International Journal of Gynecology and Obstetrics 121 (2013) 86–90

Contents lists available at SciVerse ScienceDirect

International Journal of Gynecology and Obstetrics

journal homepage: www.elsevier.com/locate/ijgo

www.figo.org

CLINICAL ARTICLE

Clinical features and short-term outcomes of triplet pregnancies in Japan

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ARTICLE INFO

Article history:
Received 5 July 2012
Received in revised form 9 October 2012
Accepted 11 December 2012

Keywords:
Fetal death
Perinatal mortality
Preterm birth
Triplet

ABSTRACT

Objective: To review clinical features and short-term outcomes of triplet pregnancies among Japanese women. *Methods:* A retrospective analysis was carried out among 320 Japanese women with triplet pregnancies (8 monochorionic, 75 dichorionic, and 150 trichorionic triplets; 87 with unknown placental chorionicity) who delivered at 22 gestational weeks or more between January 2005 and December 2008. *Results:* Delivery was by cesarean for 315 (98%) women. Gestational age at delivery was 32.3 ± 2.8 weeks (mean ± SD) and 33.2 weeks (median), and 97%, 61%, and 14% of women delivered at less than 37, less than 34, and less than 30 gestational weeks, respectively. For live-born infants, mean birth weight was 1762 ± 437 g, 1608 ± 396 g, and 1406 ± 380 g for the heaviest, middle, and lightest triplet, respectively. Eighteen (5.6%) women experienced perinatal mortality (3 triplets for 1 woman, 2 triplets for 4 women, and 1 triplet for 13 women). Perinatal mortality was 25 deaths per 1000 deliveries, and decreased with increasing number of chorionic membranes (125, 44, and 20 per 1000 mono-, di-, and trichorionic triplet deliveries, respectively). *Conclusion:* Short-term outcomes were good among triplet pregnancies in Japan. The data may be useful for counseling Japanese women with triplet pregnancies.

1. Introduction

The general clinical features of triplet pregnancy, as assessed by studies of more than 100 pregnancies, have been reported from many countries [1–4] but not Japan. Since 1998, the incidence of triplet pregnancy has decreased in England and Wales [5], as well as in Japan: according to information released by the Japanese Ministry of Health, Labour and Welfare, the annual number of triplet pregnancies has been decreasing gradually from 337 pregnancies in 1995 to 246 in 2005, 246 in 2006, 219 in 2007, 181 in 2008, and 157 in 2009 [6]. Meanwhile, approximately 1100000–1200000 neonates are currently born annually in Japan [6]. Thus, the number of triplets accounts for only 0.04%–0.08% of all neonates born in Japan.

The incidence of monozygotic twinning is relative constant throughout the world, varying between approximately 3 and 5 per 1000 pregnancies; by contrast, the rate of dizygotic twinning varied from 1.3 (Japan) to 49 (Nigeria) per 1000 pregnancies even before the era of clinically available assisted reproductive techniques [7]. Therefore, the proportions of placental chorionicity in triplet pregnancies may differ between Japanese women and women from other countries.

As a result, the aim of the present retrospective study was to review the clinical features and outcomes of triplet pregnancy among Japanese women by using a relatively large cohort of women with triplet pregnancies who participated in the registry system established by the Japan Society of Obstetrics and Gynecology (JSOG).

2. Materials and methods

Data were analyzed from women with triplet pregnancies who gave birth between January 1, 2005, and December 31, 2008, at one of approximately 120 secondary and tertiary hospitals participating in the JSOG Successive Pregnancy Birth Registry System, which collected information on successive deliveries that occurred at a gestational age of 22 weeks or more in the participating hospitals. The present study was conducted after being approved by the Ethics Committee of Hokkaido University Hospital.

The information available from this system includes maternal age; parity; gestational age at delivery; chorionicity of the placenta; sex of the infant; birth weight; live-born, stillborn, or early neonatal death (END) within 7 days of life; delivery mode; use of assisted reproductive techniques; and maternal complications such as premature membrane rupture, pregnancy-induced hypertension, placental abruption, placenta previa, feto-fetal transfusion syndrome, and hyperglycemia during pregnancy.

