

## Original Article

# Obstetric outcomes of elderly primiparous singleton pregnancies conceived by *in vitro* fertilization compared with those conceived spontaneously

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**Aim:** To examine the obstetric outcomes of elderly primiparous singleton pregnancies conceived by *in vitro* fertilization (IVF) compared with those conceived spontaneously.

**Methods:** Data were collected from primiparous women aged 35 years and older with a singleton pregnancy conceived by IVF ( $n = 89$ ) or spontaneously ( $n = 849$ ). Data included antenatal data, gestational age at delivery, obstetric complications, such as pregnancy-induced hypertension, gestational diabetes, placental previa and placental abruption, mode of delivery, birth weight, fetal demise and the Apgar score at 1 min.

**Results:** The elective Cesarean rate in pregnancies following IVF was significantly higher than that in the control group ( $P = 0.014$ ). However, there were no significant differences in obstetric outcomes between the two groups.

**Conclusions:** The current results did not support the IVF-related risks of elderly primiparous singleton pregnancies. (Reprod Med Biol 2007; 6: 219–222)

**Key words:** elderly primiparae, *in vitro* fertilization, obstetric outcomes.

## INTRODUCTION

RECENTLY, SOME SUFFICIENTLY sized and appropriately performed studies have examined the influence of assisted reproductive technology (ART) on singleton pregnancies.<sup>1–4</sup> Although the great majority of singleton ART pregnancies are uncomplicated, recent evidence has suggested higher rates of adverse outcomes in singleton ART pregnancies compared with spontaneously conceived pregnancies. In 2004, for example, Jackson *et al.*<sup>2</sup> reported that women with *in vitro* fertilization (IVF)-conceived singletons are at increased risk of perinatal complications, such as pregnancy-induced hypertension, preterm birth, low birth weight infants and placenta previa. In addition, in 2005, Shevell *et al.*<sup>3</sup> observed that there is an increased incidence of abnormal placentation in IVF pregnancies, including a 2.4-fold increased relative risk of placental abruption and a 6.0-fold increased relative risk of placenta previa, com-

pared with spontaneous pregnancies. In 2007, the same tendency was also reported from one of the largest hospitals in Japan, that is, that the incidence of placenta previa and placental abruption in pregnancies following IVF are significantly higher than those in spontaneous pregnancies.<sup>5</sup> However, some limitations, such as a bias in maternal age, have been associated with these studies. Although women treated by IVF tend to be 'elderly' primiparae, who are known to be in a high-risk group,<sup>6</sup> obstetric outcome data comparing IVF pregnancies in elderly ( $\geq 35$  years of age) women with pregnancies conceived spontaneously are limited. In the present study, therefore, we examined the obstetric outcomes of elderly primiparous singleton pregnancies conceived by IVF compared with those conceived spontaneously.

## MATERIALS AND METHODS

THE PROTOCOL FOR this study was approved by the Ethics Committee of the Japanese Red Cross Katsushika Maternity Hospital. Informed consent concerning analysis from a retrospective database was obtained from all subjects.

This was a retrospective study of women with singleton pregnancies who gave birth at the Japanese Red Cross

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Katsushika Maternity Hospital between 2002 and 2006. Data were collected from 89 'elderly' primiparous women (aged 35 years or more) conceived by IVF-embryo transfer (ET), including 24 patients who underwent intracytoplasmic sperm injection and ET, and from 849 elderly primiparous singleton pregnancies conceived spontaneously (control group). In this study, we excluded one patient who underwent gamete intrafallopian transfer, 55 patients who underwent intrauterine insemination and 41 patients who underwent ovulation induction only.

