technologies (ARTs) according to underlying male, female, or unexplained infertility.

Design: Registry-based study.

Subjects: All singleton births in Norway between 2000 and 2021 recorded in the national birth registry.

Exposure: We compared ART pregnancies with underlying male (N = 9,957), female (N = 10,031), mixed (N = 3,287), or unexplained (N = 7,178) infertility with naturally conceived pregnancies (N = 1,210,709). Information on underlying causes of infertility was reported from fertility clinics.

Main Outcomes and Measures: We compared the birthweight and pregnancy length using robust linear regression, and the risk of pre-eclampsia, cesarean section, stillbirth, preterm birth, low birth weight, small-for-gestational age and transfer to neonatal unit using logistic regression, adjusting for parental age, maternal parity, cohabitation, country of birth, and year of delivery.

Results: Pregnancy length and birthweight were lower in all ART groups compared with the naturally conceived. The shorter pregnancy length was less pronounced in ART deliveries resulting from male infertility (adjusted difference -1.24 days; 95% confidence interval [CI]: -1.43 to -1.05) than in ART deliveries resulting from female infertility (adjusted difference -1.92 days; 95% CI: -2.12 to -1.73). Similarly, the lower birthweight in ART deliveries was less pronounced in those resulting from male (adjusted difference -29 grams; 95% CI: -39 to -18) than those resulting from female (adjusted difference -49 grams; 95% CI: -59 to -39) infertility. We also observed a higher risk of most adverse perinatal outcomes in all ART groups, with the magnitude being lower for ART deliveries resulting from male infertility.

Conclusion: The increased risk of adverse perinatal outcomes in pregnancies conceived by ART was less pronounced if used for male infertility than for female infertility. This suggests that the risks in ART pregnancies are a combination of underlying factors related to female infertility and ART procedures. However, whether underlying male infertility also increases the risks cannot be excluded. (Fertil Steril® 2025;124:270-80. ©2025 by American Society for Reproductive Medicine.)

El resumen está disponible en Español al final del artículo.

Key Words: Assisted reproductive technologies, perinatal outcomes, infertility

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Data Sharing Statements: Data are not publicly available due to their containing information that could compromise the privacy of research participants. Summary data can be made available from the corresponding author at a reasonable request.

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In parallel with increasing age at first birth, the use of assisted reproductive technologies (ARTs) is increasing in most countries (1). Women with pregnancies conceived by ART have an increased risk of experiencing complications, including, for example, stillbirth, pre-eclampsia, preterm birth, low birth weight, and congenital malformations (2–5). This increased risk does not appear to be explained by a higher rate of multiple births, because it is also seen among singletons, nor does it appear to be fully explained by unmeasured confounding factors, as indicated by sibling studies (6–8). Despite this existing evidence, it remains unclear whether an increased risk of certain pregnancy complications reflects an underlying role of aspects related to ART procedures or underlying conditions related to fertility problems in the couple.

Existing studies looking into the potential role of female underlying causes of infertility resulting in the use of ART (including endometriosis and polycystic ovary syndrome) and unexplained infertility had limited sample sizes and overall unclear findings (9–12). Even less is known about whether underlying male infertility contributes to the increased risk of complications in ART births. The main indication for using intracytoplasmic sperm injection (ICSI) is to treat male infertility, although it is clear that it is increasingly used also when female infertility is the main indicator (13). Most studies report either a similar or slightly lower rate of adverse perinatal outcomes in ICSI pregnancies than in vitro fertilization (IVF) pregnancies, although the interpretation of these studies is complicated by the increasing use of ICSI even in the presence of only female infertility (14, 15). Two studies previously evaluated the risk of complications in pregnancies conceived by ART due to male infertility, specifically (16, 17). This included one large study of 117,401 live births from the United Kingdom that compared the risk of preterm birth and low birth weight in ART pregnancies (16). They found no risk differences in their comparisons pregnancies to couples with male infertility or unexplained infertility. Notably, this study was not able to compare the risk in ART birth with that in naturally conceived births.

The objective of our study was to compare the risk of adverse perinatal outcomes between naturally conceived and ART pregnancies according to underlying male, female, or unexplained infertility. If we observe an increased risk of adverse perinatal outcomes of a similar magnitude in ART birth resulting from male-only and female-only infertility, this might support a greater role for the ART procedures themselves.

MATERIALS AND METHODS

Study population

We conducted a registry-based study of all singleton births in Norway after 20 completed gestational weeks between 2000 and 2021. Information was available from the Medical Birth Registry of Norway (MBRN) (18), which includes mandatory registrations of pregnancies ending after 12 completed gestational weeks. We restricted the study population to births from 2000 onward because this was

when detailed information on primary and secondary causes for use of ART from fertility clinics became available in the MBRN.

