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ASSISTED REPRODUCTION TECHNOLOGIES

Association of multifetal gestation with obstetric and neonatal outcomes in gestational carrier pregnancies

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Abstract

Objective Multifetal gestation is more frequent among gestational carrier pregnancies than non-surrogacy IVF pregnancies. We aimed to evaluate the association between multifetal gestation and obstetric and neonatal morbidity among gestational carrier pregnancies.

Methods Pooled cross-sectional study of birth certificate data from gestational carrier pregnancies in Utah from 2009 to 2018. Our primary outcome was a composite of severe obstetric morbidity; secondary outcomes included cesarean delivery (CD), hypertensive disorders of pregnancy, preterm birth (PTB), and a neonatal morbidity composite. Logistic regression was utilized to compare odds of these outcomes between gestational carrier pregnancies with and without multifetal gestation.

Results A total of 361 gestational carrier pregnancies resulted in the delivery of 435 neonates during the study period. Of these, 284 were singleton pregnancies, and 77 were multifetal, a multifetal gestation rate of 21.3%. Baseline demographic characteristics did not differ between singleton and multifetal gestations. Multifetal gestation was not associated with higher rates of severe obstetric morbidity (odds ratio [OR] 1.87, 95% confidence interval [CI] 0.34–10.39). Multifetal gestation was associated with increased odds of neonatal morbidity (OR 9.49, 95% CI 5.35–15.83); PTB < 37, 34, and 32 weeks (OR 21.88, 95% CI 11.64–41.12; OR 11.67, 95% CI 5.25–25.91; OR 8.79, 95% CI 3.41–22.68); and CD (OR 4.82, 95% CI 2.81–8.27).

Conclusion Severe obstetric morbidity did not differ between singleton and multifetal gestations among gestational carrier pregnancies. However, multifetal gestation was associated with increased odds of neonatal morbidity, CD, and PTB. This information may be useful when counseling prospective gestational carriers and intended parents.

Keywords Multifetal gestation · Gestational carrier pregnancies · Gestational surrogacy

Introduction

Gestational carrier pregnancies are occurring with increasing frequency in the USA; in 2013 (the last year for which data was published), a woman who is a gestational carrier was involved in 2.5% of all in vitro fertilization (IVF) cycles, representing a total of 3432 cycles [1]. These pregnancies can be associated with significant costs for the intended parents (including payments to the woman who is a gestational carrier, reimbursements for medical care, IVF costs, as well as agency and attorney fees), and intended parents may consider multifetal gestation as a way to grow their family with fewer pregnancies and thereby fewer costs [2].

The American Society for Reproductive Medicine (ASRM) recommends that "special consideration should be given to transferring a single embryo in an effort to limit the risks of multiple pregnancy for the carrier," but also notes that "after appropriate counseling and agreement by all parties, additional embryos may be transferred… in an effort to improve the probability of pregnancy" [3]. Evidence exists that rates of multifetal gestation are higher among gestational carrier pregnancies than non-surrogate IVF pregnancies and that rates of adherence to single embryo transfer recommendations

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are lower in gestational carrier pregnancies than non-surrogate IVF pregnancies (42% of embryo transfers in women who are gestational carriers are adherent to single embryo transfer recommendations, versus 60% in non-surrogate embryo transfers) [1, 4]. Despite this disparity, there is a lack of information regarding how multifetal gestation impacts outcomes for both the women who are gestational carriers and the fetuses they carry, making it difficult for intended parents and women who are gestational carriers to assess the risks and benefits of multiple embryo transfer. While data has demonstrated that multifetal gestation is associated with adverse obstetric and neonatal outcomes in a general population, these risks may differ among a population of ostensibly healthy, low-risk women who are gestational carriers [5–7].

In this study, we set out to evaluate the association between multifetal gestation and obstetric and neonatal morbidity, among gestational carrier pregnancies. We hypothesized that multifetal gestation is associated with significantly increased risks of both obstetric and neonatal morbidity. The state of Utah legalized gestational surrogacy in 2005, and in 2009 began capturing involvement of a woman who is a gestational carrier on the birth certificate, allowing a unique opportunity to study outcomes in this population on a state-wide level [8].

