Comparing the course and delivery outcomes of Japanese twin pregnancies with and without gestational diabetes mellitus: a single-center retrospective analysis

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Abstract. Singleton pregnant women with gestational diabetes mellitus (GDM) are at an increased risk of adverse maternal and neonatal outcomes. Multiple pregnancies are associated with increased risks of perinatal complications; however, the impact of GDM on maternal and neonatal outcomes in multiple pregnancies is unknown, and there are currently few reports on GDM status in twin pregnancies. This study aimed to compare the background and perinatal outcomes between Japanese twin pregnancies with and without GDM at a perinatal center in Japan. Additionally, the clinical course of GDM was investigated. In this retrospective cohort study, women with twin pregnancies underwent GDM screening at Yokohama City University Medical Center from January 2011 to December 2016. Overall, 307 twin pregnancies were divided into GDM (47 cases, 15.3%) and non-GDM (260 cases, 84.7%) groups. GDM-associated pregnancy complications, GDM status, and pregnancy outcomes were ascertained. Women with GDM were older and had a higher pre-pregnancy body mass index than those without GDM. Glycemic control was good in all patients, and there was no difference in delivery outcomes between the two groups. Gestational weight gain was lower in pregnant women with GDM (+8.0 kg) than in those without GDM (+11.8 kg), suggesting the impact of strict nutritional guidance on twin pregnancies with GDM. In conclusion, twin pregnancies with GDM did not have different delivery outcomes compared to those without GDM. To manage twin pregnancies with GDM, this study suggests that it is important to monitor patients’ weight and blood glucose levels.

Key words: Gestational diabetes mellitus (GDM), Twin pregnancy, Japanese, Pregnancy outcomes

THE INCIDENCE of diabetes in pregnancy, particularly gestational diabetes mellitus (GDM), is increasing worldwide, which can be attributed to advanced maternal age [1, 2], obesity [2], and the inclusion of more stringent diagnostic criteria [3, 4]. Singleton pregnant women with GDM are at an increased risk of adverse maternal and neonatal outcomes, such as cesarean section, increased neonatal weight, large for gestational age (LGA) births, and gestational hypertension, when compared to pregnant women without diabetes [5-7]. The risk of perinatal complications, such as eclampsia, preterm labor, and intrauterine growth restriction, tend to increase in multiple pregnancies [8, 9].

Previous reports have compared twin pregnancies among women with (GDM group) or without GDM (non-GDM group). Some studies reported maternal complications during twin pregnancy, including increased risk of gestational hypertension [10] and preeclampsia [10-12], while others did not [13, 14]. The reported maternal and infant perinatal outcomes include increased neonatal intensive care unit admission [13, 14] and increased risk of asymmetric overgrowth [15]. Other studies reported no difference in most major perinatal outcomes between GDM and non-GDM twin pregnancies [11, 13, 14, 16]. Thus, the reports have been conflicting. Furthermore, most of these studies involved Westerners [10-13, 15, 16].

Of note, the incidence of monozygotic twins (MZTs) in women who underwent assisted reproductive technology (ART) was 1.4%, which is about 3.5 times higher than that of MZTs from spontaneous pregnancies (0.4%)
In particular, the MZT rate after blastocyst transfer was estimated to be 1.7%, which is 4.25 times higher than that from spontaneous pregnancies [18, 19]. Currently in Japan, the incidence of multiple pregnancies is decreasing due to restrictions on the number of embryos transferred, but the multiple pregnancy rate for fresh embryo transfers is still high, at 2.6%, while that for frozen embryo transfers is 2.9% [20]. Since the number of births by ART is increasing every year in Japan [20], there is a possibility that the number of multiple pregnancies will increase in the future.

As described above, in Japan, the number of twin pregnancies with GDM may increase in the future due to the development of ART and an increase in gestational age. However, since twin pregnancies are often excluded from GDM studies, there are few studies on twin pregnancies with GDM, and few of them involved Asians.

This study aimed to compare the background and perinatal outcomes between Japanese twin pregnancies with and without GDM at a single perinatal center in Japan. Additionally, the clinical course of GDM among Japanese women with twin pregnancies was investigated.

