Gestational surrogacy in the Czech Republic

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Background. Gestational surrogacy, is a treatment option for women with certain clearly defined medical problems, usually an absent uterus, to help them have their own genetic children. The aim of our study was to review, evaluate and share our experience and outcomes over the last 13 years of the largest surrogacy program in the Czech republic.

Methods. A total of 75 intended mothers and 82 surrogate mothers participated in this study. A retrospective cohort study was performed. Anonymized data were collected on 130 cycles of gestational surrogate (2004-2017) directly from the Clinic database.

Results. We performed 130 in vitro fertilization cycles with gestational surrogacy which involved 73 fresh embryo transfers and 57 frozen embryo transfers. We achieved 57 (43.9%) pregnancies and 42 (32.3%) live births. The rate of multiple pregnancies was only 2.3 %. The most common indication for using was an absent or damaged uterus (65%), followed by medical conditions precluding pregnancy (23%) and repeated in vitro fertilization cycles or pregnancy failure (12%).

Conclusion. In the 14 years of our experience, we have shown that treatment of young women with specific indications for gestational surrogacy is beneficial, successful and relatively free of complications. However, it is imperative to follow the medical indications for this treatment and specialist recommendations.

Key words: gestational surrogacy, surrogate mother, intended parents, pregnancy rate, live birth rate

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INTRODUCTION

Gestational surrogacy, whereby the child is conceived using the egg of an intended mother and the sperm of an intended father and the resulting embryo is transferred to the uterus of a surrogate mother, is a recent phenomenon. It was introduced only after the first in vitro child was born. Introduction of egg donation in 1983 in particular paved the way for this form of surrogacy¹. The first successful gestational surrogate pregnancy involving in vitro assisted reproductive technology (ART) was reported by Utian et al. in 1985 (ref.²).

Gestational surrogacy (GS), otherwise known as "In vitro fertilisation (IVF) surrogacy" or "full surrogacy" is a treatment option for women with certain clearly defined medical problems to help them have their own genetic children³. The indications for treatment by GS have involved over time. When surrogacy programs were initiated, the prime indication for GS was for women who had had a hysterectomy^{2,4,5}. It was later became apparent that success also could be achieved for women with Mayer-Rokitansky-Küster-Hauser syndrome^{6,7}. Afterwards, women with repeated IVF failures and those with recurrent abortions were also considered suitable for treatment by GS (ref.⁸). With increasing experience and use of GS as a

treatment option, the number of indications has increased over the last 30 years⁹. Women suffer from severe medical conditions that would cause childbearing to threaten the health or life of the recipient are also indicated for the use of GS. The largest reported series from Canada reviewed the outcomes of 333 consecutive GS cycles carried out between 1998 and 2012. They list thirty specific medical indications for GS (ref.¹⁰). The most significant recent addition to the indications for surrogacy has been for same-sex male couples who wish to have families of their own¹¹. In the Czech Republic current law prohibits ART including surrogacy for same-sex couples¹².

Treatment by GS involves routine IVF procedures for the intended mother, with the transfer of fresh or frozen-thawed embryos to the surrogate host. Surrogate mother (SM) is a woman who carries and delivers a child for another couple and who agrees that the child can be adopted. Thus surrogate hosts the pregnancy but does not have a genetic connection to the child¹.

The results of treatment using GS are good, clinical pregnancy rates achieved in large series are up to 40% per transfer³.

But surrogacy is not without its difficulties. From the medical point of view, this is not a complicated treatment, but from an ethical, legal and social point of view, it is the

most controversial form of assisted reproduction, with a number of pitfalls for intended parents, surrogate mother, and last but not least for the child¹³.

Although uncommon, the SM may change her mind and decide to keep the child. Intended parents (IPs) may also change their mind and the child might be abandoned by them in the case of unexpected complications or birth defects. In many Western countries surrogacy practice has been made illegal because of concern for the SM. There have been worries about the possibility of exploitation or coercion of women to act as gestational carriers^{14,15}.

