Title

Gestational surrogacy in Australia 2004-2011: treatment, pregnancy and birth outcomes

Short title

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Conflicts of interest

All authors have no conflict of interest in relation to this work.

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ABSTRACT

Background: Information on gestational surrogacy arrangement and outcomes is limited in Australia.

Aims: This national population study investigates the epidemiology of gestational surrogacy arrangement in Australia: treatment procedures, pregnancy and birth outcomes.

Materials and Methods: A retrospective study was conducted of 169 intended parents cycles and 388 gestational carrier cycles in Australia in 2004-2011. Demographics were compared between intended parents and gestational carrier cycles. Pregnancy and birth outcomes were compared by number of embryos transferred.

Results: Over half (54%) intended parents cycles were in women aged <35 years compared to 38% of gestational carrier cycles. About 77% of intended parents cycles were of nulliparous women compared to 29% of gestational carrier cycles. Of the 360 embryo transfer cycles, 91% had cryopreserved embryos transferred and 69% were single embryo transfer (SET) cycles. The rates of clinical pregnancy and live delivery were 26% and 19% respectively. There were no differences in rates of clinical pregnancy and live delivery between SET cycles (27% and 19%) and double embryo transfer (DET) cycles (25% and 19%). Five of 22 deliveries following DET were twin deliveries compered to none of 48 deliveries following SET. There were 73 liveborn babies following gestational surrogacy treatment including 9 liveborn twins. Of

these, 22% (16) were preterm and 14% (10) were low birthweight. Preterm birth was 13% for liveborn babies following SET, lower than the 31% or liveborn babies following DET.

Conclusions: To avoid adverse outcomes for both carriers and babies, SET should be advocated in all gestational surrogacy arrangements.

INTRODUCTION

For some women, it is too risky or impossible to carry a pregnancy through and to give birth to a healthy infant.[1] Surrogacy arrangement is one option for family formation for these women and their partners. A surrogacy arrangement is where a woman known as a carrier, who has no intention of becoming pregnant otherwise, agrees to carry a baby for another person or couple known as intended parents with the intention that the child will be raised by the intended parents.[2] A surrogacy arrangement can be classified as either traditional or gestational surrogacy. Traditional surrogacy usually occurs when the woman who has agreed to carry the pregnancy for the intended parents is inseminated with the sperm of the intended father, which means that the baby is the biological child of the gestational carrier.[1] Gestational surrogacy is when an embryo, fertilized through assisted reproductive technology (ART) procedures using the oocytes and sperm from the intended parents, donors or a combination, is transferred to the gestational carrier.[1] This means that the gestational carrier has no genetic link to the child.

Traditional surrogacy can be performed at home or in any health settings. In comparison, gestational surrogacy requires ART treatment including both clinical and laboratory procedures and is performed exclusively in fertility clinics. In 2011 in the United States, <1% of the 151,923 ART cycles were gestational carrier cycles.[3] In the same year in Australia and New Zealand, there were 177 surrogacy arrangement cycles (46 intended patients cycles and 131 gestational carrier cycles), accounting for 0.3% of all ART treatment cycles (66347) [4].

Due to the rarity of gestational surrogacy, there is no worldwide statistics on number of gestational carrier cycles and resulting pregnancy and birth outcomes. Even though gestational surrogacy treatment cycles performed in Australia were collected in Australian and New Zealand Assisted Reproduction Database (ANZARD), there is limited information published in Australia on demographics of the intended parents and gestational carriers, treatment procedures, and associated pregnancies and birth outcomes. This national population study investigates the epidemiology of gestational surrogacy treatment and resulting pregnancy and birth outcomes in Australia during 2004 to 2011.

MATERIALS AND METHODS

Data

A retrospective population study was conducted of all gestational surrogacy arrangement cycles in Australia from 1 January 2004 to 31 December 2011. The research dataset of this study was extracted from the ANZARD. The ANZARD is a census of all initiated ART treatment cycles undertaken in Australia and New Zealand. Items on ANZARD are collected annually, in a de-identified format, from all fertility centres within Australia and New Zealand. The ANZARD includes information on both the ART treatment (oocyte pick-up, fertilization procedure, use of thawed embryos, blastocyst culture, embryo transfer, donation of gametes or embryos, and surrogacy arrangement) and resulting pregnancy and birth outcomes (birth status, gestational age, and birthweight).

