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Medical intervention during labor increases after in vitro fertilization pregnancy

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Summary

Purpose of investigation: To compare the need for medical assistance during singleton deliveries between *in vitro* fertilization (IVF) pregnancy and spontaneous pregnancy (SP). *Materials and Methods:* A total of 848 women with singleton pregnancy (and who delivered at ≥ 36 weeks with problem-free pregnancy were divided into two groups. The groups were compared in terms of maternal age, parity, maternal pre-pregnancy body weight, maternal body weight at delivery, maternal weight gain, infant body weight, infant head circumference, and presence or absence of medical intervention (MI) at delivery (induction of labor, instrumental labor, or emergency cesarean section: CS). *Results:* The proportion of cases with MI was significantly higher in the IVF group (64.8%) than the SP group (39.3%). Clinical features, such as maternal age, parity, maternal body weight at delivery, infant body weight, and infant head circumference, were also extracted and compared between the two groups: MI group and non-medical intervention group. Univariate analysis showed significant differences between the MI group and the non-medical intervention group in terms of maternal age, maternal body weight at delivery, parity, infant body weight, infant head circumference, and presence or absence of IVF. Multivariate analysis of the factors that were significant in the univariate analysis showed similar trends in maternal age, parity, infant body weight, and presence or absence of IVF. In addition, the IVF group had a higher risk for requiring MI than the spontaneous pregnancy group [adjusted odds ratio (AOR) 1.74; 95% confidence interval (CI), 1.17-2.00, $p < 0.01$]. In particular, the IVF group had higher risk of needing emergency CS than the SP group (AOR 3.83; 95% CI, 1.87-7.78, $p < 0.01$). *Conclusion:* In spite of no problem in pregnancy course, the need for MI during labor increased after IVF regardless of maternal age and parity.

Key words: Infertility; Assisted reproduction; Delivery; Cesarean; Induction of labor.

Introduction

When I visited Egypt, I was shocked to see the fresco of the shrine. The drawing there depicts the instrument which is thought to have been used at the time of delivery and it resemble forceps that we always use even now. It signifies that medical intervention already existed at delivery from B.C. As society has changed, for example, both marrying and childbearing age have increased, *in vitro* fertilization (IVF), both conventional and intracytoplasmic sperm injection (ICSI), have become an essential method of treatment.

It is a well-known fact that when maternal age increases, delivery abnormality also increases, but after all will IVF pregnancy also increase tendency the risk of delivery? Is that the only reason why maternal age of IVF is older?

It has been noted that IVF is followed by an increase in abnormalities during pregnancy of the umbilical cord or placenta, including placenta previa, intrauterine growth restriction (IUGR), gestational diabetes mellitus (GDM), pregnancy induced hypertension (PIH) [1-4], and an increased probability of emergency cesarean section (CS) [5-8].

Among women with advanced maternal age, induction of labor at 39 weeks of gestation, as compared with expectant management, had no significant effect on the rate of CS and no adverse short-term effects on maternal or neonatal outcomes. However, the IVF status of the patient is not specified in this report [9]. On the other hand, there has been little investigation of medical intervention (MI) during delivery after IVF pregnancy.

In this report, the authors studied the effect of MI on the course of natural childbirth, after both spontaneous pregnancy (SP) and IVF pregnancy, in cases where delivery occurred at 36 weeks or later after a pregnancy without problems during pregnancy.

Materials and Methods

Patients who delivered at ≥ 36 weeks age of gestation between September 2013 and November 2015 were included in this study. In total, there were 848 cases in this study: spontaneous pregnancy (SP) in 689 cases and IVF, including ICSI, in 159 cases. Patients with problems during pregnancy, such as body mass index (BMI) < 30, placenta previa, low-lying placenta, umbilical cord factors, IUGR, moderate to advanced gestational hypertension, or GDM, were excluded in this study. These factors which are increased by

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Table 1. — *Comparison of clinical features during delivery, according to the need of IVF/ICSI.*

	Spontaneously pregnant (n=689)	IVF or ICSI (n=159)	*p*-value
Maternal age (years)	33	37	< 0.01
Maternal pre-pregnancy body weight (kg)	52.2	52.8	0.05
Maternal body weight at delivery (kg)	61.8	61.9	0.05
Maternal weight gain (%)	1.19	1.17	0.71
Infant body weight (grams)	3024	3090	0.21
Infant head circumference (cm)	32.6	33	< 0.01
Multiparity	277	22	< 0.01

IVF pregnancy were already reported and the patients that did not have any problems during the pregnancy were chosen.