Data included antenatal data, gestational age at delivery, obstetric complications, such as pregnancy-induced hypertension, gestational diabetes, placental previa and placental abruption, mode of delivery, birth weight, fetal demise and the Apgar score at 1 min. Pregnancy-induced hypertension was defined as blood pressure  $\geq 140/90$  mmHg measured on two or more occasions at least 6 h apart with the patient at bed rest. A 75-g, 2-h oral glucose tolerance test was carried out to diagnose gestational diabetes according to the Japan Society of Obstetrics and Gynecology (1995). Gestational diabetes was defined as a plasma glucose level meeting two of the following criteria:  $\geq 100$  mg/dL while fasting,  $\geq 180$  mg/dL after 1 h or  $\geq 150$  mg/dL after 2 h. Placental abruption was defined as complete or partial separation of a normally implanted placenta before delivery, which was confirmed at delivery by evidence of retro-placental bleeding at delivery and placental pathology. Infants who were light for dates or heavy for dates were defined as those with sex-adjusted and age-adjusted birth weights below the tenth or over the ninetieth percentile according to the fetal growth curve for Japan (Acta Neonatologica Japonica from the Japan Society of Neonatology 1998).

As an additional control group, we also examined the same variables in nulliparous women between the ages of 20–29 years at delivery ( $n = 2038$ ).

## Statistical analysis

For statistical analysis, a  $\chi^2$ -test was used to compare maternal characteristics and neonatal outcomes, and a multiple logistic regression analysis was carried out to evaluate other obstetric outcomes.  $P < 0.05$  was considered statistically significant.

## RESULTS

TABLE 1 SHOWS THE maternal characteristics and obstetric outcomes in elderly primiparous singleton

**Table 1** Maternal characteristics and obstetric outcomes in elderly primiparous singleton pregnancies conceived by *in vitro* fertilization or spontaneously conceived

	Spontaneous	<i>In vitro</i> fertilization	<i>P</i>
N	849	89	
Multigravida	292 (34)	34 (38)	0.47
Maternal age (years)			
35–39	726 (86)	70 (79)	0.086
40–44	120 (14)	18 (20)	0.12
45–49	3 (0.4)	1 (1.1)	0.29
Obstetric complications			
Pregnancy-induced hypertension	44 (5.2)	3 (3.4)	0.46
Gestational diabetes	4 (0.47)	1 (1.1)	0.42
Placenta previa	10 (1.2)	1 (1.1)	0.96
Placental abruption	10 (1.2)	3 (3.4)	0.09
Placental abruption $\geq$ Stage III†	3 (0.35)	1 (1.1)	0.33
Gestational age at delivery (weeks)			
$\leq 32$	21 (2.4)	3 (3.4)	0.61
$\leq 36$	69 (8.1)	4 (4.5)	0.22
$\geq 41$	151 (18)	21 (24)	0.18
Delivery mode			
Instrumental vaginal delivery	124 (15)	18 (20)	0.16
Elective Cesarean delivery	96 (11)	18 (20)	0.014
Emergency Cesarean delivery	120 (14)	11 (12)	0.65
Birth weight (g)			
$\leq 1500$	12 (1.4)	2 (2.2)	0.55
$\leq 2500$	110 (13)	8 (9.0)	0.31
Light for dates	68 (8.0)	6 (6.7)	0.65
Heavy for dates	41 (4.8)	7 (7.9)	0.22
Fetal demise	2 (0.23)	0 (0)	0.65
Apgar score at 1 min			
$\leq 4$	12 (1.4)	0 (0)	0.26
$\leq 7$	43 (5.1)	6 (6.7)	0.50

Data are presented as the number of cases (%).

†Stage III based on a previous report by Page *et al.* (1954).<sup>11</sup>

pregnancies conceived by IVF compared with those conceived spontaneously. The elective Cesarean rate in pregnancies following IVF was significantly higher than that in the control group. However, there were no significant differences in other variables between the two groups.