For each woman with triplets, the heaviest, middle, and lightest triplet was defined as that with the heaviest, middle, and lightest birth weight, respectively. To compare birth weight according to gestational age at delivery between triplets and singletons, we excluded stillborn triplets and used the normative birth weight of singletons according to gestational age at delivery, a benchmark that is widely used in Japan [8]. Because approximately 99.7% of all pregnant Japanese women receive

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0020-7292/$ – see front matter
http://dx.doi.org/10.1016/j.ijgo.2012.10.022

regular prenatal care, including 2–3 prenatal visits during the first trimester [9], and obstetric ultrasonography is widely used in Japan, gestational age was expected to be accurate for most of the study participants. Perinatal mortality was defined as stillbirth at a gestational age of 22 weeks or more, and END.

Statistical analyses were performed via the statistical software package StatView 5.0 (SAS Institute, Cary, NC, USA). All data are presented as the mean ± SD. The unpaired *t* test and Mann–Whitney *U* test were used to analyze the data. The Fisher exact test was used to compare the frequencies. In all analyses, a *P* value of less than 0.05 was taken to indicate statistical significance.

3. Results

A total of 320 triplet pregnancies were registered in the JSOG Successive Pregnancy Birth Registry System between January 1, 2005, and December 31, 2008, corresponding to 36% of all 892 women with triplet pregnancies occurring across Japan between these dates. Eight, 75, and 150 women were registered as having monochorionic (MC), dichorionic (DC), and trichorionic (TC) triplets, respectively; placental chorionicity was not specified for the remaining 87 women.

As expected, two-thirds of triplet pregnancies were established after treatment for infertility (Table 1). After excluding 87 women with unknown placental chorionicity, the frequency of mono-, di-, and trichorionic triplets among the remaining 233 women was 3.4%, 32%, and 64%, respectively. However, this proportion varied in accordance with the mechanism leading to triplet pregnancies: the majority of triplets were mono- or dichorionic for women who conceived spontaneously, whereas most triplets were trichorionic for women who underwent ovulation induction alone (Fig. 1). The fraction of women with spontaneously conceived triplets decreased with increasing number of chorionic membranes: such women accounted for 75% of monochorionic triplet pregnancies, but only 18% of trichorionic triplet pregnancies (Fig. 1).

Among all 320 women, 315 (98%) underwent cesarean delivery (Table 1) and 5 women gave birth to triplets vaginally at a gestational age of 22 weeks (1 woman), 24 weeks (1 woman), 32 weeks (1 woman), and 34 weeks (2 women). The mean and median gestational age at delivery was 32.3 ± 2.8 weeks and 33.2 weeks, respectively. The duration of pregnancy increased with increasing number of chorionic membranes: that of trichorionic triplets was significantly longer than those of other triplets ($P = 0.030$ vs monochorionic; $P = 0.001$ vs dichorionic; $P < 0.001$ vs unknown chorionicity).

In total, 310 (97%) of the 320 pregnancies ended in preterm delivery before 37 weeks of gestation (Fig. 2), and 927 (99%) of the 939 live-born triplets were born with a low birth weight of less than 2500 g (Table 1). The overall mean birth weight for live-born infants was 1762 ± 437 g, 1608 ± 396 g, and 1406 ± 380 g for the heaviest, middle, and lightest triplet, respectively. The corresponding birth weights were 1443 ± 496 g, 1320 ± 492 g, and 1085 ± 376 g for monochorionic

Table 1
Demographic characteristics according to placental chorionicity.

