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ASSISTED REPRODUCTION TECHNOLOGIES

Obstetric morbidity in gestational carrier pregnancies: a population-based study

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Abstract

Purpose We sought to characterize severe obstetric morbidity among women who are gestational carriers compared to other patients.

Methods This was a population-based study comparing gestational carrier pregnancies to non-surrogate pregnancies (non-surrogate IVF pregnancies, all non-gestational carrier pregnancies, and a cohort of matched controls) delivering in Utah between 2009 and 2018, using birth certificate data. Our primary outcome was a composite of severe morbidity, including death, ICU admission, eclampsia, HELLP syndrome, transfusion, and unplanned hysterectomy. Our secondary outcomes were cesarean delivery (CD) and hypertensive disorders of pregnancy.

Results During the study period, 361 gestational carrier pregnancies and 509,015 other pregnancies resulted in live births. Severe morbidity was less common among gestational carrier pregnancies than IVF pregnancies (1.7% versus 5.5%, odds ratio [OR] 0.29, 95% confidence interval [CI] 0.12–0.70), but was not different when compared to all other pregnancies (1.0%, OR 1.61, 95% CI 0.72–3.60), or a cohort of matched controls (1.0%, OR 1.37, 95% CI 0.55–3.40). CD was less common among gestational carrier pregnancies than IVF pregnancies, but not different than all other pregnancies or matched controls. While frequency of hypertensive disorders of pregnancy was lower among gestational carrier pregnancies than IVF pregnancies, it was higher than all other women who delivered and comparable to matched controls.

Conclusion Severe obstetric morbidity is uncommon among gestational carrier pregnancies. Women who are gestational carriers are at lower risk of morbidity and CD than others who conceive through IVF and do not appear to be at increased risk compared to matched controls.

Keywords Gestational surrogacy · Gestational carrier pregnancies · Severe obstetric morbidity · IVF

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Introduction

Gestational carrier pregnancies, wherein intended parents or a single intended parent contract with a woman to gestate their fetus, are becoming more frequent in the USA [1]. As of 2013, 2.5% of all in vitro fertilization (IVF) cycles reported to the Center for Disease Control and Prevention (CDC) involved a woman who is a gestational carrier, compared to1999, when 1% of IVF cycles involved a woman who is a gestational carrier [2].

Despite this rise in prevalence, little attention has been paid to the obstetric outcomes of women who are gestational carriers. An understanding of the health outcomes that women who are gestational carriers experience is important to appropriately counsel women who are considering acting as gestational carriers. Several case series and cohort studies have been published, primarily focusing on hypertensive disorders

of pregnancy, gestational diabetes (GDM), and cesarean delivery (CD) [3–5]. Many of these case series lack a control group, while others compare women who are gestational carriers to women who conceive via in vitro fertilization (IVF). But IVF may not be an appropriate control group, as women who require IVF due to underlying infertility or subfertility are likely quite different than women who are gestational carriers (who ideally should be healthy and parous), and their risks are likely quite different [1]. One single institution study compared outcomes of women who are gestational carriers to their own prior pregnancies and found increased risks of hypertensive disease of pregnancy [5]. But since all of the women serving as their own controls were older during their gestational carrier pregnancies than they were during their prior pregnancies, age was a likely confounding factor. This lack of an appropriate control group makes it challenging to counsel women who are considering acting as gestational carriers about the risks of morbidity during a gestational carrier pregnancy.

The state of Utah legalized gestational carrier pregnancies in 2005 and since 2009 has included a field for gestational carrier pregnancy in birth certificate data collection. This allows a unique opportunity to evaluate data on a population level.

Our objectives were to describe rates of severe obstetric morbidity in women who are gestational carriers and to compare these outcomes to those of other IVF pregnancies, all other pregnancies, and pregnancies of matched controls. We hypothesized that women who are gestational carriers would experience lower rates of severe morbidity than women who conceived by IVF without assistance of a woman who is a gestational carrier but higher rates of morbidity than a general obstetric population.

Materials and methods

This was a population-based study that used birth and death certificate data from the state of Utah between the years of 2009 and 2018. Deidentified data were provided by the Utah Department of Health Office of Vital Records and Statistics. All births identified as being the result of a gestational carrier pregnancy were included as the exposed cohort. The state of Utah requires a prebirth parentage order issued by a judge in order for the intended parents to be named as the legal parents of the child born via surrogacy [6].