Use of ART for male and female infertility

Assisted reproductive technology was defined as use of IVF with or without ICSI. Information on primary and secondary causes for using ART is reported to the MBRN from fertility clinics. This includes female factors such as endometriosis, polycystic ovary syndrome, amenorrhea/anovulation, reduced ovarian response, premature ovarian failure, and tubal factors. Male factors registered include reduced semen-related factors and cancer/cancer treatment. There are also “other” and “unknown” categories available for the registration of the couple. We created 4 mutually exclusive exposure groups of ART pregnancies: use of ART for male infertility was defined as having used ART where semen-related factors were defined as the primary cause and no additional female contributing causes were registered; use of ART for female infertility was defined as ART where female factors were listed as the primary cause of using ART and there was no registration of a male cause; use of ART for mixed female and male causes (this also included the “other category”); and use of ART where no underlying cause could be identified. These 4 groups of ART births were compared with naturally conceived births (non-ART conceived births).

Perinatal outcomes

Perinatal outcomes include pre-eclampsia (including registrations of pre-eclampsia, eclampsia, and “Hemolysis, Elevated Liver enzymes, and Low Platelets” syndrome), delivery by cesarean section, stillbirth, gestational age at birth in days (estimated by ultrasound [95% of pregnancies] or last menstrual period), birthweight in grams, Apgar score at 5 minutes, and transfer to a neonatal intensive care unit. We defined preterm birth as birth before 37 completed gestational weeks, low birthweight as a birthweight <2,500 grams, and small-for-gestational-age (SGA) as birthweight <10th percentile by sex and gestational age. We further examined spontaneous and iatrogenic preterm birth separately, which were distinguished based on whether the onset of labor was registered as spontaneous or initiated by medical interventions. Because we had information on all births in Norway during the study period, we created the cut-offs to define SGA based on this internal reference. No external reference was used.

Covariates

We obtained information on background characteristics that could influence both the use of ART and the perinatal outcomes of interest. This included maternal age (continuous), paternal age (continuous), parity (0, 1, 2, and 3 or more), being cohabitating/married (yes vs. no), maternal country of birth (categorized according to the global burden of disease super regions (19)), the year of delivery and maternal smoking during pregnancy (no, yes, or unknown). We accounted for the calendar year of delivery due to the

increase in ART use over time, in addition to the changes in adverse perinatal outcomes over time (1, 20).

Statistical analysis

Differences in the mean gestational age at birth and birthweight were estimated using robust linear regression, whereas differences in the odds of the binary perinatal outcomes of interest were estimated using logistic regression. We used logistic regression instead of log-binomial regression models because we experienced convergence problems for some models when attempting to run log-binomial regression. We accounted for women and men who had more than one birth during the follow-up period by using robust cluster variance estimation. The main multivariable model adjusted for parental age, parity, cohabiting/married, maternal country of birth, and calendar year of birth. Maternal and paternal age at delivery were accounted for using both a linear and a squared term, whereas the other covariates were categorized as indicated. Among those with information on maternal smoking during pregnancy (~87%), we evaluated the impact of further adjusting for this covariate. We did not conduct multiple imputations of the missing information on paternal age (~1%), maternal country of birth (~2%), or smoking during pregnancy (13%) because we had limited information to inform an imputation model. We also evaluated the robustness of our findings for outliers in birthweight and gestational length by examining differences in the median between the exposure groups using quantile regression.

We further stratified the associations by parity (nulliparous vs. parous) and maternal age (<35 vs. ≥ 35 years), where the age categories were defined according to the maternal age-associated risks observed for the pregnancy outcomes evaluated (21, 22). We also evaluated variations in the perinatal outcomes according to the use of ART for male and female infertility, further grouped by the use of ICSI and cryopreservation (fresh vs. frozen embryo transfer). To examine differences in the perinatal outcomes within the ART groups according to male and female infertility, we directly compared these groups using pregnancies conceived by ART due to female infertility as the reference. Finally, we conducted a comparison within pregnancies of the same mother, within the subgroup of women who had both a non-ART and an ART delivery, using a fixed effect linear regression for the continuous outcomes and a conditional logistic regression for the binary outcomes.

All statistical analyses were conducted using Stata version 17 (StataCorp., Texas).

Ethical approval

This registry-based study was approved by the Regional Committee for Medical and Health Ethics of South/East Norway (No. 2014/404), which waived the need for consent from participants.