The subjects were divided into a SP group and an IVF group and were comparatively studied with regards to maternal age, parity, maternal pre-pregnancy body weight, maternal body weight at delivery, maternal weight gain, infant body weight, infant head circumference, and presence or absence of MI at delivery, such as induction of labor, instrumental labor such as vacuum extraction and forceps delivery, and emergency CS. Deliveries were performed by two board-certified doctors at the same facility. The indications for MI during delivery were based on the Japan Society of Obstetrics and Gynecology criteria.

A Chi-square test was used to compare the presence or absence of MI. The Mann–Whitney U test was used for statistical analysis. Logistic regression analysis was performed on binary variables that were converted from continuous variables. In particular, maternal age, maternal body weight at delivery, and infant head circumference were each divided into two groups based on a median cut-off value. Infant body weight was divided into two groups: ≥ 3,000 g and < 3,000 g. The level of significance was set at a *p* value of < 0.05. This study was conducted with the approval of the Ethics Committee of Yanaihara Women's Clinic and with patient consent (ERBY/1, 2013).

Results

The IVF group had a significantly higher rate of cases that underwent MI than the SP group [103/159 (64.8%) *vs*. 271/689 (39.3%); $p < 0.01$]. Table 1 shows the comparison of clinical features during delivery according to the need of IVF/ICSI. Significant differences were observed in maternal age, infant body weight, and multiparity.

Table 2 shows the differences in clinical features between the MI group and the non-MI group. Significant differences were observed in maternal age (34.1 ± 4.6 *vs*. 33.1 ± 4.4 years), maternal body weight at delivery (62.7 ± 7.9 *vs*. 61.1 ± 7.1 kg), infant body weight (3,082 ± 393.9 *vs*. 3,000 ± 344.5 grams), infant head circumference (32.8 ± 1.5 *vs*. 32.6 ± 1.2 cm), and parity (56 *vs*. 243). However, the two groups were similar in terms of maternal pre-pregnancy body weight (52.6 ± 7.6 *vs*. 51.9 ± 7.0 kg) and maternal weight gain (1.19 ± 0.06% *vs*. 1.18 ± 0.06%) ($p > 0.05$).

Table 2. — *Comparison of clinical features during delivery, according to the need for medical intervention.*

	Had medical intervention (n=374)	Did not have medical intervention (n=474)	*p*-value
Maternal age (years)	34.1±4.6	33.1±4.4	< 0.01
Maternal pre-pregnancy body weight(kg)	52.6±7.6	51.9±7.0	0.13
Maternal body weight at delivery(kg)	62.7±7.9	61.1±7.1	0.01
Maternal weight gain (%)	1.19±0.06	1.18±0.06	0.10
Infant body weight(g)	3,082±393.9	3,000±344.5	< 0.01
Infant head circumference (cm)	32.8±1.5	32.6±1.2	0.04
Parity	56	243	< 0.01

Table 3. — *Multivariate analysis of clinical features that predict the need for medical intervention during delivery.*

Explanatory variable	Adjusted Odd ratio	95% Confidence interval	*p*-value
Maternal age (≥ 34 years)	1.44	1.05−1.99	0.03
Maternal body weight at delivery (≥ 63 kg)	0.97	0.79−1.06	0.57
Infant body weight (≥ 3,000 grams)	2.05	1.47−2.88	< 0.01
Infant head circumference (≥ 32.7 cm)	0.87	0.62−1.22	0.42
Multiparity	0.16	0.11−0.23	< 0.01
IVF	1.74	1.17−2.62	< 0.01

Table 4. — *Univariate analysis of clinical features affecting the need for emergency cesarean section during delivery.*

	Emergency cesarean section (n=50)	Not emergency cesarean section (n=474)	*p*-value
Maternal age (years)	35.5±4.2	33.1±4.4	< 0.01
Maternal pre-pregnancy body weight (kg)	54.4±9.0	51.9±7.0	0.05
Maternal body weight at delivery (kg)	63.8±9.4	61.1±7.1	0.05
Maternal weight gain (%)	1.18±0.06	1.18±0.06	0.71
Infant body weight (g)	3048.3±479.8	3000.2±344.5	0.21
Infant head circumference (cm)	33.3±1.7	32.6±1.2	< 0.01
Parity	7	243	< 0.01
IVF	24	56	< 0.01

Table 3 shows the results of multivariate logistic regression analysis of the predictive factors (maternal age, infant body weight, parity, and IVF) for the need for MI during delivery. Results showed that the risk factors that independently contributed to the need for MI during delivery were maternal age ≥ 34 years [odds ratio (OR) 1.44, 95% confidence interval (CI) 1.05–1.99; $p = 0.03$], infant body weight ≥ 3,000 grams (OR 2.05, 95% CI 1.47–2.88; $p <$

Table 5. — *Multivariate analysis of clinical features that predict the need for emergency cesarean section during delivery.*

Explanatory variable	Adjusted odds ratio	95% confidence interval	*p*-value
Maternal age (≥ 34 years)	1.78	0.88–3.64	0.11
Infant head circumference (≥ 33 cm)	2.11	1.11–4.13	0.02
Multiparity	0.18	0.07–0.40	< 0.01
IVF	3.83	1.87–7.78	< 0.01

0.01), multiparity (AOR 0.16, 95% CI 0.11–0.23; $p < 0.01$), and IVF pregnancy (AOR 1.74, 95% CI 1.17–2.62, $p < 0.01$).