Given the lack of a single best control group, we used three comparison groups. The first group consisted of women with live births whose pregnancies resulted from IVF without a gestational carrier. While IVF itself is not included as a field on the Utah birth certificate, all pregnancies involving "infertility drugs or treatment" were reviewed, and those with comments indicating IVF, embryo transfer, intracytoplasmic sperm injection (ICSI), donor eggs, or preimplantation genetic testing (PGT) were included in this cohort. The second comparison group consisted of all women other than gestational carriers (including those who conceived through IVF) who had live births in the state of Utah during the study period. This cohort allowed for a comparison of background obstetric outcomes in the state of Utah during our study period. For the third comparison, we curated a matched control group of 5 women who had non-IVF live births for each gestational carrier pregnancy. Due to limited demographic information for women who are gestational carriers on the birth certificate, we matched based on year of delivery, age at the time of delivery (when available, this was not reliably included on the birth certificate for women who are gestational carriers until 2016), tobacco use, chronic hypertension, preexisting diabetes, substance use, nulliparity, and number of prior CD. We felt that this matched cohort would provide important information for counseling of patients, as it allowed for a direct comparison of women who are gestational carriers to woman at similar risk of morbidity, except for IVF. We chose not to match on multifetal gestation, as rates of multifetal gestation have been reported to be significantly higher in gestational carrier pregnancies (notably, higher even than among other IVF pregnancies) and may contribute to obstetric morbidity in this population [2]. Additionally, we excluded pregnancies conceived through IVF in the matched cohort, as IVF has been proposed as a contributing factor to increased risk in women who are gestational carriers [5]. When no matched controls were available, the gestational carrier subject was excluded from the analysis.

Our primary outcome was a composite of severe obstetric morbidity and mortality. This was based on definitions of severe maternal morbidity from the World Health Organization (WHO) and Centers for Disease Control and Prevention (CDC) but was restricted to available data from the birth certificate. We therefore included in our composite primary outcome eclampsia, blood transfusion, unplanned hysterectomy, intensive care unit (ICU) admission, and death. Utah death certificate data was reviewed to determine death within 1 year of delivery. We chose to use the term "obstetric morbidity and mortality" rather than "maternal morbidity and mortality," as women acting as gestational carriers are not legally the mothers of these children, and based on qualitative studies, they do not consider themselves the mothers of these children [7–9].

Our secondary outcomes included CD and hypertensive disorders of pregnancy, including gestational hypertension, preeclampsia with and without severe features, superimposed preeclampsia, eclampsia, and HELLP syndrome.

Covariates included age at delivery, nulliparity, comorbidities (including chronic hypertension, preexisting diabetes, tobacco use, and other substance abuse), and multifetal gestation. We were unable to collect data regarding race and ethnicity, as this data is not recorded for women acting as gestational carriers

Table 1 Demographic characteristics

	Gestational carrier pregnancies ($n = 361$)	Non-gestational carrier IVF pregnancies ($n = 563$)	p value[1]	Non-gestational carrier pregnancies ($n = 509{,}015$)	p value[1]	Matched controls ($n = 1{,}800$[2])	p value[1]
Age at delivery[3]	31 (28–34)	38 (33–43)	0.0001				
Nulliparity	6 (1.7)	350 (62.2)	<0.0001	166,441 (32.7)	< 0.0001	30 (1.7)	1.00
Chronic hypertension	4 (1.1)	18 (3.2)	0.04	5549 (1.1)	0.97	20 (1.1)	1.00
Type 1 or 2 diabetes mellitus	0 (0)	6 (1.1)	0.05	3714 (0.7)	0.10	0 (0)	1.00
Tobacco use	8 (2.2)	9 (1.6)	0.42	82,354 (16.2)	0.01	40 (2.2)	1.00
Other substance use	7 (1.9)	0 (0)	0.001	5115 (1.0)	0.08	35 (1.9)	1.00
Multifetal gestation	77 (21.3)	146 (25.9)	0.11	8881 (1.7)	<0.0001	106 (5.9)	< 0.0001
Prior cesarean delivery	40 (11.1)	83 (14.7)	0.11	66,619 (13.1)	0.26	200 (11.1)	1.00

Data presented as median (IQ interval) or n (%)

IVF in vitro fertilization

[1] Gestational carrier pregnancies used as referent group

[2] No matched controls available for one subject who is a gestational carrier; comparison for matched controls was to 360 subjects who are gestational carriers

[3] Age not available for 145 subjects who are gestational carriers

on the Utah birth certificate; rather, that data is recorded for the intended parents.

