

Obstetric Outcomes of Twin Pregnancies in Japanese Women Aged 40 and Older

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Abstract

Background: The aim of this study was to compare the obstetric outcomes of twin pregnancies between Japanese women aged ≥ 40 years and their younger counterparts aged 25 - 29.

Methods: This was a retrospective study of twin pregnancies managed at Japanese Red Cross Katsushika Maternity Hospital between 2002 and 2016. Women aged 40 and older at delivery ($n = 117$) were compared with women aged 25 - 29 at delivery ($n = 536$).

Results: Although the women ≥ 40 years old were more likely to have increased risks of HELLP (hemolytic, elevated liver enzymes and low platelet) syndrome and very low birth weight neonates, there were no measurable differences in obstetric outcomes such as hypertensive disorders, premature delivery and neonatal asphyxia between the two groups.

Conclusion: Advanced maternal age did not seem to affect obstetric outcomes in twin pregnancies seriously.

Keywords: Twin pregnancy; Age 40 or older; Obstetric outcomes

Introduction

Traditionally, advanced maternal age (AMA) and twin pregnancy are both independent risk factors for adverse obstetric outcomes with an increasing incidence of hypertensive disorders, cesarean birth and maternal and (or) newborn complications [1-6]; however, our subgroup analyses of twins in 2007 have found that AMA aged 35 years and over was not associated with increased risk for adverse outcomes [7]. In recent decades, the proportion of both twin and AMA births has increased due to the advances in assisted reproductive technology (ART) and the permission of two embryos transfer in patients of advanced age [8]. Although there have been a considerable number of studies concerning maternal and perinatal outcomes of singleton pregnancy in women older than 35 - 45

years and those of twin pregnancy in women older than 35 years, those targeting of twin pregnancy in women of much older than 40 years are still limited [1-7, 9-13]. The aim of this study is to investigate maternal and neonatal outcomes in twins in Japanese women greater than 40 compared to their younger counterparts aged 25 - 29.

Materials and Methods

The protocol for this study was approved by the Ethics Committee of the Japanese Red Cross Katsushika Maternity Hospital.

This was a retrospective study of twin pregnancies managed at Japanese Red Cross Katsushika Maternity Hospital between 2002 and 2016. Based on the study design of our previous study and recent studies in twin pregnancy, Japanese women 40 years and older at delivery ($n = 117$: AMA group) were compared with Japanese women aged 25 - 29 at delivery ($n = 536$: control group).

Data included antenatal data, gestational age at delivery, mode of delivery, birth weight, Apgar score at 1 and 5 min and postpartum hemorrhage requiring transfusion. In our institute, the guidelines for vaginal delivery of twin pregnancy are: 1) without severe complications such as twin-twin transfusion syndrome, 2) without history of previous cesarean deliveries, 3) vertex presentation of the first twin, 4) gestational age at delivery ≥ 33 weeks, and 5) estimated birth weight of at least 1,500 g for each twin. In addition, we performed cesarean section for maternal request in cases of twin pregnancy.

Data are expressed as the number (percentage). SPSS Statistics software version 20 (IBM Corp., Armonk, NY, USA) was used for statistical analyses. A Chi-square test was used for categorical data, and a P-value < 0.05 was considered significant. Logistic regression analysis was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs).

Results

Table 1 shows the maternal characteristics of this study. The women ≥ 40 years old were more likely to have used ART (32% vs. 0%, $P < 0.01$). The rates of multiparous women and those with uterine myoma with a diameter of 4 cm or more in the AMA group are higher than those in the control group (multiparous: OR 2.43, 95% CI 1.5 - 3.6, $P < 0.01$; uterine myoma: OR 2.04, 95% CI 1.1 - 3.8, $P = 0.04$). There were no

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Table 1. Maternal Characteristics of Twin Pregnancy in Women Aged 25 - 29 (Control) and ≥ 40 Years (Advanced Age)

	Control		Advanced age		P-value
	Number	%	Number	%	
Total	536		117		
Maternal age at delivery					
Range	25 - 29		40 - 45		
Average	27.9 \pm 0.8		41.9 \pm 0.7		
Nulliparous	358	67	53	45	< 0.01
Maternal height	156 \pm 6		157 \pm 7		0.68
Prepregnancy body mass index	22.0 \pm 3.5		22.3 \pm 3.1		0.55
Body mass index at delivery	27.5 \pm 3.7		27.3 \pm 3.5		0.48
<i>In vitro</i> fertilization	0	0	38	32	< 0.01
Egg donor	0	0	0	0	1
Fetal reduction	0	0	1	1	0.18
Monochorionic twin pregnancy	204	38	41	35	0.46
Chronic hypertension	0	0	1	1	0.18
Pregestational diabetes	0	0	0	0	1
Low-dose aspirin in pregnancy	0	0	0	0	1
Uterine myoma with a diameter of 4 cm or more	36	7	15	13	0.04

Data are presented as number with percentage or mean \pm SD.

cases of egg donor and one case of fetal reduction.