Materials and methods

We conducted a pooled cross-sectional analysis of birth certificate data from deliveries of live-born neonates in the state of Utah from 2009 to 2018, a time period during which Utah identified gestational carrier pregnancies on the birth certificate. The state of Utah employs a pre-birth parentage process, wherein during the pregnancy, a judge affirms the contract between the intended parent(s) and the woman who is a gestational carrier; this allows the intended parents to be named the legal parents of the offspring on the birth certificate and allows for identification of these pregnancies [8].

De-identified birth certificate data for all deliveries during the study period was provided by the Utah Department of Health Office of Vital Statistics. All deliveries that were the result of a gestational carrier pregnancy were included in this study. As Utah does not issue birth certificates for stillborn fetuses or pre-viable losses, pregnancies with these outcomes were not included in this study.

Our exposure variable was multifetal gestation. This is coded on the birth certificate, regardless of whether the co-twin was live-born or stillborn.

Our primary obstetric outcome was a composite of severe obstetric morbidity. This was based on the World Health Organization and Centers for Disease Control and Prevention's definitions of maternal morbidity, but was limited to the following outcomes included on the Utah birth certificate: eclampsia, HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome, blood transfusion, intensive care unit (ICU) admission, and unplanned hysterectomy. Additionally, death within 1 year of delivery was included in this composite outcome; this was ascertained using death certificate data provided by the Utah Department of Health Office of Vital Statistics. Notably, we chose to use the term obstetric morbidity rather than maternal morbidity, recognizing that women who are gestational carriers are not the legal mothers of these children, and in qualitative studies do not identify as the mothers of these children [9–11].

Our primary neonatal outcome was a composite of neonatal death, 5 min Apgar < 7, neonatal intensive care unit (NICU) admission, respiratory distress syndrome (RDS), assisted ventilation > 6 h, and seizure. Of note, RDS was removed from the birth certificate in 2016, resulting in missing data. We therefore conducted a sensitivity analysis of the neonatal morbidity composite both including and excluding RDS.

Secondary outcomes included cesarean delivery (CD), pregnancy-related hypertension (including gestational hypertension, pre-eclampsia, superimposed pre-eclampsia, eclampsia, and HELLP syndrome), and preterm birth (PTB) < 37, < 34, and < 32 weeks.

We collected the following characteristics of the woman who is a gestational carrier as covariates: age at delivery, nulliparity, chronic hypertension, pre-existing diabetes, severe asthma, heart disease, chronic kidney disease, anxiety, depression, other mental health disorders, tobacco use, other substance use, and weight gain during pregnancy. Given recommendations for selection of a woman who is considering acting as a gestational carrier, we expected a low frequency of pre-existing health conditions [3]. Therefore, we created three composites of gestational carrier health: pre-existing medical conditions (pre-gestational diabetes, chronic hypertension, severe asthma, chronic kidney disease, and chronic heart disease), pre-existing mental health disorders (anxiety, depression, bipolar disorder, schizophrenia, substance use, tobacco use), and an overall gestational carrier health composite which combined both medical and mental health disorders. Notably, additional demographic characteristics of women who are gestational carriers, such as race and ethnicity, are not recorded on the Utah birth certificate. These characteristics are reported for the intended parents instead.

We first conducted bivariate analyses to evaluate any differences in sociodemographic and obstetric risk factors between singleton and multifetal gestational carrier pregnancies. Fisher's exact test was used for categorical variables and the Kruskal-Wallis test was utilized for continuous variables.

We then used univariable and multivariable logistic regression to assess the association between multifetal gestation and each of the primary and secondary outcomes. Cesarean birth, hypertensive disorders of pregnancy, and preterm birth were assessed at the pregnancy level. Robust standard errors were used via STATA's *robust* option to account for any

heteroskedasticity [12]. The neonatal morbidity composite and components of the composite were evaluated at the neonate level, adjusted for clustering in multifetal gestations. Adjusted binomial logistic regression was utilized to address potential confounders. We used a reverse stepwise approach to the inclusion of covariates in the models, starting with any variables that differed across the exposure of interest ($p < 0.20$) or were felt to be related to the outcomes of interest. No imputations were performed for missing data.

