

## OBSTETRICS

# Perinatal death of triplet pregnancies by chorionicity

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**OBJECTIVE:** The purpose of this study was to evaluate the perinatal risk of death by chorionicity at >22 weeks of gestation of triplet pregnancies.

**STUDY DESIGN:** In a retrospective cohort study, the perinatal data were collected from triplet pregnancies in Japanese perinatal care centers between 1999 and 2009. We included maternal characteristics and examined the following factors: prenatal interventions, pregnancy outcome, and neonatal outcome. The association between fetal or neonatal death of triplets and chorionicity was evaluated by logistic regression analysis.

**RESULTS:** After the exclusion of 253 cases, the study group comprised 701 cases: 507 trichorionic triamniotic (TT) triplet pregnancies, 144 diamniotic triamniotic (DT) triplet pregnancies, and 50 monochorionic triamniotic (MT) triplet pregnancies. The mortality rate (fetal death

at >22 weeks of gestation; neonatal death) in triplets was 2.6% and included 2.1% of TT triplet pregnancies, 3.2% of DT triplet pregnancies, and 5.3% of MT triplet pregnancies. No significant risk of death was identified in DT triplet pregnancies; however, MT triplet pregnancies had a 2.6-fold greater risk (adjusted odds ratio, 2.60; 95% confidence interval, 1.17–5.76;  $P = .019$ ) compared with TT triplet pregnancies. Prophylactic cervical cerclage did not reduce the perinatal mortality rate at >22 weeks of gestation in triplets.

**CONCLUSION:** The risk of death for MT triplet pregnancies is significantly higher than that of TT triplet pregnancies; however, the risk of death for DT triplet pregnancies is not.

**Key words:** chorionicity, fetofetal transfusion syndrome, perinatal outcome, prophylactic cervical cerclage, triplet pregnancy

Cite this article as: Kawaguchi H, Ishii K, Yamamoto R, et al. Perinatal death of triplet pregnancies by chorionicity. *Am J Obstet Gynecol* 2013;209:36.e1-7.

The incidence of multiple births, which had increased, has begun to decrease in recent years.<sup>1,2</sup> The infants of multiple pregnancies are reported to have high mortality and morbidity rates primarily because of preterm birth and/or low birthweight, compared with infants of singleton pregnancies.<sup>2-6</sup> Perinatal outcome in multiple gestations is also affected to a large degree by chorionicity.

Monochorionic twin pregnancy is associated with a higher risk of neurologic sequelae and perinatal death, which

primarily is attributed to the blood flow of intertwin placental vascular anastomoses.<sup>7,8</sup> Twin-twin transfusion syndrome,<sup>9,10</sup> selective intrauterine growth restriction,<sup>11-13</sup> and increased incidences of fetal anomalies and acute fetofetal hemorrhage before a single fetal death<sup>14</sup> are regarded to be representative complications of monochorionic twin gestation. Similarly, monochorionic triplet gestation, which includes dichorionic or monochorionic triplet pregnancies, might have an equally poor or poorer prognosis than monochorionic twin gestations.<sup>15-17</sup> Perinatal prognosis, especially regarding death, in triplet gestations has been described in several reports.<sup>5,15-23</sup> However, in those reports, the number of subjects was small, or chorionicity as a perinatal factor was not discussed.

The aim of this study was to evaluate the perinatal outcome by chorionicity in triplet gestations in Japan between 1990 and 2009 and to assess the effect of chorionicity on outcome.

## MATERIALS AND METHODS

All triplet births at >22 weeks of gestation between January 1990 and

December 2009 were included in this retrospective cohort study. The medical records of mothers and neonates who attended 91 perinatal care centers in Japan were reviewed. The subjects were enrolled in the Perinatal Research Network in Japan; all the centers are listed at the end of this article. Spontaneous abortion or at least 1 fetal death at <22 weeks of gestation, lethal malformations, acardiac twins, conjoined twins, induced abortions, and cases in which a delayed interval delivery occurred were excluded from this study. The approval of the institutional review board (Osaka Medical Center and Research Institute for Maternal and Child Health) was obtained before this study began.

Obstetric management policy, which includes whether to perform prophylactic cervical cerclage and offer hospitalization for bed rest and indications and timing of delivery, was decided at the discretion of each institution. In cases of threatened preterm labor, ritodrine hydrochloride and/or magnesium sulfate was administered for tocolysis. Tocolytic agents usually were used for maintenance tocolysis. Antenatal

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Received Dec. 6, 2012; revised Jan. 13, 2013; accepted March 7, 2013.

The authors report no conflict of interest.