When MI was compared using only emergency cesarean section, IVF cases had a higher risk for requiring emergency cesarean section than SP cases (AOR 3.83, 95% CI 1.87–7.78; $p < 0.01$) (Tables 4 and 5).

Discussion

There have been various reports on the course of pregnancy after IVF. These studies have stated that placental abnormalities, such as placenta previa and low-lying placenta, were as common as abnormalities of umbilical cord attachment, gestational hypertension, and premature birth [1, 3, 4, 7, 10–13]. Although many reports have addressed these diseases that occur during the course of pregnancy, a few have investigated on MI during delivery after a full-term, problem-free IVF pregnancy.

Older primiparas are generally known to have more abnormalities during labor [5, 13–15]. Because IVF pregnancy includes a particularly high number of older primiparas, it is assumed to include a greater number of difficult births. In fact, emergency cesarean section has been reported to have an increased likelihood after IVF at the age of 40 years or older [5, 16]. CS has been implicated in postoperative complications, such as secondary infertility and ectopic pregnancy [17]; therefore, it is better to have vaginal delivery if CS can be avoided.

Most of these previous reports did not investigate the factors that make delivery difficult. There have been observed tendencies for older mothers to have less muscle strength and weaker contractions and for primiparas to have more difficult deliveries than multiparas. Larger infants and weight gain by the mother over the course of the pregnancy tend to make delivery more difficult. Therefore, studies on medical interventions during delivery need to be assessed under conditions that exclude these factors. Masatake *et al.* stated that there was a higher probability of having CS or instrumental labor in IVF pregnancies at the age of 40 years or older [5].

In this study, MI was found to be affected by age, parity, and infant body weight. However, there was a 1.74-fold higher probability of MI during delivery in IVF pregnancies, compared with SP (95% CI 1.17–2.62, $p < 0.01$), regardless of age or parity. In particular, the risk for emergency CS was 3.83 times greater during delivery in IVF pregnancies compared with SP (95% CI 1.87–7.78, $p < 0.01$). Although a statistically significant difference was not observed, subgroup comparison of patients in the IVF group (conventional IVF group *vs*. ICSI group) showed that the ICSI group had tendency for a lower rate of MI at delivery by about 10%. Nouri *et al.* compared birth outcomes between conventional IVF and ICSI and reported that conventional IVF included more cases of pregnancy complications than ICSI [18]. Looking at the breakdown of indications for emergency CS in this present study, 24% were infant indications and 76% were maternal indications. However, because the sample size was small, statistical analysis was not possible.

The present authors have previously studied the risk for MI during delivery after artificial insemination by husband (AIH), but they did not find a significant difference with SP (data not shown). In general, AIH and ICSI are implemented in many cases of infertility that are due to male factors. In other words, the reason for the higher risk of MI during delivery in conventional IVF cases in this study was believed to be the woman's physical condition and the living environment after becoming pregnant.

An increase in convenience alongside scientific advances and the reduced body movement with the modern lifestyle are implicated in the muscle weakness reported in young people. Especially after IVF treatment, patients tend to take a physiologic rest because they tend to think that physiologic activity causes miscarriage and premature labor; therefore, the essential muscles for delivery become weaker. Although there have been reports on the physiologic and biochemical basis of dysfunctional labor, the exact mechanisms are still poorly understood and need further studies [19].

In infertility involving obesity, an improvement in physical condition before IVF reportedly improved clinical results; IVF results were believed to be better when there was daily physical activity [6, 20, 21]. Due to reports that preterm births were more frequent with general infertility [22] and from the conclusion of Ensing *et al.* that delivery by patients who have undergone medically-assisted reproduction was associated with asphyxia due to maternal characteristics [23], both pregnancy after IVF and pregnancy after general infertility may necessitate lifestyle guidance regardless of age or pregnancy calendar. Such lifestyle guidance is considered essential before and during pregnancy.

The present results implied that MI involved complex interactions of various factors. Further study is needed to validate these factors.

Conclusion

In spite of no problem in pregnancy course, the need for medical assistance during labor increased after IVF, regardless of maternal age and parity.

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