Obstetric and Perinatal Outcomes of Singleton Pregnancies After in-vitro Fertilization in Siriraj Hospital, A Matched Case-Control Study

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ABSTRACT

Objective: To compare obstetric and perinatal outcomes between singletons born after IVF and natural conception.

Methods: A total of 141 singleton pregnancies conceived by IVF were included. Another 141 singleton pregnancies conceived naturally were randomly selected as comparison group, matched by age. Data were retrospectively extracted from medical records, including baseline characteristics and delivery data. Various characteristics, including pregnancy and neonatal outcomes were compared between groups.

Results: Women in IVF group were more likely to be nulliparous and had previous miscarriage (88.7% vs. 76.6%, 0=0.003; and 26.2% vs. 14.8%, p=0.018, respectively). Underlying diseases and complications during pregnancy were comparable between the 2 groups. Mean gestational age was lower in IVF group (37.9 ± 2.0 vs. 38.4 ± 1.6, p=0.008), but without clinical significance. Primary cesarean section was significantly more common among women in IVF group (74.4% vs. 54.6%, p<0.001) and the majority were elective cases (61.9% vs. 23.4%, p<0.001). There were no significant differences in terms of rates of preterm labor, birth weight, low birth weight, small for gestational age, neonatal intensive care unit admissions, and perinatal mortality.

Conclusion: Singleton pregnancies after IVF were not associated with higher risks of adverse obstetric and perinatal outcomes, compared with naturally conceived group, but IVF pregnancies are associated with a high rate of cesarean sections.

Keywords: IVF; Natural conception; pregnancy outcomes; neonatal outcomes; cesarean (Siriraj Med J 2018; 70: 233-237)

INTRODUCTION

Since the first successful birth after in vitro fertilization and embryo transfer (IVF/ET) reported in England in 1978, the number of babies resulting from the assisted reproductive technology (ART) has increased all over the world.[1] At first, IVF was developed for the woman with tubal problem (blocked or damaged fallopian tube), but now it is the treatment of choice for other causes of infertility that are refractory to more conservative treatment.[2,3] Although most pregnancies after IVF result in normal and good outcomes, many studies reported the higher rates of the cesarean section, preterm birth, low birth weight (LBW) and poor perinatal outcomes compared with general population.[4]

Recently, there were a great number of women that had a tendency to be married and desire for pregnancy at older age. The infertility rate among that group seems to have increased. This, in turn, raises the demand for

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infertility treatment especially assisted reproduction technology. Maternal factors related to infertility are also independently associated with adverse obstetrical outcomes. For example, advancing maternal age is associated with both declining fertility and multiple adverse outcomes of ongoing pregnancy.[5] A higher incidence of obstetric complications of advanced maternal age pregnancies, including pregnancy induced hypertension (PIH), gestational diabetes (GDM), placenta previa and abnormal labor patterns, has been reported.[6,7] This observation is likely related to the underlying progressive vascular endothelial damage that occurs with aging.[7] This is of lesser parity than the average gravida, so IVF pregnancies are more likely to deliver by cesarean section.[8]

In Siriraj Hospital, the rate of IVF treatment has increased year by year. Obstetric and perinatal outcomes of the IVF pregnancies, regarding the association with adverse outcomes, are always of concern. The aim of our study was to compare obstetric and perinatal outcomes between singletons born after IVF and natural conception.

MATERIALS AND METHODS

The study was approved by the Institutional Review Board of Siriraj Hospital (Si 515/2014). 141 singleton pregnancies conceived naturally or by IVF from July 2006 to December 2013, and delivered at Siriraj Hospital were enrolled. In IVF pregnancy group, the indication for IVF included male factor, tubal factor, and peritoneal factor (e.g. pelvic endometriosis, pelvic adhesion). The analysis included only pregnancies leading to live births (less than 500 grams of birth weight).

The IVF and naturally conceived group were matched 1:1 for age (±2 years) and time of delivery (within same day). They were treated by the same obstetric service. All the data regarding the examinations, hospitalization, delivery and discharge were kept in the standardized medical records. All newborns received physical examination after birth and all abnormalities were noted. The gestational age of IVF group was calculated by adding 14 days to the day of the oocyte retrieval; while for the spontaneous conception, it was estimated based on the last menstrual period or the first ultrasound results. Retrospective chart review was performed. Data of the maternal complications during antenatal and intrapartum period, gestational age, mode of delivery, perinatal mortality and neonatal outcomes were collected.