**Materials and Methods**

This was a retrospective, single-center study using a database of medical records (UMIN Clinical Trial Registry 000042345). The ethics committee of Yokohama City University approved the study (No. B180600059). We studied the cases registered in our perinatal registration database at the Perinatal Center for Maternity and Neonate, Yokohama City University Medical Center, from January 1, 2011 to December 31, 2016. These pregnancies all resulted in delivery after 22 weeks and 0 days of gestation. A total of 324 cases extracted using the keyword “twin pregnancy” were included in the study. Fifteen cases in which a glucose tolerance assessment was not performed at the hospital owing to maternal transport and pregnancy complicated with type 1 diabetes (one case) and type 2 diabetes (one case) were excluded from the study (Fig. 1).

In our hospital, those who met any of the following conditions were treated as being at high risk of GDM: blood glucose level ≥95 mg/dL, pre-pregnancy body mass index (BMI) ≥25 kg/m², positive urine glucose test, advanced maternal age (≥35 years), diabetic first- and second-degree relatives, history of previous LGA delivery, history of shoulder dystocia, history of perinatal loss or an unexplained malformation, or history of GDM [21]. For high-risk pregnant women, a 75-g oral glucose tolerance test (OGTT) was performed without a glucose challenge test (GCT) in early pregnancy (12–15 weeks gestation). Generally, twin pregnancies are treated as high-risk groups for GDM. However, multiple pregnancies alone were not subjected to an initial OGTT at our hospital, and a 50-g GCT or 75-g OGTT was performed at the attending physician’s discretion during the first trimester (gestation up to the end of 13 weeks) and second trimester (gestation between 14–27 weeks).

A GCT was performed in the second trimester (by 24–26 weeks) for women with a normal OGTT in the first trimester or without the above risks. A 75-g OGTT was performed for cases of positive GCT or suspected elevated blood glucose levels, such as urine glucose 2+,...
levels were <120 mg/dL, patients were managed as out-patients. The GCT was performed 1 h after the administration of 50 g of glucose, and glucose levels in venous whole blood >140 mg/dL were considered positive. For the 75-g OGTT, 75 g of glucose was administered during fasting, and venous whole blood was drawn after exactly 1 h and 2 h; GDM was diagnosed if any one of the following values were exceeded: 92 mg/dL before the test, 180 mg/dL after 1 h, and 153 mg/dL after 2 h.

When GDM was diagnosed, the dietary guidance was 30 kcal × ideal body weight (IBW) + 150 kcal until 28 weeks of gestation and 30 kcal × IBW + 350 kcal after 28 weeks of gestation. For obese pregnant women with a pre-pregnancy BMI ≥25 kg/m², the nutritional guidance of 30 kcal × IBW was provided throughout the pregnancy. When two or three OGTT measurement values at diagnosis exceeded the standard value or when the HbA1c level was 5.9% or higher (or glycoalbumin was 15.9% or higher) in monthly follow-up blood sampling tests, patients were admitted to the perinatal center and were provided a 6-meal-a-day diet (each meal: breakfast, lunch, and dinner, divided into two equal portions). The patients had their blood glucose levels measured 2 hours after the start of meals. If the postprandial blood glucose levels were <120 mg/dL, patients were managed as out-patients. However, if the postprandial blood glucose levels exceeded 120 mg/dL even after the prescribed diet, the attending obstetrician judged that the patient should receive insulin, and insulin therapy was initiated with the intervention of the Department of Endocrinology and Diabetology. The number of insulin units administered and the method of dose adjustment were decided by the attending physician of the Department of Endocrinology and Diabetology.

Self-monitoring of blood glucose (SMBG) was performed by all pregnant women using insulin. Since March 2016, the indications for SMBG have been expanded to allow its use in patients with high-risk GDM who are not insulin users. According to the Japanese guidelines for insurance coverage, high-risk GDM was specifically defined as patients with HbA1c levels of <6.5% and a 75-g OGTT 2-hour value of ≥200 mg/dL; patients with abnormally high plasma glucose values for two of the three measurements in the 75-g OGTT were indicated for SMBG. SMBG was also indicated for patients considered at high risk for GDM because of a pre-pregnancy BMI of ≥25 kg/m² and at least one abnormally high plasma glucose value out of the three 75-g OGTT measurements.