Baseline characteristics, as well as primary and secondary outcomes, were compared between groups using univariate analysis with chi-square test, Fisher's exact test, and Student's *t* test, as appropriate. Multivariate logistic regression was utilized to obtain adjusted odds ratios for the primary and secondary outcomes when comparing women who are gestational carriers to other women who had IVF pregnancies and to women who gave birth after all other types of pregnancies. We included in these analyses any baseline variables that differed between groups in univariate analysis. No multivariate regression was performed for the matched cohort, as the matching process was designed to control for demographic differences and negate the need for this analysis. All tests were two-sided, and a p value of 0.05 was used to define statistical significance. Analyses were performed using Stata version 15.1 (StataCorp LLC, College Station, TX). This study was approved by the Utah Department of Health prior to initiation.

Results

A total of 509,376 pregnancies resulted in the live birth of at least one neonate in the state of Utah during the study period. Of these, 361 were to women who were gestational carriers and 563 to women who conceived through IVF without assistance of a gestational carrier.

Baseline demographic characteristics for each of these groups are reported in Table 1. Notably, we were unable to find matched controls for one woman who was a gestational carrier; she was 58 years old and was excluded from the matched control analysis. When compared to women who conceived by IVF without the assistance of a gestational carrier, women who were gestational carriers were significantly younger and less likely to be nulliparous or to have chronic hypertension but were more likely to report substance use. When compared to all other women who delivered in Utah during the study period, women who are gestational carriers were older and less likely to be nulliparous or to report tobacco use. While gestational carrier pregnancies were much more likely to be complicated by multifetal gestation than all other pregnancies (21.3% versus 1.7%, $p < 0.001$) and matched controls (21.3% versus 5.9%, $p < 0.001$), there was no difference when these pregnancies were compared to non-surrogate IVF pregnancies (21.3% versus 25.9%, $p = 0.11$).

Frequency of morbidity among women who are gestational carriers compared to all other IVF pregnancies is reported in Table 2. When compared to other IVF pregnancies, women who are gestational carriers were significantly less likely to experience severe obstetric morbidity (1.7% versus 5.5%, odds ratio [OR] 0.29, 95% confidence interval [CI] 0.12–0.70), CD (25.5% versus 60.0%, OR 0.22, 95% CI 0.17–

Table 2 Obstetric outcomes among gestational carrier and non-gestational carrier IVF pregnancies

	Gestational carrier pregnancies (n = 361)	Non-gestational carrier IVF pregnancies (n = 567)	OR (95% CI)	aOR[1] [2] (95% CI)
Primary outcome	6 (1.7)	31 (5.5)	0.29 (0.12-0.70)	0.17 (0.04-0.81)
Mortality	0 (0)	0 (0)	n/a	
ICU admission	2 (0.6)	2 (0.4)	1.56 (0.22–11.14)	
Eclampsia	0 (0)	3 (0.5)	n/a	
HELLP syndrome	1 (0.3)	5 (0.9)	0.31 (0.04–2.66)	
Transfusion	4 (1.1)	23 (4.1)	0.26 (0.09–0.76)	
Unplanned hysterectomy	0 (0)	4 (0.7)	n/a	
Cesarean delivery	92 (25.5)	340 (60.0)	0.22 (0.17–0.30)	0.42 (0.27–0.65)
Hypertensive disorders of pregnancy[3]	37 (10.2)	120 (21.2)	0.42 (0.28–0.63)	0.86 (0.45–1.64)

Data presented as n (%)

ICU intensive care unit, *HELLP syndrome* hemolysis, elevated liver enzymes, low platelets, *OR* odds ratio, *CI* confidence interval, *aOR* adjusted odds ratio

[1] Adjusted for age, nulliparity, chronic hypertension, substance use

[2] Adjusted odds ratios not calculated for rare outcomes

[3] Pre-eclampsia, gestational hypertension, HELLP, and superimposed pre-eclampsia

0.30), or hypertensive disorders of pregnancy (10.2% versus 21.2%, OR 0.42, 95% CI 0.28–0.63). After adjusting for demographic differences (age, nulliparity, chronic hypertension, and substance use), the association persisted between gestational carrier pregnancy and decreased odds of severe obstetric morbidity (adjusted OR 0.15, 95% CI 0.03–0.80) and CD (a secondary outcome; adjusted OR 0.42, 95% CI 0.27–0.65), but not hypertensive disorders of pregnancy (another secondary outcome; adjusted OR 0.86, 95% CI 0.45–1.64).