Table 2 shows the maternal characteristics and obstetric outcomes in spontaneous primiparous pregnant women

**Table 2** Maternal characteristics and obstetric outcomes in spontaneous singleton primiparous pregnant women aged 20–29 years

	N (%)	P1	P2
Total	2038	–	–
Multigravida	638 (31)	0.11	0.17
Obstetric complications			
Pregnancy-induced hypertension	76 (3.7)	0.07	0.86
Gestational diabetes	6 (0.29)	0.46	0.18
Placenta previa	13 (0.63)	0.13	0.58
Placental abruption	15 (0.74)	0.24	0.0070
Placental abruption ≥ Stage III†	4 (0.20)	0.13	0.012
Gestational age at delivery (weeks)			
≤32	61 (3.0)	0.44	0.84
≤36	179 (8.8)	0.57	0.16
≥41	395 (19)	0.32	0.33
Delivery mode			
Instrumental vaginal delivery	158 (7.8)	<0.001	<0.001
Elective Cesarean delivery	123 (6.0)	<0.001	<0.001
Emergency Cesarean delivery	164 (8.0)	<0.001	0.15
Birth weight (g)			
≤1500	49 (2.4)	0.10	0.92
≤2500	284 (14)	0.48	0.18
Light for dates	157 (7.7)	0.79	0.74
Heavy for dates	119 (5.8)	0.28	0.43
Fetal demise	8 (0.39)	0.51	0.55
Apgar score at 1 min			
≤4	24 (1.2)	0.60	0.30
≤7	124 (6.1)	0.28	0.80

P1, *P*-value versus elderly primiparous singleton pregnancies conceived by spontaneously; P2, *P*-value versus elderly primiparous singleton pregnancies conceived by *in vitro* fertilization.

†Stage III based on a previous report by Page *et al.* (1954).<sup>11</sup>

aged 20–29 years old. The rate of interventional delivery, such as instrumental vaginal and Cesarean delivery, in elderly pregnant women was significantly higher than that in women aged 20–29 years, irrespective of IVF. In addition, the incidence of placental abruption in elderly pregnancies conceived by IVF was significantly higher than that in the younger group ( $P = 0.0070$ ; odds ratio = 4.1, 95% confidence intervals = 1.43–11.8).

## DISCUSSION

RECENTLY, SOME SUFFICIENTLY sized studies found an association between IVF (or ART) and an increased rate of poorer perinatal outcome in singleton pregnancies.<sup>1–4</sup> However, there have been no observations that have been adjusted for maternal age.<sup>1–4</sup> Thus, we have demonstrated for the first time that, after adjusting maternal age, IVF itself does not increase the likelihood of a poor obstetrical outcome.

In this study, the elective Cesarean rate was the only significant difference observed between pregnancies following IVF and spontaneously conceived pregnancies. The reason for this result is not clear, although physician counseling may be one factor. As our policy, we do not perform Cesareans as a result of ‘patient request’. Thus, a further examination may be needed to clarify the adequacy of our medical intervention.

In this study, the incidence of placental abruption in elderly primiparae who conceived by IVF was fourfold that in spontaneous primiparae with a maternal age of 20–29 years. However, the difference in the incidence of placental abruption between elderly primiparae with IVF conception and elderly primiparae spontaneous conception did not reach statistical significance. In addition, there were no significant differences in other obstetric complications between the two elderly primiparous groups. One reason for this could be the small sample size in this study, because there were only three cases of placental abruption in the IVF group. Another possible reason is that IVF alone may not affect the obstetric outcome or that it may not be possible to separate IVF-related risks from those secondary to the underlying reproductive pathology.

In developed countries, there is a tendency to become pregnant at later ages, and this is associated with the societal advances of women and/or an increased use of ART. A higher incidence of obstetric complications in pregnancies at later ages, including pregnancy-induced hypertension, gestational diabetes, placenta previa and abnormal labor patterns, has previously been reported.<sup>6–10</sup> This observation is likely to be related to the underlying progressive vascular endothelial damage that occurs with aging.<sup>6,7</sup> In this study, the interventional delivery rate in elderly pregnant women was significantly higher than that in younger women, irrespective of IVF. Thus, the current results also support these previous studies.<sup>5–9</sup>

In conclusion, the current results did not support previous studies<sup>1–5</sup> that show IVF-related risks of singleton pregnancies. A further large-scale study is needed to clarify the effect of IVF.

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