For multivariable logistic models in which the outcome had a significant association with multifetal gestation, the average marginal probability of the outcome as it relates to the multifetal gestation specifically were computed using STATA's *margins* command [7]. Marginal probabilities provide an intuitive interpretation of logistic regression data. Fundamentally, the average marginal probability estimates the change in the probability of the outcome (when the outcome is binary) for a given change in a predictor with all other covariates held constant. In this case, the marginal probability represents the increased probability of the outcome associated with a change from singleton to multifetal gestation.

All statistical analysis was performed using STAT/MP 14.2 (StataCorp LLC, College Station, TX). This study was approved by the Utah Department of Health.

Results

A total of 361 gestational carrier pregnancies resulted in the delivery of 435 live-born neonates in the state of Utah during the study period. Of these, 284 of these pregnancies were of singletons, while 77 pregnancies were multifetal (resulting in 151 live-born neonates). Baseline demographic characteristics of women who are gestational carriers for these pregnancies did not differ among cohorts (Table 1).

Table 2 provides the results of unadjusted and adjusted logistic models for obstetric outcomes. The rate of the primary outcome, severe obstetric morbidity, among all participants was 1.7% ($n = 6$). Notably, 5 out of 6 instances of obstetric morbidity occurred in subjects who delivered preterm. Rates of severe obstetric morbidity were not significantly different among multifetal pregnancies compared to singleton pregnancies in both unadjusted and adjusted models (2.6% vs 1.4%, adjusted odds ratio 5.60, 95% confidence interval 0.28–110.6). The adjusted model included gestational carrier's age at delivery and history of preterm birth. Of note, a significant proportion of participants ($n = 145$) were missing data for gestational carrier age at delivery. Models of the primary outcome which included gestational carrier age at delivery demonstrated better model fit, and more conservative point estimates of effect, and thus, we retained this covariate. Other covariates demonstrated significant collinearity and were therefore excluded. A post hoc power calculation demonstrated that this study had 80% power to detect an 8.1% difference in the primary obstetric outcome.

Rates of CD were higher in multifetal pregnancies than in singleton pregnancies (51.9% vs 18.3%, odds ratio 4.8, 95% confidence interval 2.81–8.3). Even in women without a prior CD, the rate of CD was significantly higher in multifetal gestations (46.2% versus 12.5%, odds ratio 6.0, 95% confidence interval 3.3–11.1). In adjusted models, rates of CD remained higher (adjusted odds ratio 5.60, 95% confidence interval 3.1–10.2). Covariates included in the adjusted models were pre-pregnancy health composite, history of prior CD, and history of PTB. Age at delivery was not significant in these models and did not improve model fit nor substantively alter the point estimates. Therefore, we chose to exclude this covariate in favor of retaining data. Rates of hypertensive disease of pregnancy did not differ between groups (Table 2). Rates of preterm birth < 37 weeks, < 34 weeks, and < 32 weeks were all significantly higher among multifetal than singleton pregnancies (Table 2). In adjusted models (adjusting for history of PTB and pre-pregnancy health composite; again age was not included in favor of retaining data), rates of PTB remained higher (adjusted odds ratio 29.30, 95% confidence interval 11.01–77.96; adjusted odds ratio 12.52, 95% confidence interval 5.5–28.3; and adjusted odds ratio 8.93, 95% confidence interval 3.4–23.4).