Surrogacy cycles in this study were chosen based on a surrogacy flag in ANZARD. The final analysis included 169 intended parents cycles and 388 gestational carrier cycles during 2004 to 2011 with resulting pregnancy and birth outcomes between 2004 and 2012.

Definitions

Age of the gestational carrier and age of the female partner of the intended parents were in completed years at time of treatment. Parity was grouped as previous pregnancy of greater than 20 weeks (parous) versus no previous pregnancy (nulliparous). Embryo transfers were defined by the following: oocytes fertilized by in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI); fresh or cryopreserved; cleavage (day 2-3) or blastocyst (day 5-6) embryo; and number of embryos transferred (1 or ≥2).

A clinical pregnancy was defined as satisfying one of the following criteria: evidence by ultrasound of intrauterine sac(s) or fetal heart(s); examination of products of conception reveal chronic villi; an ectopic pregnancy that had been diagnosed laparoscopically or by ultrasound. A live delivery is a birth event in which one or more baby is liveborn of ≥ 20 weeks gestation or of ≥ 400 grams birthweight.

Statistical analysis

Descriptive statistics were generated for the gestational surrogacy cycles. Proportion of preterm birth (< 37 weeks of gestation) and low birthweight (< 2500 grams of birthweight) was calculated for liveborn babies following surrogacy treatment were presented. Adverse pregnancy and birth outcomes

were by number of embryos transferred was compared by Chi-square test. Data were analysed using the Statistical Package for Social Sciences (SPSS), version 22.

Ethics

This project was approved by the University of New South Wales Human Research Ethics Advisory Panel (Reference Number: 2011-7-03). Approval for use of the data was given by the Fertility Society of Australia.

RESULTS

There were a total of 557 surrogacy cycles during 2004-2011. These include 169 intended parents cycles and 388 gestational carrier cycles, with an average of 2.3 gestational carrier cycles per every intended parents cycle. Of the 557 surrogacy cycles, 56.2% (313) were from New South Wales, 26.0% (145) were from Australian Capital Territory. The remaining 17.8% (99) cycles were from Queensland, Victoria, South Australia and Western Australia. The number of surrogacy cycles increased from 34 in 2004 to 129 in 2011.

The age range of intended parents (females: 20 to 58 years; males: 26 to 70 years) compared to 22 to 45 years for gestational carriers. Over half (53.8%) intended parents cycles were in women aged less than 35 years, in contrast to less than 40% of gestational carrier cycles. The main cause of infertility of intended parents cycles was female only (45.0%), with 9.4% combined male-female, 16.6% unexplained and 29.0% where infertility was not stated. Over three quarters of intended parents cycles were of nulliparous women compared to 29.1% of gestational carrier cycles (Table 1).

Of the 169 intended parents cycles, 12 (7.1%) used donated oocytes. Husband or partner's sperm was used in all intended parents cycles.

Of the 388 gestational carrier cycles, 92.8% (360) had at least one embryo transferred. The mean number of embryos transferred was 1.4 and ranged from 1 to 3. Of embryo transfer cycles, 91.1% used cryopreserved embryos and 8.9% used fresh embryos. Single embryo transfers (SET) counted for 68.9% embryo transfer cycles (Table 2).

Of the 360 carrier embryo transfer cycles, 26.4% (95) resulted in a clinical pregnancy and 18.9% (68) resulted in at least one live delivery. Of the 110 double embryo transfer (DET) carrier cycles, 27 (24.5%) resulted in a clinical pregnancy and 21 (19.1%) in a live delivery. This was not significantly different from the 27.4% clinical pregnancy rate (p=0.57) and the 19.0% live delivery rate (p=0.99) of SET carrier cycles (68 clinical pregnancies and 47 live deliveries from 248 SET carrier cycles). The overall multiple delivery rate following gestational carrier cycles was 7.1% (5 twin deliveries and 65 singleton deliveries). There were no multiple births following SET compared to 22.7% for DET. The proportion of women giving birth by caesarean section in a gestational surrogacy arrangement was 47.1% (33 of 70 deliveries).