RESULTS

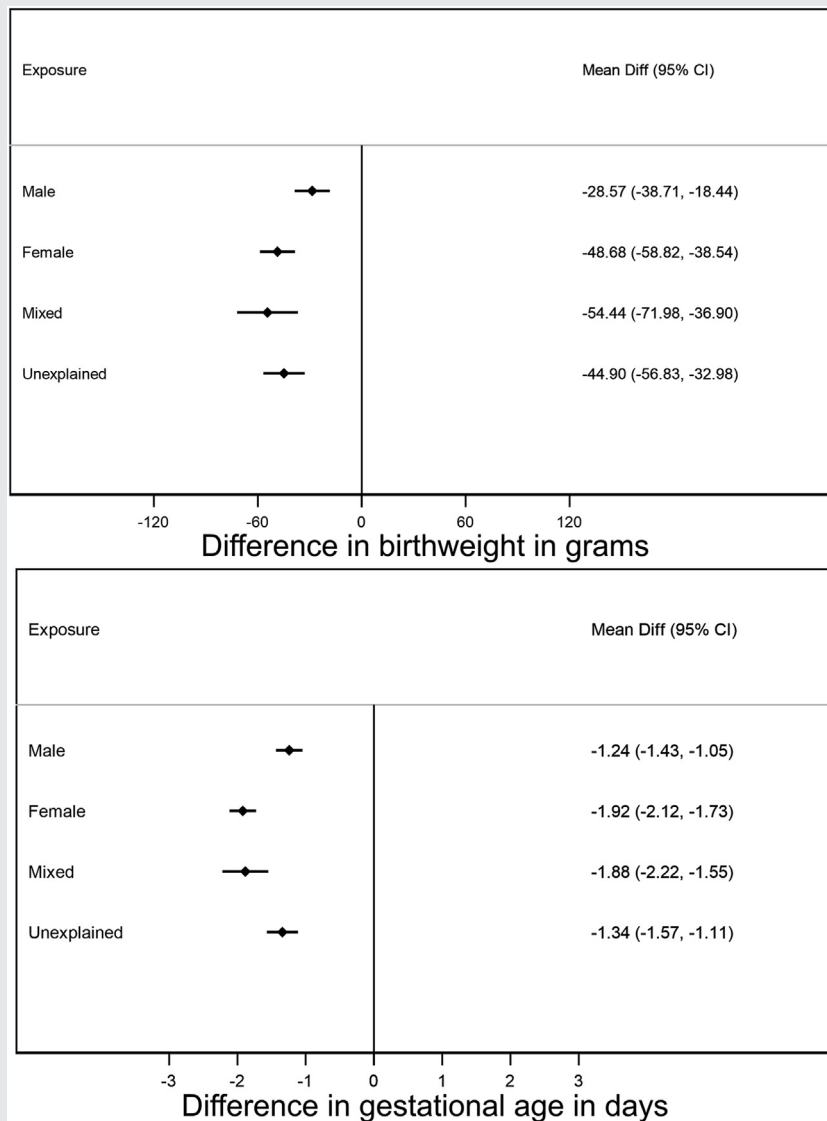
A total of 1,245,577 singleton births (34,868 ART births) after 20 completed gestational weeks were registered in the MBRN

between 2000 and 2021. After excluding ART births without information on underlying causes for infertility (n = 4,335), and ART births where male cancer/cancer treatment was listed as a main or contributing cause for using ART (n = 80), we were left with 30,453 ART births and 1,210,709 non-ART births for analysis. Of the ART births, 9,957 (32.7%) were registered with male infertility as the only cause, 10,031 (32.9%) were registered with only female infertility, 3,287 (10.8%) were due to a combination of male and female infertility, whereas 7,178 (23.6%) had unexplained infertility. Parents with ART births were older, more likely to be first-time parents, and more likely to be cohabiting/married than single (Supplement Table 1, available online).

Overall, the mean gestational age among all deliveries was 278 days (SD 14), whereas the mean birthweight was 3,534 g (SD 579) (Supplement Table 2, available online). We observed a lower gestational age and birthweight in all groups of ART deliveries compared with natural deliveries (Fig. 1). However, the decrease in gestational age was less pronounced in ART deliveries resulting from male infertility (adjusted difference -1.24 days; 95% CI: -1.43 to -1.05), than in ART deliveries resulting from female infertility (adjusted difference -1.92 days; 95% CI: -2.12 to -1.73). Similarly, compared with naturally conceived deliveries, the decrease in birthweight was less pronounced in ART deliveries due to male infertility (adjusted difference -29 grams; 95% CI: -39 to -18) than in ART deliveries due to female infertility (adjusted difference -49 g; 95% CI: -59 to -39). The differences in mean gestational age and birth weight according to use of ART for female and male infertility are emphasized by the nonoverlapping CIs. Differences in gestational age and birthweight in deliveries after the use of ART for mixed reasons were similar to ART deliveries due to female infertility. Unadjusted differences are shown in Supplement Figure 1, available online. Additional adjustments for maternal smoking during pregnancy did not change our findings (Supplement Fig. 2, available online). The observed differences in mean birthweight and gestational age resulting from the robust linear regression analyses were similar to the observed differences in the median for these 2 outcomes resulting from the quantile regression analyses (Supplement Fig. 3, available online).

The overall risk of adverse perinatal outcomes ranged from 0.4% for stillbirth to 15% for cesarean section delivery (Supplement Tables 2 and 3, available online). Compared with naturally conceived deliveries, we observed an increased risk of all adverse perinatal outcomes in the 4 groups of ART deliveries, with the exception of SGA (Fig. 2). The estimates for the risk of cesarean section delivery and preterm birth according to ART showed a notable difference according to whether it was used for male or female infertility, as indicated by the nonoverlapping CIs. Overall, we did not observe that the use of ART for a combination of both female and male infertility was associated with an additional increased risk of adverse perinatal outcomes beyond what was observed for couples who only had female infertility. Unadjusted estimates are shown in Supplement Figure 4, available online. The results did not change notably with additional adjustment for maternal smoking during pregnancy (Supplement Fig. 5, available online).

FIGURE 1



Adjusted mean differences in birthweight and gestational age between pregnancies conceived by assisted reproductive technologies and naturally conceived pregnancies according to the underlying cause for infertility. Adjusted for parental age, in addition to maternal parity, being married/cohabitating, country of birth, and year of delivery.