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0002-9378/\$36.00

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<http://dx.doi.org/10.1016/j.ajog.2013.03.003>

**TABLE 1**  
**Baseline characteristics of 701 women with triplet pregnancies**

Variable	Total (n = 701)	Triplet pregnancies			P value
		Trichorionic triamniotic (n = 507)	Dichorionic triamniotic (n = 144)	Monochorionic triamniotic (n = 50)	
Maternal age, y <sup>a</sup>	31 (17–48)	31 (20–48)	32 (21–41)	31 (17–40)	NS
Mode of conception, n/N (%)					< .001
Spontaneous pregnancy	104/694 (15.0)	26/505 (5.1)	45/139 (32.4)	33/50 (66.0)	
Ovulation induction	318/694 (45.8)	272/505 (53.9)	37/139 (26.6)	9/50 (18.0)	
Assisted reproductive technology	272/694 (39.2)	207/505 (41.0)	57/139 (41.0)	8/50 (16.0)	
Nulliparous, n/N (%)	503/696 (72.3)	389/506 (76.9)	91/140 (65.0)	23/50 (46.0)	< .001
Body mass index, kg/m <sup>2a</sup>	20.4 (14.5–42.0)	20.3 (14.5–37.6)	20.7 (16.4–42.0)	20.3 (15.6–32.7)	NS
Previous preterm delivery, n/N (%)	14/193 (7.3)	11/117 (9.4)	2/49 (4.1)	1/27 (3.7)	NS

NS, not significant.

<sup>a</sup> Data are given as median (range).

Kawaguchi. Risk of death for triplet pregnancies. *Am J Obstet Gynecol* 2013.

corticosteroids were used when indicated at <34 weeks of gestation. Neither selective feticide by cord occlusion for any situation nor fetoscopic laser surgery for fetofetal transfusion syndrome (FFTS) was a management option in our setting.

Based on macroscopic placental examination in addition to early obstetric ultrasonography, triplet gestations were categorized into 3 groups: trichorionic triamniotic (TT), dichorionic trichorionic (DT), or monochorionic triamniotic (MT). The main study outcome was death, which included both intrauterine fetal death at >22 weeks of gestation and neonatal death (all deaths at ≤28 days' gestation). Maternal baseline characteristics included mode of conception, prenatal interventions such as prophylactic cervical cerclage, hospitalization for bed rest, intravenous tocolytic agents, maternal corticosteroids, preterm premature rupture of membranes, pregnancy-induced hypertension, and gestational diabetes mellitus. FFTS, gestational age at delivery, mode of delivery, and neonatal status at birth (which included birthweight and Apgar scores at 5 minutes) were compared among the groups with the use of the  $\chi^2$  test for nominal variables or

the Kruskal-Wallis test for continuous variables. Additionally, the incidence of neonatal complications (admission to the neonatal intensive care unit, respiratory distress syndrome, grade III or IV intraventricular hemorrhage, necrotizing enterocolitis, retinopathy of prematurity, and neonatal sepsis) were evaluated for each group. The odds ratio was used to evaluate the influence of chorionicity on death. Univariate analyses were used to estimate the crude odds ratios and the 95% confidence interval of the prenatal factors at <20 weeks of gestation; these factors included maternal baseline characteristics (with or without prophylactic cerclage) and chorionicity. A multiple logistic regression model for the death of triplets was constructed with the variables that had been selected by stepwise selection (significance level for entering into the model,  $P < .2$ ). The reported probability values were 2-sided. Analyses were performed with SPSS software (version 20; SPSS Inc, Chicago, IL).

## RESULTS

During the study period, 954 triplet pregnancies were identified. A total of 253 pregnancies were excluded because of a lack of detailed information

(n = 222), intrauterine fetal death at <22 weeks of gestation (n = 20), spontaneous abortion (n = 3), induced abortion (n = 3), delayed interval delivery (n = 2), and lethal malformations (n = 3). Among the 701 remaining triplet pregnancies, there were 507 TT triplet pregnancies, 144 DT triplet pregnancies, and 50 MT triplet pregnancies. There were no cases with monoamniotic or diamniotic triplet pregnancies in our database. Maternal characteristics by chorionicity are presented in Table 1. The median and range of maternal age at delivery was 31 years (range, 17–48 years). Nulliparous women accounted for 76.9% of TT triplet pregnancies, 65.0% of DT triplet pregnancies, and 46.0% of MT triplet pregnancies; these differences were statistically significant ( $P < .001$ ). The rate of spontaneous pregnancy was 15.0%; the rate after ovulation induction that included artificial insemination was 45.8%, and the rate of assisted reproductive technology was 39.2%. Among MT triplet pregnancies, 66.0% were conceived naturally; however, 94.9% of TT triplet pregnancies and 67.6% of DT triplet pregnancies were impregnated by fertility treatments such as ovulation induction or assisted reproductive

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