The most important concern related to surrogacy treatment is anxiety about possible harmful medical and psychological consequences for the child. A large systematic review has shown that the perinatal outcome of the children is comparable to standard IVF and oocyte donation and there is no evidence of harm to the children born as a result of surrogacy¹⁶. The findings from the studies of surrogacy that currently exist, indicate that families formed in this way are generally functioning well, suggesting that the absence of a gestational link between the parents and the child does not jeopardize the development of positive family relationships or positive child adjustment¹⁷⁻²¹.

Our clinic has been dealing with GS since 2004. In the Czech Republic surrogacy is not regulated by law but also not prohibited. In 2012, the Committee for Assisted Reproduction (CAR) of the Czech Gynaecological and Obstetrical Society approved the guidelines according to which individual IVF centers should proceed in the treatment of infertility with the use of surrogacy²². Surrogacy is an ART procedure reserved for medical indications only. For social reasons it is unacceptable. In accordance with the recommendations of an International Federation of Gynecology & Obstetrics (FIGO) Committee report, only gestational surrogacy is acceptable at this time. The autonomy of the SM should be respected at all stages, including any decision about her pregnancy, which may conflict with the commissioning couple's interest. Surrogacy arrangements should not be commercial. The choice of the SM is of the highest importance for the successful outcome of the treatment¹⁶. To minimize the medical risks to the SM, criteria were established which follows the latest recommendations drawn up by specialist groups in ESHRE, ASRM and FIGO (ref.²³⁻²⁵). To avoid unnecessary endangerment of the health of the surrogate and the future child it is strongly recommended that only one embryo at a time is transferred to the surrogate²³. A legal contract signed by all parties after obtaining independent legal advice, a thorough psychosocial assessment and counselling regarding all types of issues is essential and is mandatory in our program.

The purpose of our study was to evaluate and share our experience over the last 14 years with 130 GC cycles that were performed in the Clinic of Reproductive Medicine and Gynecology in Zlin. This represents, to our knowledge, the largest GS program in the Czech Republic.

MATERIALS AND METHODS

Subjects

A total of 75 intended mothers and 82 surrogate mothers participated in this study. A retrospective cohort study was performed. Anonymized data were collected regarding 130 cycles of gestational surrogate (2004-2017) directly from the IVF Clinic database. This study was approved by the Ethics Committee of the IVF Clinic.

The intended parents are responsible for recruitment of surrogate mothers. The IVF clinic has never been involved in this process. All surrogate mothers were examined and consulted according to CAR (Committee of Assisted Reproduction) recommendations²². A cycle coordination was achieved by the use of GnRH analogue. Surrogate mother receptivity preparation is carried out using oral estradiol to build up the endometrial lining, followed by progesterone administered by vaginal capsules. Embryo transfer was carried out 5 days after oocyte retrieval. Ovarian stimulation of the intended mother before oocyte retrieval was performed using a short protocol with GnRH antagonists.

Statistical analysis

Data from 130 IVF were analyzed for 73 fresh embryo transfers and 57 frozen embryo transfers. Categorical variables were expressed as number (n) and percentage of occurrence (%). Continuous variables were expressed as means $\pm$ standard deviation (SD). Odds ratio and Fisher exact test were computed to estimate the association of two binary variables and Pearson chi-square test was used to test association for a non-binary categorical variable. The significance level for hypothesis rejecting was 0.05 and statistical software SAS 9.3 (SAS Institute Inc., Cary, NC, USA) was used for all analysis and graphs.

RESULTS

We performed 130 IVF cycles with GS which involved 73 fresh embryo transfers and 57 frozen embryo transfers. We defined a cycle as a transfer of fresh or frozen-thawed embryo into the uterus of the surrogate mother. Our study included 75 intended mothers and 82 surrogate mothers. The difference between the number of intended mothers and surrogate mothers was due to the fact that some intended mothers underwent treatment using GS repeatedly with more than one surrogate mother to achieve pregnancy. Of these 130 cycles, we achieved 57 (43.9%) pregnancies, 15 resulted in a miscarriage (11.5%) and 42 (32.3%) resulted in a live birth. As is shown in Table 1, no statistically significant differences in results were found between fresh embryo transfer and frozen-thawed embryo transfer. The rate of multiple pregnancies was only 2.3% in our study. The elective single-embryo transfer (eSET) took place in our program in the last 7 years.