Table 3 provides results from adjusted and unadjusted models of neonatal morbidity. Adjusted models included pre-pregnancy health composite, history of PTB, cesarean birth (at index pregnancy), and accounting for clustering in multifetal gestations. In adjusted models, rates of the neonatal morbidity composite were significantly higher among multifetal gestations compared to singletons (51.7% vs 9.5% of neonates; adjusted odds ratio 9.39, 95% confidence interval 4.8–18.4). NICU admission > 24 h (adjusted odds ratio 9.70, 95% confidence interval 4.9–19.2), respiratory distress syndrome (adjusted odds ratio 11.11, 95% confidence interval 2.8–44.8), and assisted ventilation for > 6 h (adjusted odds ratio 7.2, 95% confidence interval 2.8–18.4) all remained significantly associated with multifetal gestation in adjusted models. Of note, the relationship between neonatal morbidity and multifetal gestation is completely mediated by preterm gestational age at delivery (analyses not shown). Missing data on RDS prompted us to conduct a sensitivity analyses assessing the importance of respiratory distress syndrome to the neonatal morbidity composite. In analyses not shown, no cases of the neonatal morbidity composite were included due solely to a diagnosis of RDS.

We next computed the average marginal predicted probabilities for each of the outcomes associated with multifetal gestation (CD, PTB < 37 weeks, and neonatal morbidity composite) using the adjusted logistic regressions reported in Tables 2 and 3 (Table 4). Figure 1 demonstrates the increased marginal probabilities across a range of parturient age for each

Table 1 Demographic and obstetric characteristics of GC pregnancies by gestation type[1]

	Multifetal gestation ($n = 77$)	Singleton gestation ($n = 284$)	p value[2]
Gestational carrier age at delivery	30 (27–33)	31 (28–35)	0.26
Previous preterm birth	7 (9.1)	27 (9.5)	1.00
Previous cesarean birth	12 (15.6)	28 (9.9)	0.16
Nulliparous	2 (2.6)	9 (3.2)	1.00
Pre-existing health conditions composite[3]	4 (5.2)	39 (13.7)	0.05
Chronic hypertension	1 (1.3)	3 (1.1)	1.00
Pre-gestational diabetes	0	0	n/a
Tobacco use	0	8 (2.9)	0.21
Substance use	0	7 (2.5)	0.35
Mental health disorders[4]	3 (3.9)	30 (10.6)	0.08
Medicaid Insurance	0	8 (2.8)	0.21

Missingness: age at delivery: 145, smoking: 27; chronic heart disease and chronic kidney disease: 216; gestational weight gain: 30

[1] Data presented as median (IQ range) or n (%)

[2] Fisher's Exact for categorical variables and Kruskal-Wallis test for medians as appropriate

[3] GC health composite includes: pre-gestational diabetes, chronic hypertension, severe asthma, chronic kidney disease, chronic heart disease, anxiety, bipolar disorder, depression, schizophrenia, substance use, and tobacco use

[4] Mental health disorders includes anxiety, depression, bipolar disorder, schizophrenia, substance use, and tobacco use

outcome, with CD in panel a, PTB < 37 weeks in panel b, and neonatal morbidity in panel c. The marginal probability listed in Table 4 is the average absolute difference between the predicted probability for singleton gestations (the blue lines) and the predicted probability for multifetal gestations (the red lines) in Fig. 1. At age 30 (approximately the median age of women who are gestational carriers in this study), CD is predicted in 18.5% (95% confidence interval 13.4–23.6%) of singleton gestations, and in 53.2% (95% confidence interval 37.1–69.4%) of multifetal gestations. Similarly, PTB < 37 weeks at age 30 is predicted in only 11.0% (95% confidence interval 6.1–16.0%) of singleton gestations, but 76.4%

Table 2 Obstetric morbidity among multifetal and singleton gestational carrier pregnancies