Table 2 shows the maternal and neonatal outcomes. The difference in the incidence of hypertensive disorders between the two groups did not reach statistical significance ($P = 0.09$); however, the incidence of HELLP syndrome (hemolytic, elevated liver enzymes and low platelet syndrome) in the AMA group was higher than that in the control group (3% vs. 0%, $P < 0.01$). On the other hand, the incidence of preterm delivery at < 32 weeks in the AMA group was lower significantly than that in the control group (OR 0.107, 95% CI 0.018 - 0.62). The difference in the incidence of neonatal birth weight discordance $\geq 20\%$ did not reach statistical significance ($P = 0.53$). However, the incidence of neonatal low birth weight in smaller twin in the AMA group was higher than that in the control group ($< 1,500$ g: OR 2.23, 95% CI 1.2 - 4.2, $P = 0.02$; $< 2,500$ g: OR 2.68, 95% CI 1.1 - 6.6, $P = 0.04$), while the incidence of neonatal low birth weight in larger twin in the AMA group was lower than that in the control group ($< 1,500$ g: OR 0.236, 95% CI 0.088 - 0.63, $P < 0.01$; $< 2,500$ g: OR 0.366, 95% CI 0.23 - 0.58, $P < 0.01$).

Discussion

In this study, it was found that AMA Japanese women were more likely to have used ART for twin pregnancies and were complicated by uterine myoma. These findings are supported by some previous studies [1-13]. In our earlier study, the rate of cesarean delivery in AMA women was higher than that in younger women [7]; however, in the current study, the differ-

ence in the rate of cesarean delivery did not reach statistical significance. This may be due to the recent dramatic increase in the overall cesarean delivery rate of twin pregnancies [14, 15]. The increase has been supposed to be due to physician counseling and maternal request for elective cesarean delivery to avoid perinatal asphyxia especially in the second twin and/or combined vaginal-cesarean delivery [16-18].

Based on the current study, AMA did not seem to be a risk factor for the development of hypertensive disorders or gestational diabetes in twin pregnancy. It may support our previous study [7]; however, the current results may be against a recent study indicating the high rates of cesarean delivery, preeclampsia and gestational diabetes in twin pregnancies in women 45 years of age or older [3]. In some earlier studies in twin pregnancies, an increased incidence of preeclampsia has been reported to be associated with nulliparity [19, 20]. In this study, the lower rate of nulliparous women in the AMA group may be associated with the similar rate of hypertensive disorders between the two groups. Instead, severe cases of hypertensive disorders such as HELLP syndrome might be more common in AMA women with twin pregnancy. A recent large study by Premru-Srsen et al [21] shows that nulliparity is also significantly associated with twin very preterm birth.

In this study, the rate of very low birth weight neonates in the AMA group was higher than that in the control group. Based on the current results of the neonatal birth weight, the incidence of negligible birth weight discordance between the twins seemed to be more frequently in AMA women than that in the control. The reason leading to the observation is not clear. One possible reason may be the higher rate of uterine

Table 2. Obstetric Outcomes of Twin Pregnancy in Women Aged 25 - 29 (Control) and ≥ 40 Years (Advanced Age)

	Control		Advanced age		P-value
	Number	%	Number	%	
Total	536		117		
Gestational age at delivery					
< 28 weeks	12	2	0	0	0.14
< 32 weeks	40	7	1	1	0.01
< 34 weeks	72	13	16	14	0.95
< 37 weeks	303	57	75	64	0.15
Cesarean delivery					
Elective	351	65	80	68	0.59
After labor	42/185	23	11/37	30	0.40
Hypertensive disorder	48	9	17/116	15	0.09
HELLP syndrome	0	0	3	3	< 0.01
Gestational diabetes	8	1	0	0	0.36
Placental abruption	6	1	1	1	1.00
Placenta previa	1	0	0	0	1.00
Either twin fetal demise	0	0	0	0	1.00
At 12 - 21 weeks	0	0	0	0	1.00
At ≥ 22 weeks	3	1	0	0	0.96
Birth weight of smaller twin					
< 1,500 g	33/533	6	15	13	0.02
< 2,500 g	476/533	88	112	96	0.04
Birth weight of larger twin					
< 1,500 g	70	13	4	3	< 0.01
< 2,500 g	461	86	81	69	< 0.01
Birth weight discordance $\geq 20\%$	33	6	9	8	0.53
Neonatal outcomes of first twin					
Apgar score at 1 min < 7	18	3	0	0	0.06
Apgar score at 5 min < 7	1	0	0	0	1.00
Neonatal outcomes of second twin					
Apgar score at 1 min < 7	33/533	16	2	2	0.07
Apgar score at 5 min < 7	1/533	0	0	0	1.00
Postpartum hemorrhage requiring transfusion	8	2	4	4	0.24

Data are presented as number with percentage. HELLP: hemolytic, elevated liver enzymes and low platelet.

myoma in AMA women. The presence of myoma might contribute to the development of difference in fetal blood flow distribution between the twins associated with the irregularities of the uterine cavity due to myoma.

We understand that there are some limitations in this study. The current results were obtained from a small sample size. In addition, we could not examine the influence of very advanced maternal age (> 45 years old), egg donation, and/or nulliparity on obstetric outcomes in twin pregnancies. Donor egg has been a well-known risk factor for the development of preeclampsia [22]. In Japan, legislation for egg donation has

not been in place and social consensus in egg donation or fetal reduction has not been well acquired. Thus, a further study will be needed with a large sample size.

In conclusion, advanced maternal age of ≥ 40 years did not seem to be associated with serious adverse obstetric outcomes in twin pregnancies.

Competing Interests

The author has declared that no competing interests exist.

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