The indications for a GC were divided into three groups. Group 1 included the women without a uterus or with uterine damage (Table 2). This group consisted of

Table 1. Pregnancy, miscarriage and live birth rates in our gestational surrogacy program.

Embryo transfer	n	Pregnancy n (%)	Live birth n (%)	Miscarriage n (%)
Fresh embryo transfer	73	34 (46.57)	26 (35.62)	8 (10.95)
Frozen-thawed embryo transfer	57	23 (40.35)	16 (28.07)	7 (12.28)
Total	130	57 (43.85)	42 (32.31)	15 (11.53)
odds ratio (95% CI) fresh vs frozen		1.29 (0.64; 2.60)	1.42 (0.67; 3)	0.88 (0.3; 2.59)
<i>P</i>		0.593	0.45	1

Odds Ratio and 95% confidence interval is estimated.

Table 2. Distribution of the ET+KET, pregnancy, delivery and abortion grouped based on the diagnose.

Medical indications for GS	n	Total ET+KET	Pregnancy	Delivery	Abortion
<i>P</i>			0.846	0.955	0.748
Group 1:					
Mayer-Rokitansky-Küster-Hauser syndrome	13	27	10	8	2
Hysterectomy for cervical carcinoma	9	17	8	5	3
Hysterectomy for postpartum bleeding	9	12	5	4	1
Hysterectomy for hypochromic anaemia	1	2	1	1	0
Hysterectomy for teratoma	1	1	1	1	0
Hysterectomy for postpartum sepsis	1	1	0	0	0
Hysterectomy for hematometer	1	1	1	1	0
Hysterectomy for myomatosis	3	7	2	1	1
Hysterectomy for pelveoperitonitis	1	2	1	1	0
Hysterectomy for adenomyosis and metrorrhagia	1	2	1	1	0
Status after repeated Section Caesarea	3	7	2	1	1
Myomatosis gravis	4	7	5	3	2
Asherman's syndrome	2	5	1	1	0
Total	49	91	38	28	10
Group 2:					
Diabetes mellitus 1	2	4	2	2	0
Status post renal transplantation	4	5	2	1	1
Status post hepatic transplantation	1	1	1	1	0
Sclerosis multiplex	1	2	1	1	0
Chronic renal disease	1	2	0	0	0
Lupus erythematosus	2	2	1	0	1
Immunological disease	1	3	1	0	1
Status post treatment of breast cancer	1	1	1	0	1
Astrocytoma brain tumour	1	3	1	1	0
Dilated cardiomyopathy (DCM)	1	1	1	1	0
Testicular feminization syndrome	1	1	1	1	0
Rh incompatibility	1	2	1	1	0
Total	17	27	13	9	4
Group 3:					
Unsuccessful repeated IVF	2	4	1	1	0
Repeated pregnancy failure	7	8	5	4	1
Total	9	12	6	5	1

Group 1 consists of patients without uterus or with uterine damage. Group 2 consists of patients that have disease with contraindication of pregnancy. Group 3 consists of repeated failure IVF or repeated pregnancy failure. Pearson chi-square tests were used to compare relationships between group

In line with the recommendations of the CAR all surrogate mothers were at least one child in our study²². More than half of them were under the age of 30 years (n=42, 51.2%). The basic characteristic of the SMs are shown in Table 3.

Table 3. The background characteristics of the surrogate mothers.

Characteristics of the SMs	Groups	n	%
Marital status	Single	38	46.3
	Married	33	40.2
	Divorced	11	13.4
Children	1 child	36	43.9
	2 children	32	39.0
	3 or more children	14	17.1
Age	Age under 30 years	42	51.2
	Age from 30 to 35 years	21	25.6
	Age over 36 years	20	24.4

49 patients (mean age 35.16; SD=4.46) who completed 91 embryo transfers. Hysterectomy was the most common indication for using a GC (27 cases), followed by MRKH syndrome (13 cases), myomatosis gravis (4 cases), status post repeated Caesarean section (3 cases) and Asherman's syndrome (2 cases). Reasons for hysterectomy are listed in the Table 2. In this group, we achieved 41.8% clinical pregnancy rate (CPR) and 30.8% live birth rate (LBR) per embryo transfer (no cases involved oocyte donors).