Frequency of morbidity among women who are gestational carriers and all other pregnancies is described in Table 3. There were no differences in rates of the primary outcome (1.7% versus 1.0%, odds ratio [OR] 1.61, 95% confidence interval [CI] 0.72–3.60), though women who are gestational carriers were significantly more likely to be admitted to the ICU (0.6% versus 0.1%, OR 4.60, 95% CI 1.14–18.50). They were also more likely to develop hypertensive disorders of pregnancy (10.2% versus 5.8%, OR 1.84, 95% CI 1.31–2.59). There were no differences in rate of CD (25.5% versus

Table 3 Obstetric outcomes among gestational carrier and non-gestational carrier pregnancies

	Gestational carrier pregnancies n = 361	Non-gestational carrier pregnancies n = 509,015	OR (95% CI)	aOR[1] [2] (95% CI)
Primary outcome	6 (1.7)	5296 (1.0)	1.61 (0.72-3.60)	1.03 (0.51-2.07)
Mortality	0 (0)	256 (0.05)	n/a	
ICU admission	2 (0.6)	616 (0.1)	4.60 (1.14–18.50)	
Eclampsia	0 (0)	609 (0.1)	n/a	
HELLP syndrome	1 (0.3)	1061 (0.2)	1.33 (0.19–9.48)	
Transfusion	4 (1.1)	3408 (0.6)	1.66 (0.62–4.46)	
Unplanned hysterectomy	0 (0)	251 (0.04)	n/a	
Cesarean delivery	92 (25.5)	111,870 (22.0)	1.21 (0.96–1.54)	1.06 (0.90–1.25)
Hypertensive disorders of pregnancy[3]	37 (10.2)	29,756 (5.8)	1.84 (1.31–2.59)	1.44 (1.13–1.84)

Data presented as n (%)

ICU intensive care unit, *HELLP syndrome* hemolysis, elevated liver enzymes, low platelets, *OR* odds ratio, *CI* confidence interval, *aOR* adjusted odds ratio

[1] Adjusted for age, nulliparity, tobacco

[2] Adjusted odds ratios not calculated for rare outcomes

[3] Pre-eclampsia, gestational hypertension, HELLP, and superimposed pre-eclampsia

22.0%, OR 1.21, 95% CI 0.96–1.54). After controlling for demographic differences (age, nulliparity, and tobacco use), the associations between gestational carrier and CD did not persist. In contrast, the association between gestational carrier and hypertensive disorders of pregnancy persisted (adjusted OR 1.44, 95% 1.13–1.84).

When compared to matched controls, there were no differences in rates of the primary outcome, CD, or hypertensive disorders of pregnancy (Table 4).

Comment

In this study, we found that rates of severe obstetric morbidity were low in gestational carrier pregnancies. In line with our hypothesis, women who are gestational carriers had much lower risks of severe obstetric morbidity, CD, and hypertensive disorders of pregnancy compared to other women who conceive through IVF. Contrary to our hypothesis, however, their obstetric risks appear to be similar to the general obstetric population, with the exception of an increased risk of hypertensive disorders of pregnancy. Furthermore, risk for women who are gestational carriers was comparable to a cohort of matched controls. These findings can inform counseling of women who are considering acting as gestational carriers so that they can better assess risks before proceeding.

The finding that obstetric morbidity is less common in women who are gestational carriers than in women who conceive through IVF without the assistance of a gestational carrier is in line with other studies, which have demonstrated lower rates of hypertensive disorders of pregnancy, placenta previa and abruption, and CD [3, 4]. Demographic differences, as demonstrated in this study, likely contribute to higher rates of morbidity among women who conceive by non-surrogate IVF. However, even after adjusting for demographic differences, severe morbidity was less common among women who are gestational carriers than other women who conceive through IVF. This suggests that underlying medical conditions contributing to subfertility and infertility may contribute to risk of morbidity in women who require IVF to conceive, rather than the IVF process itself. There may also be differences in IVF itself (e.g., use of PGT or fresh versus frozen embryo transfer) among women who are gestational carriers and other women who conceive through IVF that could attribute to differences in outcomes. Unfortunately, the nuances of IVF treatment are not captured reliably by the Utah birth certificate and could not be assessed by this study.

Perhaps the more surprising finding of this study is that women who are gestational carriers do not appear to be at increased obstetric risk compared to other obstetric patients. To evaluate these associations, we took two approaches: (i) we compared gestational carrier pregnancies with all non-gestational carrier pregnancies, controlling for baseline differences in statistically adjusted multivariable models, and (ii) to make a more direct clinical comparison, we compared gestational carrier pregnancies to controls randomly matched on key baseline risk characteristics. Prior to the study, we hypothesized that gestational carriers would be at higher risk of obstetric morbidity owing to risks associated with IVF and a higher rate of multifetal gestation. However, our findings do not support this conclusion. Instead, our data suggest that gestational carrier pregnancies may not be associated with

Table 4 Obstetric outcomes among gestational carrier and matched control pregnancies