There were 73 liveborn babies following gestational surrogacy treatment including 9 liveborn twins. Of the 73 liveborn babies, 21.9% (16) were preterm and 13.7% (10) were low birthweight. Of the 47 liveborn babies following SET, 5 (10.6%) were low birthweight. In comparison, of the 26 liveborn babies following DET, 5 (19.2%) were low birthweight (p=0.31). Preterm birth was 12.8% for

liveborn babies following SET and 30.8% or liveborn babies following DET (p=0.07).

DISCUSSION

Surrogacy Australia estimates that more than 350 children have been brought back to Australia as a result of overseas gestational surrogacy arrangements in 2011.[5, 6] This is in stark contrast to the eight babies born on average per year through surrogacy arrangements in Australia between 2004 and 2010. Australian-based altruistic surrogacy is extremely rare accounting for 0.13% of all ART treatment cycles between 2004 and 2011 with an estimated utilization of 9 gestational carrier cycles per million women of reproductive age.

There is no federal legislation regarding gestational surrogacy arrangements in Australia and no national monitoring of outcomes for the gestational carriers and the infants born following surrogacy. In Australia, altruistic (uncompensated) surrogacy (the carrier does not receive any compensation beyond the reimbursement of medical and other reasonable expenses) is regulated at a state and territory level in Australia with seven jurisdictions having legislation.[7-13] State legislation also sanctions aspects of surrogacy arrangement such as ethics, eligibility, age limits, acceptance, compensation, safety, adoption for the recognition of the intended parents as the legal parents, and disclosure of the identity of the gestational carrier.[14]

This first national study details current surrogacy practice in Australia and the pregnancy and perinatal outcomes of surrogates. From 2004-2011, 388 altruistic gestational carriers cycles were performed in Australia, resulting in 360

embryos transfers, 95 clinical pregnancies, 68 live deliveries and 73 liveborn babies. The rates of clinical pregnancy (95/360, 26.4%) and live delivery (68/360, 18.9%) are comparable to the rates of autologous thaw cycles in Australian and New Zealand in 2011 (27.3% and 20.7% respectively).[4] The caesarean section rate (47.1%) is slightly lower than overall caesarean section rate in Australian and New Zealand in 2011 (49.5%).[4] Of the 73 liveborn babies in this study, the rates of preterm birth (21.9%) and low birthweight (13.7%) were slightly higher than the rates in Australian and New Zealand in 2011 (17.3% and 13.1% respectively). [4] However, there is no mechanism for national monitoring of the physical and psychosocial health and wellbeing of gestational carriers, intended parents and their offspring.

It is without doubt that the interests and safety of all parties in the surrogacy arrangement need to be paramount. In Australia, there is no national regulation to protect such interests and safety. Each State has its own legislation that differs considerably regarding eligibility, age limits, compensation, and safety. A recent study by Everingham et al. shows that State level legislations have many perceived barriers and stigma to using surrogacy arrangements in Australia.[6] As a result most couples consider or use compensated surrogacy arrangements overseas, mainly in the United States, India and Thailand.[6] As suggested by Everingham and colleagues, there is a need to review State level regulations, processes and requirements. A national approach to gestational surrogacy that ensures the interests and safety of all parties in the surrogacy arrangement and optimizes the perinatal outcomes should be supported.

There are a number of ethical issues that this study raise in relation to surrogacy arrangement and ART practice in Australia. Firstly, of the 200 gestational carrier cycles where parity was available, over one third were in nulliparous women. The literature shows that gestational carriers have potential risk of adverse maternal outcomes which would subsequently impact future pregnancies and family formation. [15, 16] Any risk to the gestational carriers and their potential for future family formation is ethically unacceptable. [16] It is not clear how these arrangements with nulliparous women were made. However, only two states in Australia, Victoria and Western Australia require carriers to have completed their desired family.[9, 11] Legislation and practice alike should be harmonized with Victoria and Western Australia to allow surrogacy only in parous women. [9, 11]

Secondly, this study found that, of gestational carrier cycles, 91.1% used cryopreserved embryos and 8.9% used fresh embryos. To avoid the potential risk of infectious disease transmitted to the carrier, it was recommend in Australia that all gametes to be transferred to a third person, should be cryopreserved.[17] The 91.1% of gestational carrier cycles using cryopreserved embryos are likely related with this recommendation. However, for the remaining 8.9% cycles where fresh embryos were transferred, we are unable to investigate why fresh embryos were used and how the potential risk of infectious disease was assessed. An ethical audit is needed to review how fresh embryos transfers were arranged.