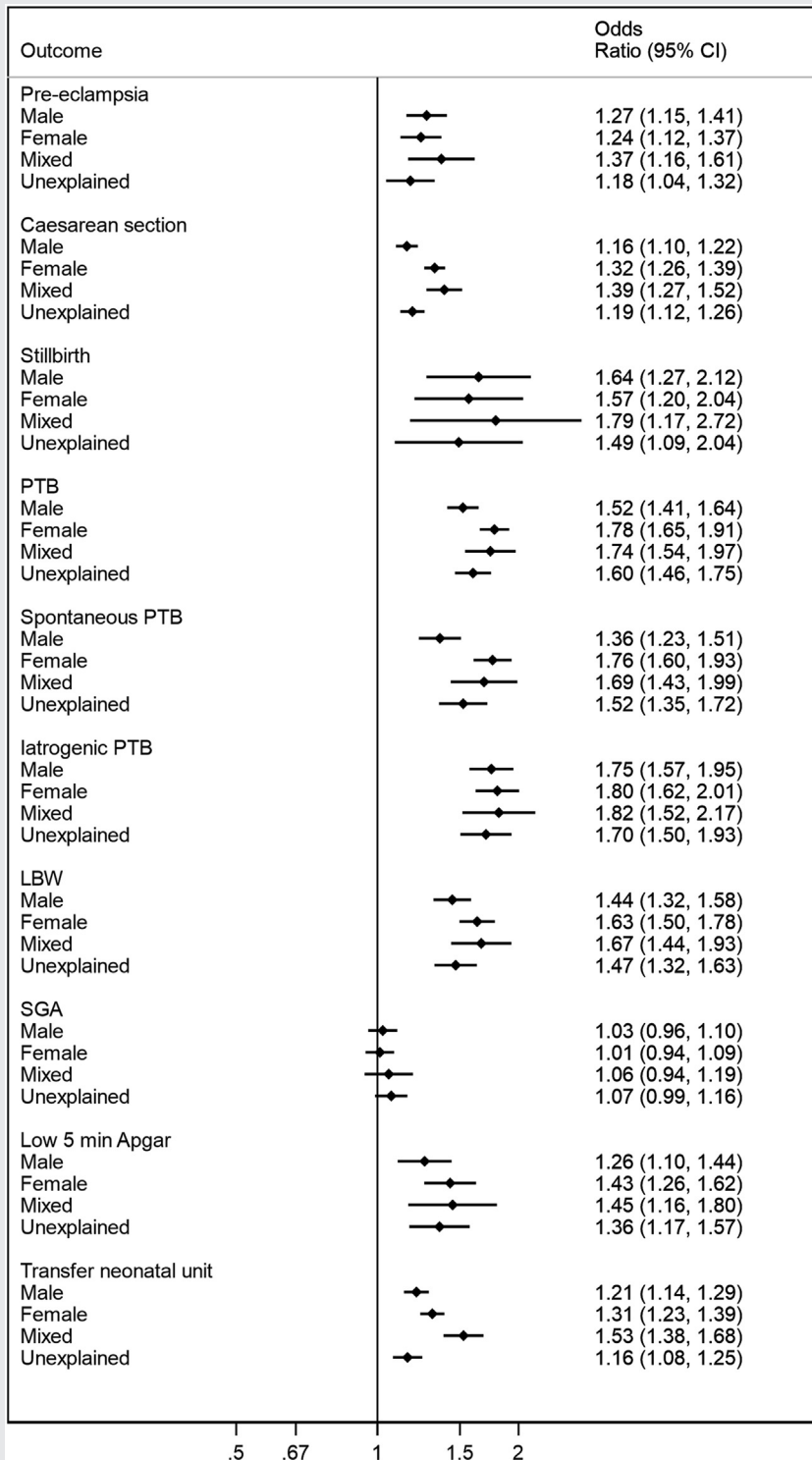
Magnus. ART indication and perinatal outcomes. *Fertil Steril* 2025.

Compared with the naturally conceived, the difference in birthweight and gestational age at birth was smaller among ICSI pregnancies than IVF pregnancies, regardless of the underlying reason for infertility, although the absolute smallest difference was seen when ICSI was used for male infertility (Fig. 3). When we examined differences in the risk of adverse perinatal outcomes according to whether the couple used ART for male or female infertility in combination with IVF or ICSI, the CIs were mostly overlapping (Fig. 4). An exception was the risk of spontaneous preterm birth, where the adjusted odds ratio (OR) was 1.78 (95% CI: 1.61–1.96) for pregnancies conceived by IVF due to female

infertility vs. 1.34 (95% CI: 1.20–1.50) for pregnancies conceived by ICSI due to male infertility, without overlapping CIs.

