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Genetic counseling decisions in gestational carrier pregnancies

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Abstract

Objective Pregnancies conceived as contracted gestational carriers are a relatively new phenomenon for reproductive medicine. Since the intended parents control genetic screening decisions, there may be differences in genetic decisions made for gestational carrier (GC) in vitro fertilization (IVF) pregnancies as compared to traditional non-gestational carrier IVF pregnancies. Our goal was to investigate the frequency and types of these genetic testing decisions.

Methods We performed a retrospective study of GC pregnancies counseled at a private maternal–fetal medicine practice between January 2006 and January 2021. Inclusion criteria were pregnancies that completed counseling with a certified genetic counselor and obtained high-resolution imaging. Controls were non-GC IVF pregnancies seen in the same period matched by parity, estimated delivery date (EDD), and the oocyte age utilized in conception. Statistical analysis included patient demographics, pre-implantation genetic testing (PGT-A) frequency and results, ultrasound imaging results, and the frequency with results of prenatal genetic screening (first or second-trimester serum screens), non-invasive prenatal testing (NIPT), or diagnostic testing (chorionic venous sampling (CVS) or amniocentesis).

Results One hundred and ninety one gestational carrier pregnancies were identified and 167 met inclusion criteria. Gestational carrier pregnancies were significantly more likely to pursue PGT-A, PGT-A with NIPT, first-trimester screening, and second-trimester screening. There were no differences in rates of amniocentesis or CVS over controls.

Conclusions Regarding genetic counseling and screening options, our series is the first to demonstrate that gestational carrier parents seek additional genetic counseling resources, even with reassuring PGT-A and ultrasound.

Keywords Third party reproduction · Gestational carriers · PGT · IVF · Genetic testing · Aneuploidy

Introduction

Assisted reproductive technology (ART) methods such as intrauterine insemination and in vitro fertilization (IVF) offer many couples the opportunity for parenting. For some patients, there is a decision to use gestational carriers (GC) as an option to achieve a viable pregnancy. GC have become more common in ART, accounting for 2.5% of IVF cycles in 2013 compared to 1.0% in 1999 [1]. The proposed reasons for the increase in the utilization of GC include an increasing number of clinics performing GC cycles, court cases establishing legal frameworks for the practice, and general awareness and acceptance of this option for family building [1]. In vitro fertilization often enhances successful implantation, ongoing clinical pregnancy, and improved live birth rates with GC cycles compared with non-gestational carrier cycles. These improved success rates contribute to increasing popularity and recommendation for gestational carrier conception, gestation, and delivery [2].

The literature is scare on the genetic counseling decisions which gestational carriers undertake. During IVF, patients can assess the pre-implanted embryos for aneuploidy or chromosomal abnormalities using preimplantation genetic testing (PGT-A) [3–7]. PGT-A aims to identify aneuploidy using 24-chromosome comprehensive screening techniques through two common methods, array comparative genomic hybridization, and single-nucleotide polymorphism (SNP) arrays [8]. The goal of PGT-A is to avoid transfer of atypical genetic embryos to increase the likelihood of a successful pregnancy free from a numerical chromosomal abnormality.

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PGT-A of embryos has been shown to increase the likelihood of having a live birth in women over the age of 37 by selectively eliminating aneuploid embryos [9, 10]. Despite the PGT-A reassurance, detailed genetic counseling in gestational carriers is recommended to meet parenting needs.

While PGT-A is done prior to implantation to screen for aneuploidy, non-invasive prenatal testing (NIPT) through the analysis of cell-free (cf) DNA allows for prenatal screening for fetal aneuploidy. Due to apoptosis of cells, DNA fragments circulate in plasma and are considered cfDNA. Placental cells and fetal cells undergo apoptosis and DNA fragments that circulate in maternal blood can be captured and tested. Currently, cfDNA can include shotgun massive parallel sequencing, targeted massive parallel sequencing, and SNP differences between mother and fetus [11]. Joint guidelines by the American College of Obstetrics and Gynecology (ACOG) and the Society for Maternal Fetal Medicine state that prenatal genetic screening and diagnostic testing options should be discussed and offered to all pregnant patients regardless of age or risk for chromosomal abnormality [12].

The purpose of this study is to investigate the genetic screening and diagnostic decisions of gestational carrier gestations with access to maternal fetal medicine care and genetic counseling. We hope to define the similarities and differences in preimplantation genetic testing, prenatal screening, and prenatal diagnostic testing decisions in GC IVF pregnancies versus non-GC IVF pregnancies.