Thirdly, this study found that the proportion of SET in gestational carrier cycles was 68.9% which is close to the 73.2% of SET cycles in Australia and New

Zealand in 2011 [4]. Interestingly, there is no difference in the clinical pregnancy rates between SET and DET in this study. However, this study found that of pregnancies where fetal hearts were detected, 20.8% (5 of 24) pregnancies following DET were twin pregnancies. This is significantly higher than the twin rate of 1.8% (1 of 57) for pregnancies following SET. Multiple pregnancies including twin pregnancies are the most notable complication following ART treatment, with demonstrated poorer perinatal outcomes, increased risk of maternal complications and a great socioeconomic burden on the parents and health care system.[17-21]

On the other hand, multiple pregnancies following ART treatment are preventable by reducing the number of embryos per transfer. [19, 20] Since gestational carriers usually do not have subfertility and the pregnancy rate of DET is the same as SET, this study advocates that transfer of a single embryo in all gestational carrier cycles to reduce the potential risk of pregnancy related complication of carriers. It would also improve perinatal outcomes of the babies and minimise the socioeconomic burden due to multiple pregnancy following transfers of multiple embryos. [17-21]

Finally, this study found that only five of the 388 gestational carrier cycles were in carriers aged less than 25 years. This reflects nationally consistent younger age limit for gestational carriers being 25 years or older, supported by the current State legislations of New South Wales, Victoria, Queensland, Western Australia and Tasmania that prevent surrogacy in young women.[7-9, 11, 12] Of note, 60% of gestational carrier cycles were in women aged 35 years or older compared to 50% of intended parents cycles. This disproportion might have

been related to that some clinics in Australia require a pre-existing relationship of at least three years between intended patients and gestational carriers. [22-25] It might also be explained by the circumstances that some mothers and older sisters carrying a pregnancy for their daughters and younger sisters respectively .[26-29]

In conclusion, this first national study reported a number of ethical issues in relation to eligibility criteria to gestational carrier and ART practice. It may be undesirable practices where more than 25% of gestational carrier cycles were in nulliparous women. In addition, that about 9% of gestational carrier cycles used fresh embryos without cryopreservation and quarantining raise ethical concerns. To avoid potential risk of infectious disease and multiple pregnancy for gestational carriers, this study suggests that transfer of single cryopreserved embryo should be advocated for in all gestational surrogacy arrangements.

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Table 1: Surrogacy arrangement in Australia

Characteristics	Intended Parents		Gestational Carrier	
	Number	**Per cent**	**Number**	**Per cent**
Age (years)				
< 25	7	4.1	5	1.3
25-30	21	12.4	36	9.3
30-34	63	37.3	105	27.1
35-39	43	25.4	139	35.8
≥40	35	20.7	103	26.5
Cause of infertility				
Male only	---	---	---	---
Female	76	45.0	---	---
Combined female/male	16	9.4		
Unexplained	28	16.6	---	---
Not stated	49	29.0	---	---
Parity				
Nulliparous	130	76.9	113	29.1
Parous	23	13.6	180	46.4
Not stated	16	9.5	95	24.5

Table 2: ART treatment procedures gestational carrier cycles compared with embryos transferred

ART procedures	Carrier cycles	
	Number	**Per cent**
Fresh/Thaw		
Fresh	32	8.9
Thaw	328	91.1
Type of fertilization		
IVF	196	54.4
ICSI	101	28.1
Missing	63	17.5
Stage of embryos		
Cleavage	173	48.1
Blastocyst	187	51.9
Number of embryos transferred		
1	248	68.9
≥ 2	112	31.1

Table 3: Pregnancy outcomes of gestational carrier cycles by number of embryos transferred

ART procedures and outcomes	Single embryo transfer	Double embryo transfer	Total
Embryo transfer cycles	248	110	360*
Clinical pregnancies	68	27	95
Deliveries	48	22	70
– Singleton deliveries	48	17	65
– Twin deliveries	0	5	5
Live deliveries	47	21	68
Number of babies	48	27	75
Number of liveborn babies	47	26	73
Clinical pregnancy rate	*27.4*	*24.5*	*26.4*
Live delivery rate	*19.0*	*19.1*	*18.9*
Multiple delivery rate	*0.0*	*22.7*	*7.1*

* Include cycles where 3 or more embryos were transferred.