Stratifying by parity, the differences between ART and naturally conceived pregnancies were larger among the parous, but the differences were of a more modest magnitude among ART pregnancies conceived due to male infertility in both strata (Supplement Figs. 6 and 7, available online). When stratifying by maternal age <35 or ≥35 years, the estimated differences were overall similar in the 2 groups, and the differences observed in pregnancies conceived by ART due to male infertility were smaller than those observed for

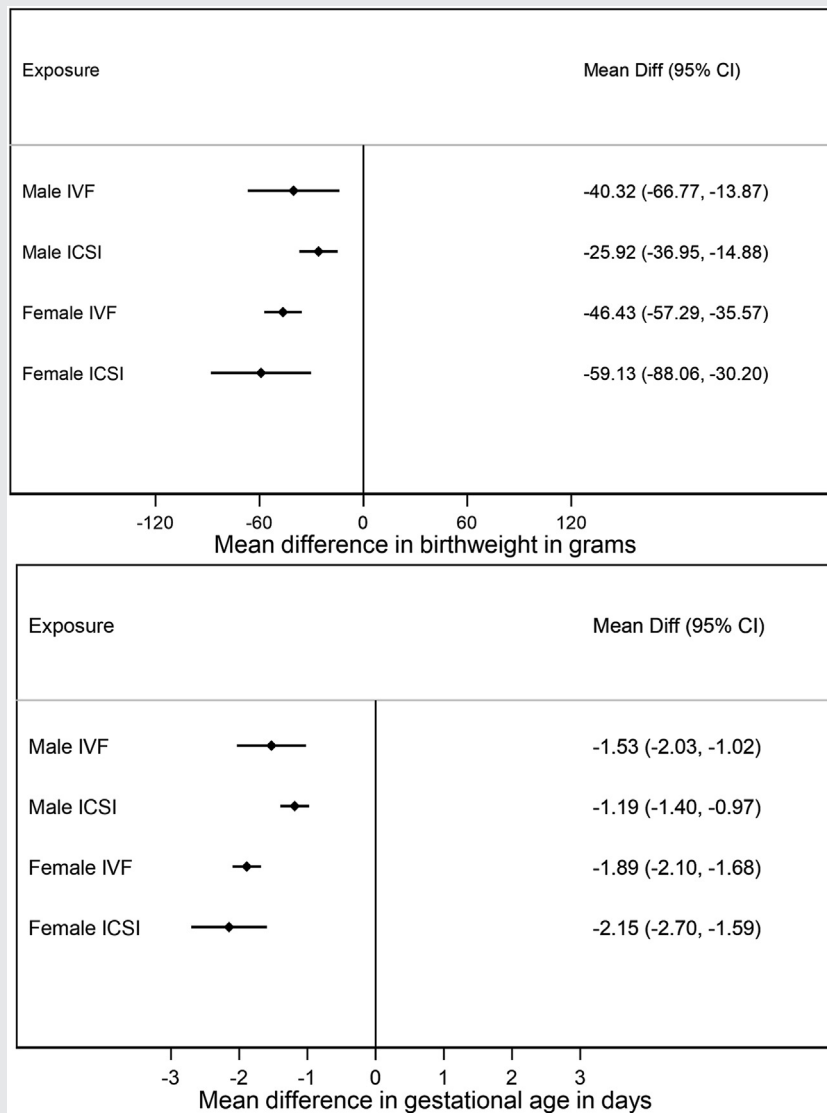
FIGURE 2



Adjusted odds ratios for perinatal birth outcomes comparing pregnancies conceived by assisted reproductive technologies and naturally conceived pregnancies according to the underlying cause for infertility. Adjusted for parental age, in addition to maternal parity, being married/cohabitating, country of birth, and year of delivery. PTB = preterm birth; LBW = low birthweight; SGA = small-for-gestational-age

Magnus. ART indication and perinatal outcomes. *Fertil Steril* 2025.

FIGURE 3



Adjusted mean differences in birthweight and gestational age between pregnancies conceived by assisted reproductive technologies and naturally conceived pregnancies according to the underlying cause for infertility and use of intracytoplasmic sperm injection (ICSI). *Note:* Adjusted for parental age, in addition to maternal parity, being married/cohabitating, country of birth, and year of delivery.