	Gestational carrier pregnancies (n=360[a])	Matched control pregnancies[b] (n = 1800)	OR (95% CI)
Primary outcome	6 (1.7)	22 (1.2)	1.37 (0.55-3.40)
Mortality	0 (0)	0 (0)	n/a
ICU admission	2 (0.6)	3 (0.2)	3.35 (0.55–20.10)
Eclampsia	0 (0)	3 (0.2)	n/a
HELLP syndrome	1 (0.3)	7 (0.4)	0.71 (0.09–5.82)
Transfusion	4 (1.1)	11 (0.6)	1.83 (0.58–5.77)
Unplanned hysterectomy	0 (0)	2 (0.1)	n/a
Cesarean delivery	91 (25.3)	390 (21.7)	1.22 (0.94–1.59)
Hypertensive disorders of pregnancy[3]	36 (10.0)	153 (8.5)	1.20 (0.82–1.75)

Data presented as median (IQ interval) or n (%)

ICU intensive care unit, *HELLP syndrome* hemolysis, elevated liver enzymes, low platelets, *OR* odds ratio, *CI* confidence interval, *aOR* adjusted odds ratio

[a] One gestational carrier pregnancy excluded, as no matched controls could be identified

[b] Matched on year of delivery, age (when available), nulliparity, number of prior cesarean deliveries, chronic hypertension, preexisting diabetes, tobacco use, drug use

[3] Pre-eclampsia, gestational hypertension, HELLP, and superimposed pre-eclampsia

additional risks beyond any other pregnancy in the same cohort of women.

Whether women who are gestational carriers are at increased risk of hypertensive disorders is not clearly resolved by this study. A previous study found that women who acted as gestational carriers were at higher risk of hypertensive disorders of pregnancy in that pregnancy than in their prior pregnancies [5]. But since patients were their own controls, the study could not account for the important confounding variable of maternal age. While we found no increased risk of hypertensive disorders of pregnancy compared to a cohort of matched controls, we did find an increased risk when compared to the general obstetric population. It is possible that the increased risk was small enough that our cohort of matched controls was underpowered to detect this difference. Alternatively, it could be that there were significant differences in the women who are gestational carriers and the general obstetric population that we were unable to control for. Patients considering acting as gestational carriers should be aware of this potential risk.

Another important finding is the high rate of multifetal gestation in gestational carrier pregnancies. This is in line with other studies [2]. As a potentially modifiable risk factor for obstetric and neonatal morbidity (with the employment of single embryo transfer), this is an important consideration for women who are gestational carriers and their physicians.

The main strengths of this study are its size and population-based design. We were able to assess risk of relatively rare outcomes that other studies of gestational carrier pregnancies could not. Even this large study, however, was likely underpowered to detect subtle differences in the very rare outcomes (e.g., maternal death). Additionally, as a population-based study, this study reduces referral bias and problems of lost to follow-up that can occur in studies within referral centers.

Our study has limitations as well. Birth certificate data may be incomplete or incorrect, and our outcomes of interest were limited to those that were collected on the Utah birth certificate. In particular, birth certificate data only collects information on live births; pregnancies resulting in stillbirth or previable delivery, which may be risk factors for obstetric morbidity, were therefore not included [10]. While prior studies have suggested that risk of miscarriage in gestational carrier pregnancies is comparable to other IVF pregnancies, as well as in the same women's own non-gestational carrier pregnancies, there is less data on stillbirth or previable delivery in these patients [2, 5]. Additionally, it is very likely that IVF pregnancies not involving a gestational carrier were underreported and thus could have been included in the general obstetric population or matched control group. We would not expect that this would systematically alter risk in the IVF group, but it may have biased our other analyses toward the null since miscoded IVF pregnancies would likely add obstetric risk to the general obstetric population and to the matched cohort. And although our subjects represent the population of an entire state, the demographics of Utah may not match those of other states, limiting somewhat the generalizability of these data.

While our study provides insight into morbidity associated with gestational carrier pregnancies, there are numerous questions that cannot be answered with retrospective birth certificate data. Prospective studies that include all gestational carrier pregnancies (including those that result in previable loss or stillbirth) would be valuable.

Overall, we found that rates of severe obstetric morbidity were lower in gestational carrier pregnancies than in other IVF pregnancies and largely similar to the general obstetric population. These findings may be reassuring to women who are considering becoming gestational carriers and to obstetric providers. More work is needed to understand the unique and additional risks borne by women who are gestational carriers.

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Authors' contributions All authors contributed to the study conception and design. Data analysis was performed by the first author. 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

Conflict of interest The authors declare that they have no conflicts of interests.

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).

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