	Overall	MC	DC	TC	Unknown	*P* value
Mothers/infants	320/960	8/24	75/225	150/450	87/261	
Nullipara	225 (70.3)	5 (62.5)	48 (64.0)	108 (72.0)	64 (73.6)	0.481
Age, y	31.7 ± 4.1	32.9 ± 4.4	31.6 ± 4.0	32.1 ± 4.1	31.1 ± 4.1	0.263
Spontaneous	109 (34.1)	6 (75.0)	31 (41.3)	27 (18.0)	45 (51.7)	0.001 (MC vs TC) <0.001 (DC vs TC)
IVF	84 (26.3)	2 (25.0)	32 (42.7)	45 (30.0)	5 (5.7)	<0.001 (DC, TC vs unknown)
Induced ovulation[a]	127 (39.7)	0 (0.0)	12 (16.0)	78 (52.0)	37 (42.5)	0.006 (MC vs TC) 0.008 (MC vs unknown) <0.001 (DC vs TC, unknown)
PIH	11 (3.4)	0 (0.0)	3 (4.0)	5 (3.3)	3 (3.5)	0.999
Hyperglycemia	4 (1.3)	0 (0.0)	0 (0.0)	2 (1.3)	2 (2.3)	0.620
Placenta previa	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0.531
FFTS	2 (0.6)	1 (12.5)	1 (1.3)	0 (0.0)	0 (0.0)	0.051
Cesarean delivery	315 (98.4)	8 (100)	73 (97.3)	148 (98.7)	86 (98.9)	0.752
Pregnancy duration, wk	32.3 ± 2.8	30.3 ± 15.4	31.7 ± 8.3	33.1 ± 7.4	31.6 ± 5.5	0.030 (MC vs TC) 0.001 (DC vs TC) <0.001 (TC vs unknown)
<37 weeks	310 (96.9)	8 (100)	75 (100)	140 (93.3)	87 (100)	0.033 (DC vs TC) 0.015 (TC vs unknown)
<34 weeks	195 (60.9)	6 (75.0)	51 (68.0)	71 (47.3)	67 (77.0)	0.004 (DC vs TC) <0.001 (TC vs unknown)
<30 weeks	45 (14.1)	3 (37.5)	16 (21.3)	12 (8.0)	14 (16.1)	0.029 (MC vs TC) 0.009 (DC vs TC)
Birth weight[b], g	1592 ± 433 (n = 939)	1300 ± 498 (n = 21)	1520 ± 444 (n = 216)	1798 ± 419 (n = 442)	1494 ± 396 (n = 260)	<0.001 (MC, DC, unknown vs TC)
<2500 g	927 (98.7)	21 (100)	210 (97.2)	437 (98.9)	259 (99.6)	0.120
<2000 g	778 (82.9)	19 (90.5)	186 (86.1)	338 (76.5)	235 (90.4)	0.004 (DC vs TC) <0.001 (TC vs unknown)
<1500 g	375 (39.9)	14 (66.7)	106 (49.1)	122 (27.6)	133 (51.2)	<0.001 (MC, DC, unknown vs TC)
<1000 g	97 (10.3)	5 (23.8)	28 (13.0)	33 (7.5)	31 (11.9)	0.031 (MC vs TC) 0.022 (DC vs TC)
Female infant	501 (52.2)	10 (41.7)	131 (58.2)	218 (48.4)	142 (54.4)	(0.018) DC vs TC
Perinatal mortality	24 (2.5)	3 (12.5)	9 (4.0)	9 (2.0)	3 (1.1)	0.019 (MC vs TC) 0.009 (MC vs unknown)
Stillbirth	21 (2.2)	3 (12.5)	9 (4.0)	8 (1.8)	1 (0.4)	0.014 (MC vs TC) 0.002 (MC vs unknown) 0.007 (DC vs unknown)
END	3 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	2 (0.8)	0.486

Abbreviations: MC, monochorionic; DC, dichorionic; TC, trichorionic; IVF, in vitro fertilization; PIH, pregnancy-induced hypertension (including gestational hypertension, pre-eclampsia, and eclampsia); END, early neonatal death within 7 days of life; FFTS, feto-fetal transfusion syndrome.

[a] Induced ovulation indicates pregnancy conceived after ovulation induction without the aid of IVF.

[b] Birth weight included only live-born infants.