Materials and methods

We conducted a retrospective study of consecutive GC pregnancies seen at a private high-risk pregnancy center between January 2006 and January 2021. Institutional Review Board approval was obtained from the Kirk Kerkorian School of Medicine of UNLV. Eligible pregnancies had complete sessions with certified genetic counselors and high-resolution ultrasounds. The patients had IVF with or without PGT-A at various fertility clinics prior to being referred for Maternal Fetal Medicine care. The participants were matched to non-gestational carrier control IVF pregnancies with similar completion of full genetic counseling and high-resolution ultrasounds. Controls were matched by parity, estimated date of delivery (EDD), and age of oocyte utilized in conception. Exclusions were patients who declined or failed to complete genetic counseling or ultrasound imaging. Study variables were patient demographics, decision to undergo PGT-A, results of PGT-A, and frequency of first trimester nuchal translucency-PAPP-A, second-trimester serum screen, non-invasive prenatal testing (NIPT), amniocentesis, or chorionic villus sampling. For patients pursuing diagnostic testing, ultrasound findings were reviewed. Descriptive statistical analysis, chi-square analysis, and Fisher's exact test were performed. All statistical tests were done with a p-value of 0.05 required for statistical significance.

Results

From January 2006 to January 2021, there were 191 GC pregnancies, with 167 eligible for inclusion in the study. Controls were found in a 1:1 fashion and are shown in Table 1. Average age at time of oocyte retrieval was 30 ± 6.69 years in GC pregnancies and 32 ± 5.55 years in non-GC IVF pregnancies ($p = 0.002$). There were 23 twin gestations and three triplet gestations among GC pregnancies. There were 35 twin gestations and two triplet gestations among non-GC IVF controls.

Patient's decisions to undergo prenatal genetic screening are shown in Table 2. Of included pregnancies, more of the gestational carriers had PGT-A than non-GC IVF controls (64.1 ($n = 107$) vs 46.7% ($n = 78$), $p = 0.002$). GC

Table 2 Pre-implantation and prenatal screening among gestational carriers compared to IVF controls

Genetic screening	GC IVF pregnancies ($n = 167$)	Control IVF pregnancies ($n = 167$)	P value
PGT-A	107 (64.1%)	78 (46.7%)	* 0.002
NIPT	57 (34.1%)	66 (39.5%)	0.364
First trimester screen	39 (23.3%)	19 (11.4%)	* 0.006
Second trimester screen	26 (15.6%)	13 (7.8%)	* 0.04
Sequential screen	5 (3.0%)	5 (3.0%)	1
AFP only	12 (7.18%)	13 (7.8%)	1
NIPT after PGT-A	37/70 (34.6%)	21/78 (26.9%)	* 0.001
NIPT after no PGT-A	20/60 (33.3%)	45/78 (57.7%)	* 0.005

Table 1 Demographics of gestational carriers ($n = 167$) and non-carrier ($n = 167$) IVF pregnancies

Variable	Gestational carrier IVF pregnancies	Non-gestational carrier IVF pregnancies	P value
Age (y) at oocyte retrieval	30.26 ± 6.69	32.62 ± 5.55	* 0.002
Singleton	$N = 141$ (84.4%)	$N = 130$ (77.8%)	0.162
Twin gestation	$N = 33$ (19.8%)	$N = 35$ (21.0%)	0.892
Triplet gestation	$N = 3$ (1.8%)	$N = 2$ (1.2%)	0.725

pregnancies were significantly more likely to have first-trimester and second-trimester screening than non-GC IVF pregnancies (23.3 ($n=39$) vs 11.4% ($n=19$), $p=0.006$, and 15.6 ($n=26$) vs 7.6% ($n=13$), $p=0.040$, respectively). GC status was not correlated with non-invasive prenatal testing (34. 1 ($n=57$) vs 39.5% ($n=66$), $p=0.364$). GC pregnancies were more likely to opt for both PGT-A and NIPT (34.6 ($n=37$) vs 26.9% ($n=21$), $p=0.001$).

GC pregnancies were not statistically different in their utilization of diagnostic testing such as CVS or amniocentesis (3.59 ($n=6$) vs 5.39% ($n=9$), $p=0.599$). Six GC pregnancies had CVS or amniocentesis done (Table 3). Two had low-risk PGT-A and low-risk NIPT but had sonographic soft-markers for trisomies such as echogenic intracardiac focus and echogenic bowel. These two resulted in normal CVS and amniocentesis results. One patient had 45 X on NIPT but normal amniocentesis. One patient had no PGT-A or NIPT but multiple fetal anomalies on ultrasound such as absent septi pellucidi, ventriculomegaly, and echogenic intracardiac focus. She had normal amniocentesis results and opted for termination at 19 weeks. Two patients had normal ultrasound, one with normal second trimester screen, and opted for elective diagnostic testing which resulted in normal CVS and amniocentesis.