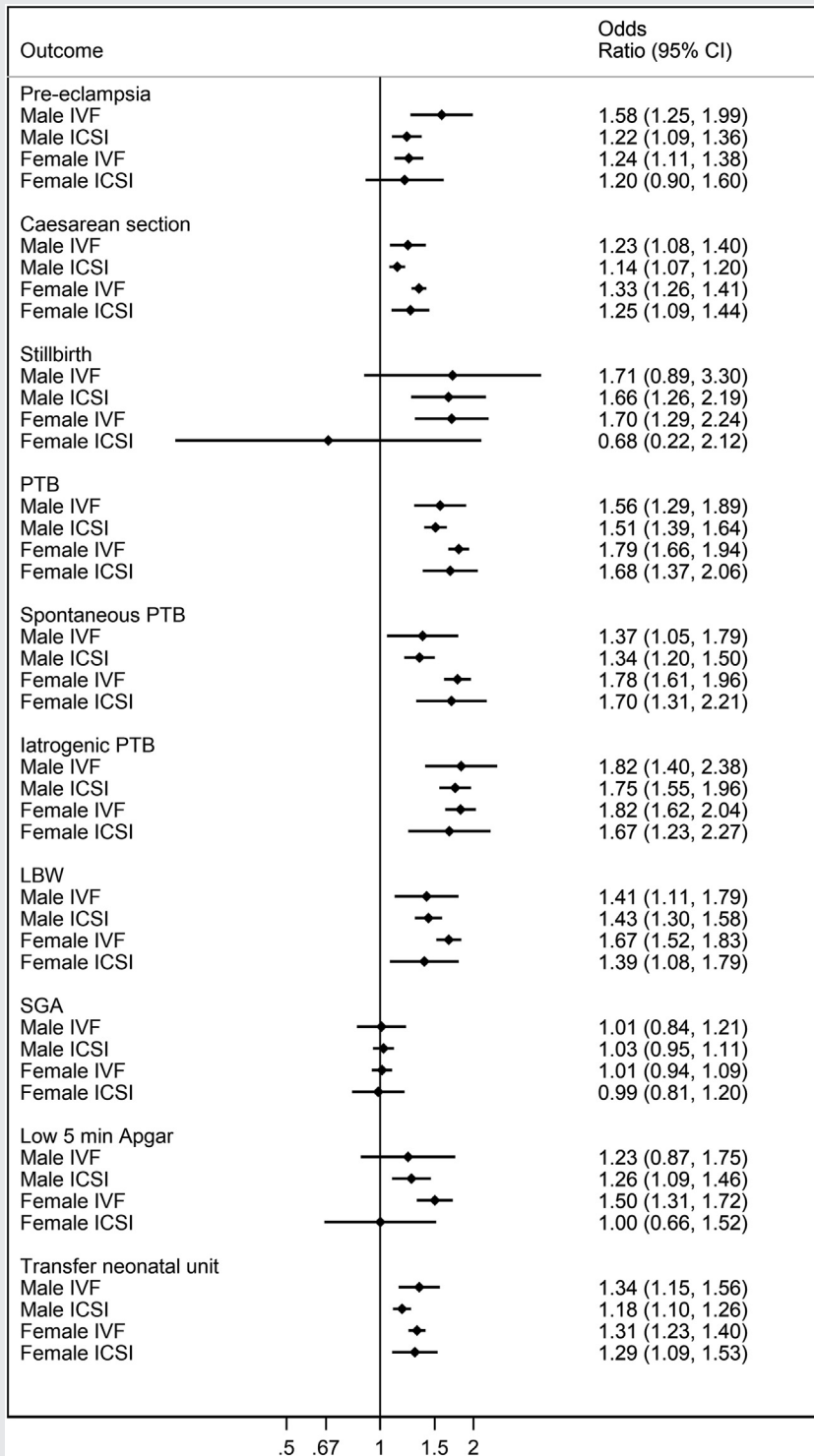
Magnus. ART indication and perinatal outcomes. *Fertil Steril* 2025.

pregnancies conceived by ART due to female infertility in both strata (Supplement Figs. 8 and 9, available online). We further directly compared ART pregnancies using those conceived by ART due to female infertility as the reference, indicating a higher birthweight and gestational age at birth, in addition to a lower risk of cesarean section delivery and spontaneous preterm birth, among pregnancies conceived by ART due to male infertility (Supplement Figs. 10–13, available online). When we further subgrouped our exposure groups according to whether fresh or frozen embryo transfer had been used, we observed the well-known pattern of a higher birthweight and an increased risk of pre-eclampsia in ART pregnancies conceived by frozen embryo transfer

regardless of male or female infertility problems, whereas the magnitude of the differences appeared to be lower for frozen embryo transfer pregnancies resulting from male infertility compared with those from female infertility (Supplement Figs. 14 and 15, available online).

We also conducted a sibling comparison in the subgroup of couples with at least one ART and one non-ART delivery ($n = 7,679$). Most effect estimates for ART deliveries conceived due to female infertility appeared to attenuate toward the null value (Supplement Figs. 16–18, available online). The same did not seem to be the case for the estimates for ART deliveries conceived due to male infertility, where the risk of some outcomes was even strengthened compared with

FIGURE 4



Adjusted odds ratios for perinatal outcomes comparing pregnancies conceived by assisted reproductive technologies and naturally conceived pregnancies according to the underlying cause for infertility and use of intracytoplasmic sperm injection (ICSI). Adjusted for parental age, in addition to maternal parity, being married/cohabitating, country of birth, and year of delivery. PTB = preterm birth; LBW = low birthweight; SGA = small-for-gestational-age.

Magnus. ART indication and perinatal outcomes. *Fertil Steril* 2025.

the main analysis for some estimates. However, in this latter analysis, the confidence intervals were wide.

DISCUSSION

In this large registry-based study, we observed a modest decrease in the mean gestational age and birth weight and higher risk of most adverse perinatal outcomes in pregnancies conceived by ART compared with naturally conceived deliveries, regardless of whether ART had been used for male, female, or unexplained infertility. Although the magnitude of the differences in the continuous outcomes was modest, this translated to notable increases in the risk of low birthweight and preterm birth. Most associations were of lower magnitude for ART deliveries after male infertility alone than in ART deliveries after female or mixed infertility, and the lowest increase in risk was in pregnancies conceived by ICSI due to male infertility. However, only the risk of cesarean section delivery and preterm birth were significantly different according to whether the ART was used for male or female infertility. Sibling analyses resulted in a greater attenuation of the estimates for female than for male infertility, supporting a stronger role of underlying female fertility factors in pregnancy complications. We did not adjust for multiple testing due to the close correlation between the outcomes evaluated, but we acknowledge that our findings need to be replicated in an independent sample.