Group 2 included the women with medical conditions precluding pregnancy. This group consisted of 17 patients (mean age 33.35; SD=5.06) with different diseases. A list of all diagnoses are summarized in table 2. We performed 27 embryo transfers in this group, in two cases we used oocytes from an oocyte donor (breast cancer, testicular feminization syndrome). 48.1% CPR and 33.3% LBR per transfer were achieved.

Group 3 included repeated IVF failure or repeated pregnancy failure. This group involved only 9 patients (mean age 38.67; SD=4.03) who underwent 12 embryo transfers, in four cases we use donated oocytes. In this group, we had 50% CPR and 41.7% LBR per transfer.

DISCUSSION

The intended mothers

Surrogacy is a highly debated method mainly used for treating women with infertility caused by uterine factors¹⁶. For those women, it is often a tremendous opportunity for family building.

Satisfactory pregnancy and delivery rates per IP and per SM are generally being achieved, as would be expected from the transfer of embryos derived from young women and transferred to fit, fertile women who are also young³. In GS programs, the clinical pregnancy rate per embryo transfer has been reported as being between 19 and 33%, with between 30 and 70% of the couples succeeding in becoming parents as a result of the arrangement^{4,6,10,16,26-29}. In our study the CPR was 43.9% per embryo transfer and 56% of the intended couples have become parents through this treatment. The live birth rate are comparable to conventional IVF (ref.²⁵). The newest retrospective cohort

study compared clinical outcomes of IVF cycles with the use of GC (24,269) and non-GC IVF cycles (1,313,452). The highest LBR occurred when the indication for GC was uterine factor infertility³⁰.

In our study, 49 of the 75 intended mothers (65.3%) underwent treatment with GS due to uterine factor infertility (congenital or acquired absence of a functioning uterus, Asherman's syndrome or significant structural abnormalities or uterine damage).

The most common indication for using a GC in our study was hysterectomy. The loss of the uterus prior to having children or completing family could have a significant adverse effect on the lives of most women⁴. Young fertile women with normally functioning ovaries might lose their uterus in connection with serious obstetric complications, such as intra- or post-partum heavy bleeding or rupture of the uterus. Medical diseases of the uterus, most often cervical cancer or uterine leiomyoma in many cases with severe menorrhagia will also lead to hysterectomy and uterine infertility. A UK series, in which all the female partners of the intended couples had had a hysterectomy, achieved a CPR 37.5% per embryo transfer⁴. We had 27 patients after hysterectomy, they underwent 45 stimulation cycles, including fresh and frozen embryo transfers with GS, 15 newborns (only singletons) were delivered. We achieved 44.4% (20/45) CPR and 33.3% (15/45) LBR per embryo transfer.

Patients with MRKH syndrome lack a functional uterus at birth. But when treated by IVF and GS they have a fair chance of achieving a live birth. Recently a comprehensive review of published research was conducted, on the reproductive potential of patients with MRKH syndrome using IVF with GS (ref.⁷). The 14 studies included in this review were published between 1988 and 2011. From a cohort of 140 patients with MRKH syndrome, only four studies contained data on more than 10 patients^{26,28,31,32}. The available data from these studies allowed the following calculations to be made: 22.7% CPR and 18% LBR per transfer. In our study 13 patients with MRKH underwent 27 cycles of IVF with GS and 9 newborns were delivered (in one case twins). We achieved 37% (10/27) CPR and 29.6% (8/27) LBR per transfer. As patients with MRKH syndrome have no alternative but to conceive using assisted reproduction techniques,

they will seek treatment at a relatively young age⁷. That could explain why patients with MRKH syndrome were the youngest group in our series; mean age 31.9 year.