Among non-GC IVF pregnancies who pursued amniocentesis or CVS, three had neither PGT-A nor NIPT prior to diagnostic testing; however, one had ultrasonographic soft markers for trisomy such as a choroid plexus cyst and an echogenic intracardiac focus. The other two had normal ultrasound. Two patients had normal PGT-A, no NIPT, and normal amniocentesis. Another patient had normal PGT-A and normal NIPT with no ultrasound abnormalities and normal CVS. Abnormal results included two trisomy 21 and one trisomy 18 among IVF controls. All three results were preceded with NIPT for the same chromosomal abnormality. One of the two patients with trisomy 21 had sonographic soft markers for trisomy such as absent nasal bone while the other had a normal ultrasound. The patient with trisomy 18 had multiple sonographic abnormalities consistent with the diagnosis such as omphalocele, microganthia, clenched hands, and rocker feet as well as cardiac defect of Tetralogy of Fallot.

The overall rate of abnormal diagnostic testing was not statistically significant between the two groups (16.7 ($n=1$) vs 33.3% ($n=3$), $p=0.585$).

Table 3 Diagnostic testing among gestational carriers compared to IVF controls

Genetic testing	GC IVF pregnancies ($n=167$)	Control IVF pregnancies ($n=167$)	*P* value
CVS or amniocentesis	6/167 (3.59%)	9/167 (5.39%)	0.599
Abnormal CVS or amniocentesis	1/6 (16.7%)	3/9 (33.3%)	0.585

Discussion

This study is the first to identify the genetic counseling decisions of gestational carrier pregnancies. We found no previous articles with similar data for gestational carrier management and outcomes. We identified that GC pregnancies were more likely to undergo PGT-A and first or second-trimester screening compared to non-GC IVF pregnancies. GC pregnancies were also more likely to opt for both PGT-A and NIPT. There was not a significant difference in utilization of diagnostic testing (3.59 ($n=6$) vs 5.39% ($n=9$), $p=0.599$) or in rates of abnormal diagnostic testing (16.7 ($n=1$) vs 33.3% ($n=3$), $p=0.585$) between GC and controls. In both groups, diagnostic testing was most often preceded by abnormal screening or ultrasound. Gestational carriers were more likely to pursue diagnostic testing in the absence of abnormal pre-implantation or screening results, leading to trends towards lower rates of abnormal diagnostic testing.

We were interested to see the frequency of follow-up testing after PGT-A. Our study shows that NIPT is still requested for patients with reassuring PGT-A in gestational carrier management. In this cohort, GC pregnancies were nearly twice as likely to opt for both PGT-A and NIPT. In our study, there was one patient who had discordant genetic screening results with normal PGT-A and abnormal NIPT. Amniocentesis found that aneuploidy from NIPT was a false positive.

To our knowledge, this is the first study to focus on GC pregnancies that have previously undergone preimplantation genetic testing, received normal results, and continued to undergo further prenatal genetic testing and screening. The reasons why GC pregnancies pursue additional genetic testing have not been studied and further studies could help elucidate needs of gestational carriers and better guide genetic counseling sessions.

We acknowledge the limitations that exist in this study. First, the study had a small sample size. Therefore, some trends may be adjusted in a study with a larger sample size. Secondly, the results of maternal genetic carrier testing and positive family history for genetic diseases could have influenced decisions for preimplantation genetic testing and prenatal genetic screening. Additionally, due to the nature of the study, there may have been differences in the content and depth of discussion between genetic counselors with GC pregnancies and non-GC pregnancies. Additionally, general obstetricians may have already ordered NIPT for patients or influenced their discussion to pursue the screening. Lastly, the study could contain a selection bias of high-risk pregnancies given that the patients sampled were patients referred to a maternal fetal medicine practice. We, therefore, conclude that a large, multi-practice study should be completed to confirm these results.

Conclusions

While many factors influence decisions to pursue preimplantation genetic testing and prenatal genetic screening, gestational carrier pregnancies had significantly higher use of PGT-A, PGT-A with NIPT, first trimester screening, and second trimester screening compared to IVF controls. There was no difference in amniocentesis or CVS use. However, gestational carriers were more likely to pursue diagnostic testing in the absence of abnormal pre-implantation or screening results, leading to trends towards lower rates of abnormal diagnostic testing. We conclude that genetic counseling pathways for gestational carrier pregnancies have distinct differences compared to IVF pregnancies without gestational carrier contracts. This study identifies an area that needs to be further studied in order to understand what exactly the needs and motivation of this population are.

Data availability Requests for data can be made to melody.rasouli@unlv.edu.

Code availability Not applicable.

Declarations

Ethics approval Not applicable.

Consent to participate Not applicable.

Consent for publication Not applicable.

Conflict of interest The authors declare no competing interests.

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