	Multifetal gestation ($n = 77$)	Singleton gestation ($n = 284$)	OR (95% CI)	aOR[1] (95% CI)
Obstetric morbidity composite[2]	2 (2.6)	4 (1.4)	1.9 (0.3–10.4)	5.60 (0.6–56.5)
Mortality	0 (0)	0 (0)		
ICU admission	1 (1.3)	1 (0.4)		
Eclampsia	0 (0)	0 (0)		
HELLP syndrome	0 (0)	1 (0.4)		
Transfusion	1 (1.3)	3 (1.1)		
Unplanned hysterectomy	0 (0)	0 (0)		
Cesarean delivery[3]	40 (52.0)	52 (18.3)	4.82 (2.8–8.3)	5.60 (3.1–10.2)
Hypertensive disorders of pregnancy[4]	10 (13.0)	28 (9.9)	1.36 (0.6–3.0)	1.39 (0.6–3.0)
Preterm birth				
Preterm birth < 37 weeks	59 (76.6)	37 (13.0)	21.88 (11.6–41.2)	29.30 (11.01–77.96)
Preterm birth < 34 weeks	23 (29.9)	10 (3.5)	11.67 (5.3–25.9)	12.52 (5.5–28.3)
Preterm birth < 32 weeks	14 (18.2)	7 (2.5)	8.79 (3.4–22.7)	8.93 (3.4–23.4)

OR odds ratio, *aOR* adjusted odds ratio, *CI* confidence interval; data presented as n (%) and OR (95% CI)

[1] Except where noted, models are adjusted for gestational carrier health composite and history of preterm birth

[2] Obstetric morbidity model additionally adjusted for gestational carrier age

[3] Cesarean delivery model additionally adjusted for previous cesarean delivery

[4] Includes gestational hypertension, preeclampsia with and without severe features, HELLP syndrome, and eclampsia

Table 3 Neonatal morbidity among neonates of multifetal and singleton gestational carrier pregnancies[1]

	Multiple gestation ($n = 151$)	Singleton gestation ($n = 284$)	OR (95% CI)	aOR[2] (95% CI) ($n = 435$)
Neonatal morbidity	78 (51.7)	27 (9.5)	10.17 (5.6–18.3)	9.39 (4.8–18.4)
Neonatal death	3 (2.0)	3 (1.1)	1.90 (0.4–9.6)	1.19 (0.2–12.7)
5 min Apgar < 7	6 (4.0)	3 (1.1)	3.86 (1.0–15.6)	4.10 (0.8–22.3)
NICU admission > 24 h	76 (50.3)	25 (8.8)	10.50 (5.8–19.1)	9.70 (4.9–19.2)
Respiratory distress syndrome[3]	17 (21.8)	3 (2.9)	9.48 (2.5–36.4)	11.11 (2.8–44.8)
Assisted ventilation > 6 h	29 (19.2)	8 (2.8)	8.2 (3.5–19.5)	7.20 (2.8–18.4)
Seizure	0 (0)	0 (0)	n/a	n/a

GC gestational carrier, *NICU* neonatal intensive care unit, *OR* odds ratio, *aOR* adjusted odds ratio, *CI* confidence interval

[1] Data presented as *n* (%) and odds ratio (95% CI)

[2] Adjusted for GC pre-pregnancy health composite, history of preterm birth, cesarean birth, and clustering in multifetal gestations

[3] Respiratory distress syndrome not reported for 252 neonates, % and models based on $n = 183$

(95% confidence interval 62.6–90.3%) of multifetal gestations. At the median age of women who are gestational carriers in this study, neonatal morbidity is predicted to occur in 9.0% (95% CI 4.0–14.1%) of singleton gestations, while this outcome is predicted in 43.6% (95% CI 26.8–60.5%) of multifetal gestations.

Comment

In this population-based study of gestational carrier pregnancies in Utah, we found multifetal gestation was associated with significant increases in odds of CD, neonatal morbidity, and PTB, but not with an increased risk of other obstetric morbidities.