Data were analyzed using SPSS ver. 17.0 (An IBM Company). The statistical significance of differences was assessed by chi-square test and unpaired t-test. A p-value of < 0.05 was considered statistically significant.

RESULTS

Maternal characteristics

The mean maternal age was similar in both groups (Table 1). The frequency of nulliparity in the IVF group was significantly higher than that in the spontaneous conceived group (88.7% vs. 76.6%, P = 0.015). Poor outcome of previous pregnancy was more frequent in the IVF group (P = 0.018). There were no significant differences in pre-gestational underlying disease.

Obstetric complications

There were no statistically significant differences in the obstetric complications between the IVF and the spontaneous conceived groups (Table 2). The rates of GDM, PIH, anemia, preterm labour, preterm PROM and intrauterine growth retardation (IUGR) were similar in both groups.

Labor and delivery characteristics

Mean gestational age at delivery was significantly lower in IVF group (37.9 ± 2.0 vs. 38.4 ± 1.6; P = 0.008), although there was no clinical significance. Normal vaginal delivery was found in significantly fewer patients in the IVF group. This was attributed mainly to the significantly higher primary cesarean section, as well as the elective cesarean section rate, in the IVF group compared with the control group (Table 3).

Neonatal outcome

No differences were noted between the IVF and spontaneous conceived groups in terms of mean birth weight, the incidence of very low birth weight (< 1,500 g) and low birth weight (1,500-2,500 g) (Table 4). The frequencies of SGA, asphyxia and neonatal intensive care admissions were also not significantly different.

DISCUSSION

The present study showed the IVF outcomes of singleton pregnancy compared with natural conceived baby in Siriraj Hospital, Thailand. The results in the study revealed that IVF pregnancies were mostly primiparous and have history of a poor pregnancy outcome as shown in previously reports.[4,9,10] These characteristics were associated with obstetric risk and adverse outcome leading to the explanation of the different outcome between IVF groups and natural conceived groups.[11] Several literatures have reported controversial data regarding the rate of obstetric complications during pregnancies.[12,13] Some studies that have similar findings showed that IVF pregnancies did not increase risk for most obstetric complications such

TABLE 1. Maternal characteristics between IVF and Spontaneous pregnancies.

Characteristics	IVF (N=141)	Spontaneous (N=141)	P value
Mean maternal age ± SD (years)	34.5 ± 3.6	34.1 ± 3.6	0.400
Nulliparous	125 (88.7%)	108 (76.6%)	0.015
Outcome of previous pregnancy			
Miscarriage	37 (26.2%)	21 (14.9%)	0.018
Pre-gestational underlying disease			
Chronic hypertension	3 (2.1%)	3 (2.1%)	1.000
Pre-gestational DM	0 (0%)	2 (1.4%)	0.156

TABLE 2. Antepartum complications between IVF and spontaneous pregnancies.

Characteristics	IVF (N=141)	Spontaneous (N=141)	P value
GDM			
GDMA1	11 (7.8%)	9 (6.4%)	0.643
GDMA2	1 (0.7%)	2 (1.4%)	0.562
Pregnancy-induced hypertension			
Gestational hypertension	4 (2.8%)	1 (0.7%)	0.176
Preeclampsia	1 (0.7%)	1 (0.7%)	1.00
Anemia	0 (0%)	1 (0.7%)	0.316
Preterm labor	16 (11.3%)	14 (9.9%)	0.699
Preterm PROM	4 (2.8%)	6 (4.3%)	0.520
IUGR	4 (2.8%)	1 (0.7%)	0.176

TABLE 3. Labor and delivery characteristics between IVF and spontaneous pregnancies.