A few studies investigated the potential role of underlying causes of infertility on the risk of complications in ART pregnancies, mostly focusing on aspects related to female infertility. An older matched case-control study, including 69 ART offspring of parents with unexplained infertility, found no difference in the rate of obstetric and perinatal outcomes when compared with either 345 naturally conceived offspring or 1,901 ART offspring of parents with known infertility causes (10). An increased risk of gestational diabetes, hypertensive disorders of pregnancy, preterm birth, and large-for-gestational age was identified in one study from Canada when comparing ART pregnancies to women with polycystic ovary syndrome (71 women) to those without (323 women) (12). A systematic review further reported an increased risk of preterm birth, cesarean section delivery, and transfer to a neonatal unit among women with endometriosis compared with those without endometriosis undergoing ART, whereas there appeared to be no increased risk of SGA, pre-eclampsia or post-partum hemorrhage (9).

Limited evidence exists regarding the risk of complications in pregnancies conceived by ART due to male infertility. A United Kingdom study including 117,401 live births (16), found no difference in the risk of preterm birth (adjusted OR: 1.01; 99.5% CI: 0.93–1.10) or low birth weight (adjusted OR: 0.95; 99.5% CI: 0.87–1.03) in pregnancies conceived by ART due to male infertility compared with ART pregnancies with unexplained infertility. This is in line with what we observed in our study, where the increased risk of adverse perinatal outcomes was largely similar in pregnancies conceived by ART due to male infertility or unexplained infertility when these 2 groups of ART pregnancies were compared with naturally conceived pregnancies. Another

considerably smaller Finnish study, including 255 ART pregnancies and 26,870 naturally conceived pregnancies, found that offspring conceived by ART due to male infertility were more likely to be transferred to the neonatal intensive care unit compared with naturally conceived pregnancies (17), which we also observed in our study.

Compared with the naturally conceived, we observed an increased risk of all adverse perinatal outcomes in pregnancies conceived by ART due to male infertility, except for SGA, which provides some important insight. A priori, we hypothesized that if we only observed an increased risk of adverse perinatal outcomes in pregnancies conceived by ART due to female or mixed causes for infertility and no increased risk in pregnancies conceived by ART due to male infertility, this could support a role for underlying contributing causes for female infertility. Because we observed an increased risk of most adverse perinatal outcomes also in pregnancies conceived by ART due to male infertility in adverse pregnancy outcomes compared with the naturally conceived, this may point to a role for aspects related to the ART procedures themselves. Furthermore, because the risk associated with use of ART for female infertility was greater than observed for male infertility, this appears to point toward a role of underlying factors related to female infertility also contributing to the pregnancy outcomes.

Potential relevant aspects related to ART procedures include, for example, the influence of the growth medium on embryonic development and the hormonal stimulation of the intrauterine environment (23). Specifically, a few studies have reported differences in birth weight according to the type and age of the culture media used (23). Existing studies indicate a difference in the risk of complications in ART pregnancies depending on whether the embryo was transferred during a programmed or natural cycle, further supporting the notion that the intrauterine environment might be influenced by hormonal stimulation with consequences for the risk of complications (24–26). We have also previously described clear differences in cord blood DNA methylation between ART and non-ART births (27) and shown that the decreased birthweight in ART births might indeed be partly explained by differences in DNA methylation patterns (28). Future studies should also look more into these potential epigenetic mechanisms in relation to other pregnancy complications.

Strengths of this study include the size, the population-based nature, and the comparison of the associations according to the couple's underlying cause of infertility. Our study also has limitations worth noting. We relied on the accurate registrations of the primary and secondary causes for using ART by fertility specialists. It might not always be easy to isolate such causes, and they were largely restricted by the answer options available to them, as listed in the methods section. We also relied on the fertility specialists indicating "sperm-related factor" as the main cause for using ART to define use of ART for male infertility. No information was available on other contributing factors to male infertility, such as, for example, hormonal imbalances, history of varicoceles, and infections, among others. This could have resulted in an underestimation of which ART pregnancies were the

result of male vs. female infertility. We included births between 2000 and 2021 in our study, and we acknowledge that the ART procedures have changed substantially over this time period, which also could have influenced the association with the risk of adverse perinatal outcomes. Furthermore, we were not able to adjust for any paternal characteristics except for paternal age. We did not have information on uterine pathology (such as fibroids or polyps). Because we only had information on the duration of the infertility for 31% of the ART pregnancies, we did not explore additional adjustments for this. This could have resulted in unmeasured confounding, which should be explored in future studies. We also had limited measures available to account for the influence of the couple's socio-economic position or lifestyle characteristics. We observed a higher rate of inductions in the ART deliveries (35%) than in the naturally conceived deliveries (25%). The difference in the overall rate of induction was partly explained by maternal age, parity, and an increase in inductions over time, and therefore, attenuated after adjustment for these 3 factors (adjusted OR: 1.25; 95% CI: 1.22–1.28). We did not adjust for or stratify by induction because this would be highly problematic and would complicate the interpretation of the estimates but we propose that our adjustment for the 3 major drivers of the difference in induction partly accounts for this issue. Our results are likely only generalizable to populations of similar ethnic composition with a universal healthcare system.