These data are important because multiple gestation may be a modifiable risk factor for gestational carrier pregnancies. Prospective intended parents and women who will be gestational carriers should be aware of the risk of multifetal gestation when making complex decisions about the number of embryos to transfer. While intended parents may consider multifetal gestation a way to build their families at lower costs (given the high cost of each additional surrogate pregnancy), significantly increased risks of PTB and neonatal morbidity (with associated short term costs related to hospital stay, potential long term costs related to additional care required for morbidity related to prematurity, and emotional costs related to parenting a child in the NICU) may offset these perceived lower costs. These additional costs may be borne by not only intended parents, but also the medical system and society as a whole, making these decisions even more ethically complex. For women who are gestational carriers, this analysis suggests CD would complicate, on average, over half of multifetal gestation pregnancies, which may have implications for both short-term health (i.e., a longer recovery postpartum) and long-term health, particularly should they desire additional pregnancies. Additionally, while we were underpowered for the primary outcome, the association between PTB and obstetric morbidity may be important for women who are gestational carriers to consider when making decisions regarding the number of embryos to transfer.

Table 4 Marginal predicted probabilities of obstetric and neonatal outcomes associated with multifetal gestation in gestational carrier pregnancies

	Marginal predicted probability	95% CI
Neonatal morbidity[1, 2]	33.1%	27.0–39.3%
Preterm birth (< 37 weeks' gestation)[3]	64.3%	54.2–74.4%
Cesarean birth[4]	31.3%	19.3–43.4%

CI confidence interval, *NICU* neonatal intensive care unit

[1] Analyzed at the neonatal level, adjusted for GC pre-pregnancy health composite, history of preterm birth, cesarean birth, and clustering in multifetal gestations

[2] Composite includes perinatal death, 5 min Apgar < 7, NICU admission > 24 h, respiratory distress syndrome, assisted ventilation > 6 h, seizure

[3] Analyzed at the pregnancy level, adjusted for GC pre-pregnancy health composite, history of preterm birth

[4] Analyzed at the pregnancy level, adjusted for GC pre-pregnancy health composite, history of preterm birth, and previous cesarean birth

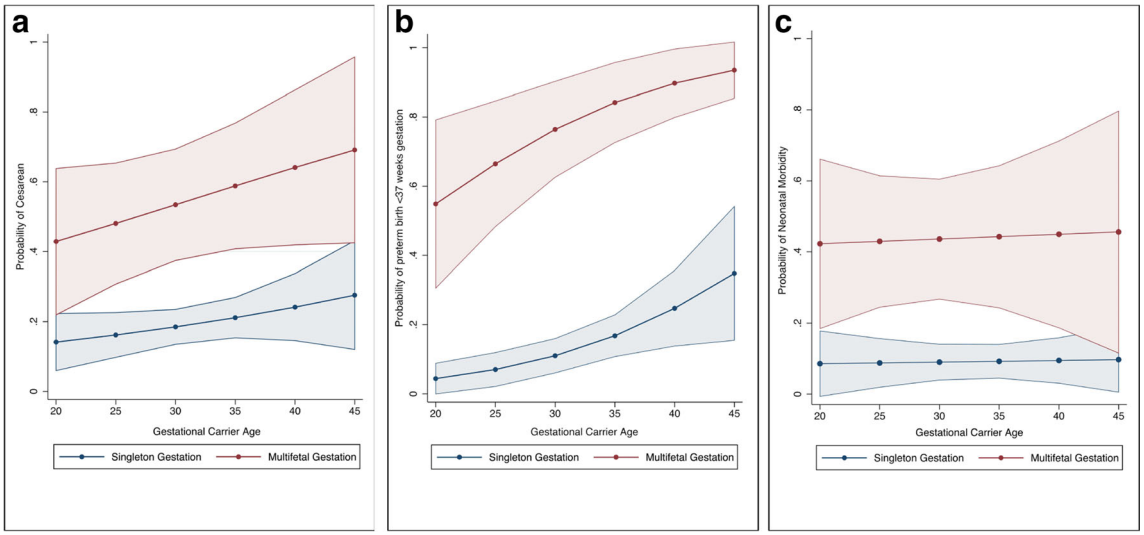

Fig. 1 Demonstrates the increased marginal probabilities across a range of parturient age for each outcome, with cesarean birth in panel **a**, preterm birth in panel **b**, and neonatal morbidity in panel **c**