Characteristics	IVF (N=141)	Spontaneous (N=141)	P value
Mean gestational age at delivery ± SD (weeks)	37.9 ± 2.0	38.4 ± 1.6	0.008
Gestational age at delivery			
< 34 weeks	6 (4.3%)	2 (1.4%)	0.333
34 – 36 weeks	10 (7.1%)	12 (8.5%)	
≥ 37 weeks	125 (88.7%)	127 (90.1%)	
Route of delivery			
Vaginal delivery	18 (12.8%)	53 (37.6%)	<0.001
Repeat cesarean section	18 (12.8%)	11 (7.8%)	0.085
Primary cesarean section	105 (74.4%)	65/105 (61.9%)	<0.001
Elective cesarean section	77 (54.6%)	18/77 (23.4%)	<0.001
Postpartum hemorrhage	4 (2.8%)	2 (1.4%)	0.684

TABLE 4. Neonatal outcomes between IVF and spontaneous pregnancies.

Characteristics	IVF (N=141)	Spontaneous (N=141)	P value
Mean birth weight ± SD (g)	3,008.6 ± 571.5	3,030.5 ± 452.7	0.721
Birth weight			
<1,500 g	3 (2.1%)	0 (0%)	0.145
1,500-2,500 g	14 (9.9%)	10 (7.1%)	
>2,500 g	124 (87.9%)	131 (92.9%)	
SGA	5 (3.5%)	2 (1.4%)	0.447
Birth asphyxia	1 (0.7%)	2 (1.4%)	0.562
NICU admission	5 (3.5%)	6 (4.3%)	0.758
Sex ratio (Male:Female)	1.01	0.99	0.905

as PIH, GDM, preterm birth, PPROM and IUGR.[12-15] This may be due to our matching method and the same treatment protocols in the university hospital. On the other hand, there is a study which found that various gestational complications occurred more frequently in IVF group.[16] One can speculate that the intense surveillance and careful monitoring of IVF pregnancies may have resulted in the higher rate of diagnosis of complications, whereas it remained undetected among spontaneous conceived group.

The authors found that the rate of preterm delivery, low birth weight and perinatal outcomes in IVF and spontaneous conceived groups were similar, and the results of preterm delivery rate and low birth rate in the study were compatible with previous study of preterm delivery in Siriraj Hospital (9-13%) and low birth weight rate of Thailand (8.1%).[17] This was opposed to the research which reported the increased prematurity and low birth weight after IVF compared to the general population.[12,14,18] However, there was also a study which was consistent with our results.[9] In that detailed analysis, it revealed that the trend toward an increased prematurity rate after conceived IVF mainly resulted from a non-significantly increased incidence of preterm cesarean sections, rather than premature spontaneous deliveries. Various obstetric complications were managed in IVF group by cesarean sections in the preterm period.[19] In Siriraj Hospital, the survival rate of premature infants has increased due to the establishment of obstetric and newborn care team including excellent equipment and well-trained neonatologists which result in the good outcome of premature newborns. This, therefore, was a possible explanation of similar perinatal outcomes of both groups. However, there were 2.1% of VLBW in the IVF group while there was no incidence of VLBW in the spontaneous conceived group. Although the number of SGA and IUGR were not significantly different between the groups, the frequencies of IUGR and SGA in IVF groups were 4 and 2-fold higher than that of the naturally conceived groups, respectively. A larger sample size may be required in future study to clarify these.

The incidence of cesarean section was higher in the IVF group than in the comparison group. Similar results have been reported in many studies.[20,13] Although the repeated cesarean section was excluded, the rate of primary cesarean section remained statistically significantly higher among the IVF pregnancies compared with spontaneous conceived pregnancies. The higher frequency in the IVF group is explained by the increase in elective cesarean section due to minimized maternal complication during the late term pregnancy or post term pregnancy. The high cesarean section rate in spontaneous conceived pregnancies (about 31% excluded elective C/S) was found with uncertain reason. Nevertheless, it is consistent with previous study that reported a trend in methods of delivery[21] and is now far beyond the rate suggested by WHO.

There are advantages of this study, the obstetric outcome of IVF patients from a single unit was compared with that of spontaneous conceived group with matching and included only singleton pregnancies to avoid the possible confounding effects of multiple pregnancies.

The limitations of the study are small sample size and we cannot record all data of every IVF patient because they have delivered in another hospital.

In conclusion, after matching the maternal age, location and date of delivery, the risk of preterm birth, low birth weight and poor perinatal outcomes, as well as obstetric complication were not associated with IVF. However, there were some poorer outcomes in the IVF group. Thus, may require a larger sample size and further research to evaluate the factors that affect the outcome of babies born after IVF.

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