CONCLUSION

In conclusion, the higher risk of adverse perinatal outcomes in pregnancies conceived by ART was less pronounced when ART was used due to male infertility than in ART pregnancies with female infertility. This supports that the risks observed in ART pregnancies are a combination of underlying factors related to both female infertility and the ART procedures themselves. However, underlying conditions related to female fertility seem to play a stronger role than underlying male infertility in the risk of adverse pregnancy outcomes in ART pregnancies. We acknowledge that we were looking at the risk of short-term health outcomes in relation to the use of ART for male vs. female infertility. Additional studies are warranted, looking into more long-term outcomes (such as neurodevelopmental disorders or metabolic disturbances).

CRedit Authorship Contribution Statement

Maria C. Magnus: Writing – review & editing, Writing – original draft, Project administration, Methodology, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Karoline H. Skåra:** Writing – review & editing, Methodology, Investigation. **Ellen Ø. Carlsen:** Writing – review & editing, Methodology, Investigation. **Miriam Gjerdevik:** Writing – review & editing, Methodology, Investigation. **Cecilia H. Ramlau-Hansen:** Writing – review & editing, Methodology, Investigation. **Mikko Myrskylä:** Writing – review & editing, Methodology, Investigation. **Liv-Bente Romundstad:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Siri E. Håberg:** Writing –

review & editing, Methodology, Investigation, Funding acquisition, Conceptualization.

Declaration of Interest

M.C.M. reports funding from the Research Council of Norway and the European Research Council for the submitted work. K.H.S. has nothing to disclose. E.O.C. reports funding from the Research Council of Norway, the Centers of Excellence funding scheme, project number 262700, and the European Research Council funding scheme, project number BIOSFER, 101071773, for the submitted work. M.G. reports the research was supported by the Research Council of Norway through its Centers of Excellence funding scheme (project No. 262700). C.H.R.-H. has nothing to disclose. M.M. has nothing to disclose. L.-B.R. has nothing to disclose. S.E.H. reports funding from the Research Council of Norway and the European Research Council outside the submitted work.

SUPPLEMENTAL MATERIAL

Supplemental data for this article can be found online at <https://doi.org/10.1016/j.fertnstert.2025.02.013>.

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Uso de técnicas de reproducción asistida para la infertilidad masculina, femenina y sus resultados perinatales

Objetivo: Comparar los resultados perinatales adversos entre embarazos concebidos naturalmente y aquellos concebidos mediante técnicas de reproducción asistida (TRA), según la causa de infertilidad: masculina, femenina o de origen desconocido.

Diseño: Estudio de cohortes basado en registros nacionales.

Sujetos de estudio: Todos los nacimientos de embarazos únicos en Noruega, entre los años 2000 y 2021, registrados en el registro nacional.

Exposición: Se compararon los embarazos por TRA debido a infertilidad masculina (N = 9.957), femenina (N = 10.031), mixta (N = 3.287) o de causa desconocida (N = 7.178), con embarazos concebidos de forma natural (N = 1.210.709). La información sobre las causas de infertilidad fue proporcionada por clínicas de fertilidad.

Medidas: Se compararon el peso al nacer y la duración del embarazo mediante regresión lineal con estimadores robustos. Asimismo, se evaluó el riesgo de preeclampsia, cesárea, muerte fetal intraúterina, parto prematuro, bajo peso al nacer, recién nacido pequeño para la edad gestacional y necesidad de ingreso en unidad neonatal mediante regresión logística, ajustando por edad de los padres, paridad materna, situación de convivencia, país de nacimiento y año del parto.

Resultados: La duración del embarazo y el peso al nacer fueron inferiores en todos los grupos de TRA en comparación con los embarazos concebidos naturalmente. La reducción en la duración del embarazo fue menos pronunciada en los partos por TRA debidos a infertilidad masculina (diferencia ajustada: 1,24 días; intervalo de confianza [IC] del 95%: -1,43 a -1,05), que en aquellos por infertilidad femenina (diferencia ajustada: 1,92 días; IC del 95%: -2,12 a -1,73). De forma similar, la reducción del peso al nacer fue menos pronunciada en los embarazos por TRA por causa masculina (diferencia ajustada: 29 gramos; IC del 95%: -39 a -18) que en los debidos a infertilidad femenina (diferencia ajustada: 49 gramos; IC del 95%: -59 a -39). También se observó un mayor riesgo de la mayoría de los resultados perinatales adversos en todos los grupos de TRA, aunque con una magnitud menor en los embarazos por TRA con indicación de infertilidad masculina.

Conclusión: El riesgo aumentado de resultados perinatales adversos en embarazos concebidos mediante TRA fue menos pronunciado cuando estas se emplearon por infertilidad masculina, en comparación con infertilidad femenina. Esto sugiere que los riesgos asociados a los embarazos por TRA se deben a una combinación entre factores subyacentes relacionados con la infertilidad femenina y los propios procedimientos de reproducción asistida. No obstante, no puede descartarse que la infertilidad masculina también contribuya al aumento del riesgo.