There are several differences between our findings and previously reported data. Our rate of multifetal gestation in gestational carrier pregnancies, 18%, is significantly lower than has been previously reported. Between 1999 and 2013, the Center for Disease Control reported a multifetal gestation rate of 36% among gestational carrier pregnancies [1]. It is possible, then, that our study represents a low-end estimate of neonatal risk in gestational carrier pregnancies from a public health perspective. On the other hand, our cohort is more contemporary, spanning 2009–2018, and likely represents a trend towards single embryo transfer consistent with a recent decreasing rate of multifetal gestation in both gestational carrier and non-surrogate IVF pregnancies that has been reported in other studies [4]. Among multifetal gestations, our rate of preterm birth (76.6%) is significantly higher than anticipated; in the year 2013, the preterm birth rate of twins born in the USA was 57% [13]. Underlying differences in our population may contribute to this difference; notably, 9.4% of all subjects had a history of PTB in a previous pregnancy. Additionally, IVF is associated with higher rates of PTB, which may contribute to this difference [14]. While history of PTB is not listed as a criterion for consideration of a woman interested in acting as a gestational carrier by the ASRM, this is in line with previous studies suggesting that in practice, women who are gestational carriers may not always be ideal candidates [3, 15]. It is interesting that rates of hypertensive disease of pregnancy did not differ among multifetal and singleton gestations in our cohort, while previous studies have shown increased rates in multifetal pregnancies [5, 6]. Our study may have been underpowered to detect a more subtle difference in hypertensive disease of pregnancy. One notable difference between this study and many other studies is that all of our subjects conceived by IVF; it may be that among IVF pregnancies, differences in rates of hypertensive disease of pregnancy are less significant between multifetal gestations and singleton gestations. Previous studies have also demonstrated higher rates of severe obstetric morbidity and mortality among multifetal gestations compared to singleton gestations [7]. Our study was underpowered to detect significant differences in this rare outcome.

This study has several strengths. We address the impact of multifetal gestation on health outcomes of both the women who are gestational carriers and the children they deliver, which can inform counseling of both intended parents and women who are gestational carriers when considering the number of embryos to transfer. This study includes a large number of gestational carrier deliveries and includes deliveries across the state of Utah, representing the practices of numerous obstetricians and reproductive endocrinologists.

This study has several limitations as well. As a study of birth certificate data, there may be data that is absent or inaccurate. We were limited to outcomes included on the birth certificate; other outcomes that may be of interest to women who are gestational carriers considering the number of embryos to transfer, such as antepartum hospitalization, could not be included in this study. Although this was a large study of outcomes among women who are gestational carrier and the infants they deliver, we were still underpowered to detect rare outcomes, such as severe obstetric morbidity and neonatal death. Additionally, we were unable to assess pre-viable loss and stillbirth, as these outcomes do not result in a birth certificate in the state of Utah. As these outcomes are higher among multifetal gestations, we are likely underestimating the true risk of multifetal gestational in gestational carrier pregnancies. These outcomes are certainly of interest to intended parents when considering the number of embryos to transfer. Pre-viable delivery and stillbirth are also associated with higher risk of obstetric risk; as these could not be included in this

study, this likely underestimates the risk of obstetric morbidity [16]. Additionally, the population of patients delivering in Utah may differ from other locations, and limit the generalizability of this data. Lastly, we did not have access to infertility records to determine the number of embryos transferred, and can therefore only presume that many multifetal pregnancies were the result of implanting more than a single embryo. Despite these limitations, our study is one of the first to evaluate the role multifetal gestation plays in obstetric and neonatal morbidity among gestational carrier pregnancies.

Conclusions

Our data suggest that multifetal gestation in gestational carrier pregnancies is associated with increased rates of PTB, CD, and neonatal morbidity. When possible, and consistent with the informed wishes of intended parents and women who are gestational carriers, single embryo transfer should be encouraged. Larger studies that can assess the risk of severe obstetric morbidity are warranted to better counsel women who are gestational carriers about the risks to their own health. Additionally, studies that address the underlying reasons for high rates of multifetal gestation within this population, and how intended parents and women who are gestational carriers assess these risks, would be extremely valuable.