Until recently, successful transplantation of a uterus to a woman with MRKH syndrome or who had had a hysterectomy was an aspiration and dream that, despite attempts by many researchers over the years, had not been successful. However Brännström et al. in 2015 reported the first birth of a healthy baby following uterus transplantation in a 35-year-old woman, using the uterus of a living 61-year-old woman³³. This success was achieved after at least 11 other attempts worldwide. Even though several healthy children have been born from donated transplanted wombs and the acceptance of uterus transplantation as infertility treatment for women with uterine factor of infertility is high, the procedure still remains in its infancy³⁴. The process of uterus transplantation is not without its ethical controversy either. It would be safer for the uterus donor to act as a surrogate rather than undergo the big operation that is much more extensive than a standard hysterectomy. This solution also would be more economical for society in general. In addition, the side effects of immune suppression in the recipient, such as increasing risk of infection and tumors, could be avoided. This aside, the overwhelming majority of surveyed women in the United Kingdom, a country which permits surrogacy, preferred transplantation of uterus over GS and adoption³⁴. We can anticipate that when transplantation of the uterus becomes more available and successful, then the demand for GS will become less in the future.

But surrogacy still remains the only option for having a biological child for women with severe medical conditions where pregnancy could pose a significant health risk or maternal medications used to treat a disease, which are, or could potentially be, teratogenic.

This treatment should be provided only when the intended mother is healthy enough to take care of a child after birth and that her life expectancy is reasonable³. We treated 17 patients with different medical co-morbidities precluding pregnancy. They underwent 27 cycles with GS and 10 newborns were delivered (in one case twins). We achieved 48.1% (13/27) CPR and 33.3% (9/27) LBR per transfer.

GS may be considered for couples with repeated unexplained IVF failures despite retrieval of good-quality embryos or for couples with repeated miscarriages²⁵. We did not have many patients with this indication. For these women the treatment of first choice is their own IVF with donated oocytes. Only 9 women with these indications were treated using GS and 6 newborns were delivered (in one case twins); 50% (6/12) CPR and 41.7% (5/12) LBR were achieved. Our results in this group of patients are comparable with the largest study on outcomes of GS (ref.¹⁰). They also reported 50% CPR and 34.8% LBR in a group of patients with recurrent implantation failure and previous poor pregnancy outcomes. In four of cases donated oocytes were used.

The surrogate mothers

Surrogacy implies that a woman becomes pregnant and gives birth to a child with the intention of giving the child away to another person or couple, commonly referred to as the intended parents²³. The IPs are responsible for recruitment of SMs. In most cases they were found using the internet. In only four cases, the SM was a sister of intended mother in our study.

According to the recommendations of the CAR, a SM should be between the age of 21 and 35 years and she should have at least one child. Her previous pregnancies must have been full-term and uncomplicated. Women, who have had previous adverse obstetric outcomes should not be accepted. The pregnancy history of the surrogate candidate may be more predictive of obstetric complications than her age³⁵. In our study all SMs had at least one child, more than half of them were under the age of 30 years ($n=42$, 51.2%). We have no serious maternal complication in accordance with other studies^{10,16,27}. This relatively low rate of maternal complications is consistent with the fact that all SMs were multiparas and they had no significant complications in prior pregnancies¹⁰. Furthermore, as the risk of almost all maternal complications is increased by multiple pregnancies, elective single-embryo transfer took place in our program in the last 7 years. The rate of multiple pregnancies was 2.3% in our study. A systematic review reported 2.6-75% of multiple pregnancies in surrogacy programs¹⁶.

One reason for regarding surrogacy as problematic and controversial is the risk of dispute between the surrogacy mother and the intended parents as to the custody of the child.

We have no cases in which surrendering the child was problematic after birth. Surrogate mothers generally report being satisfied with their experiences³⁶. Follow-up studies have shown that there were no significant difficulties for the SMs in handing over the children to the IPs and that surrogates do not suffer any long-term psychological harm^{10,36-39}.

CONCLUSION

Gestational surrogacy offers an alternative way for a small group of women to have their own genetic children. In the 14 years of our experience we have shown that treatment of young women with specific indications for treatment with GS is beneficial and relatively free of complications. The surrogacy program has been successfully implemented and has become an integral part of the treatment of some causes of infertility. However, it is imperative to follow the medical indications for this treatment and follow the recommendations of expert groups. Careful counselling of all parties involved is essential. Also close cooperation between the medical, legal and social professionals is a prerequisite for satisfactory results in the vast majority of cases.

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