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Authors' contributions All authors contributed to the study conception and design. Data analysis was performed by the first and second authors. The first draft of the manuscript was written by the first author. All authors read and approved the final manuscript prior to submission.

Data availability With the approval of the State of Utah Department of Health Office of Vital Records and Statistics, we will provide our data if requested.

Compliance with ethical standards

Conflicts of interest/competing interests No authors have conflicts of interest or competing interests to disclose.

Ethics approval This study was approved by the State of Utah Department of Health Office of Vital Records and Statistics.

Consent to participate As only deidentified, publicly available birth certificate data was utilized, no consent to participate was obtained.

Consent for publication As only deidentified, publicly available birth certificate data was utilized, no consent for publication was obtained.

Code availability All statistical analysis was performed using Stata version 15.1 (StataCorp LLC, College Station, TX).

References

1. Perkins KM, Boulet SL, Jamieson DJ, Kissin DM. Nass group. Trends and outcomes of gestational surrogacy in the United States. Fertil Steril. 2017;106(2):435–42.
2. Swanson K, Ayala NK, Barnes RB, Desai N, Miller M, Yee LM. Understanding gestational surrogacy in the United States: a primer for obstetricians and gynecologists. Am J Obstet Gynecol. 2020;222(4):330–7.
3. Recommendations for practices utilizing gestational carriers: a committee opinion. Fertil Steril. 2017;107(2):e3–10.
4. White PM. Commercialization, altruism, clinical practice: seeking explanation for similarities and differences in Californian and Canadian gestational surrogacy outcomes. Womens Health Issues. 2018;28(3):239–50.
5. Day MC, Barton JR, O'Brien JM, Istwan NB, Sibai BM. The effect of fetal number on the development of hypertensive conditions of pregnancy. Obstet Gynecol. 2005;106(5 Pt 1):927–31.
6. Buhling KJ, Henrich W, Starr E, Lubke M, Bertram S, Siebert G, et al. Risk for gestational diabetes and hypertension for women with twin pregnancy compared to singleton pregnancy. Arch Gynecol Obstet. 2003;269(1):33–6.
7. Santana DS, Cecatti JG, Surita FG, Silveria FG, Costa ML, Souza JP, et al. Twin pregnancy and severe maternal outcomes: the World Health Organization multicountry survey on maternal and newborn health. Obstet Gynecol. 2016;127(4):631–41.
8. Utah State Legislature. Utah uniform parentage act. Gestational agreement authorized. Utah Code Ann. § 78B-15-801.
9. Berend Z. The online world of surrogacy (fertility, reproduction, and sexuality: social and cultural perspectives). New York: Berghahn Books; 2016.
10. Jacobson H. Labor of love: gestational surrogacy and the work of making babies. New Brunswick: Rutgers University Press; 2015.
11. Jadva V, Murray C, Lycett E, MacCallum F, Golombok S. Surrogacy: the experiences of surrogate mothers. Hum Reprod. 2003;18(10):2196–204.
12. Williams R. Using the margins command to estimate and interpret adjusted predictions and marginal effects. Stata J. 2012;12(2):308–31.
13. Martin JA, Hamilton BE, Osterman MJ, Curtin SC, Matthews TJ. Births: final data for 2013. Natl Vital Stat Rep. 2015;64(1):1–65.
14. Sunderam S, Kissin DM, Crawford SB, Folger SG, Boulet SL, Warner L, et al. Assisted reproductive technology surveillance – United States, 2015. MMWR Surveill Summ. 2018;67(3):1–28.
15. Swanson K, Letourneau JM, Kuppermann M, Einerson BD. Association of obstetric and neonatal outcomes with deviation from guidelines for gestational carriers. Obstet Gynecol. 2020;136(2):387–93.
16. Wall-Wieler E, Carmichael SL, Gibbs RS, Lyell DJ, Girsen AI, El-Sayed YY, et al. Severe maternal morbidity among stillbirth and live birth deliveries in California. Obstet Gynecol. 2019;134(2):310–7.