Delivery management was performed at our perinatal center, and a postpartum 75-g OGTT was performed at the perinatal center or the Department of Endocrinology and Diabetology.

We examined the following parameters: maternal age at delivery; pre-pregnancy BMI; nulliparity or not; history and type of fertility treatments; maternal history of smoking, alcohol consumption, and hypertension; the gestational weeks at 50-g GCT and 75-g OGTT and their results; the frequency of nutritional guidance sessions and the recommended caloric intake (kcal); treatment of GDM and glycemic control status; gestational age at delivery (weeks) and mode of delivery (scheduled cesarean-, vaginal-, or emergency cesarean delivery); the number of live births; gestational weight gain; total placental weight; and birthweight, BMI, and sex. Pregnancy and delivery outcomes, such as the Apgar score, Apgar score of <7, neonatal hospitalization, hypoglycemia with a plasma glucose level of <40 mg/dL, and neonatal hyperbilirubinemia, respiratory distress, early neonatal deaths, and malformations, were compared between the GDM and non-GDM groups. “Early neonatal deaths” were child deaths occurring within the first week after birth. Information on malformations in neonates were extracted from their medical records. Malformations such as ventricular septal defects, polydactyly, external auditory canal defects, microcephaly, pulmonary artery stenosis, necrotizing enterocolitis, funnel chest, pulmonary artery stenosis, focal pulmonary artery stenosis, hypospadias, first and second branchial arch syndrome, anterior encephalocele, ptosis, accessory ear, undescended testis, umbilical hernia, inguinal hernia, congenital hydronephrosis, malformation of the auricle, cleft lip, and Down syndrome were included.

Since our study was conducted using only existing information without obtaining new samples or information, it was not feasible to obtain written consent from the participants. Therefore, information about the research was disclosed to the participants (posted on the website of the Yokohama City University Hospital, Yokohama City University Civic General Medical Center), and participants had the option to withdraw from this study.

Statistical analysis

Pregnancy outcomes were compared using the Wilcoxon signed-rank test for quantitative variables and the chi-squared test or Fisher’s exact test for categorical variables. Multiple logistic regression was applied to assess the influence of potential confounders on the association between GDM and the outcomes. We used JMP
version 15.0 (SAS Institute, Cary, NC, USA) for data analysis. Statistical significance was set at a \( p \)-value of \(<0.05\).

**Results**

**Characteristics of the study population**

The clinical characteristics of twin pregnancies with and without GDM are outlined in Table 1. GDM twin pregnancies were common in older pregnant women with a higher pre-pregnancy BMI.

Of the 307 eligible twin pregnancies in this study, 123 underwent a GCT in the first trimester. Twenty-four pregnancies had a positive GCT and subsequently underwent a 75-g OGTT: two were diagnosed with GDM. Of the 99 twin pregnancies with a negative GCT, 87 underwent a subsequent OGTT: six were diagnosed with GDM. There were 184 pregnant women with suspected elevated blood glucose levels, for example those with urine glucose 2+, who underwent an OGTT without having a GCT in early or mid-pregnancy; 39 were diagnosed with GDM. Finally, 47 (15.3%) pregnancies were diagnosed with GDM, and 260 (84.7%) did not have GDM (Fig. 1).

The timing of the 75-g OGTT was studied in 295 of 307 patients. Specifically, of the 295 twin pregnancies, 71 (24.1%) underwent a 75-g OGTT in the first trimester, and 198 (67.1%) underwent a 75-g OGTT in the second trimester, 21 (7.1%) in the third trimester, and 5 cases with unknown timing. Most patients underwent OGTT in the first and second trimester.

| Table 1  | Clinical characteristics of twin pregnancies with and without GDM |
|----------|---------------------------------------------------------------|
|          | Twin pregnancies with GDM \( (n = 47) \) | Twin pregnancies without GDM \( (n = 260) \) | \( p \)-value |
| Maternal age (years) | 36 (31–39) | 33 (30–36) | \(<0.01\) |
| Pre-pregnancy BMI (kg/m\(^2\)) | 21.5 (20.0–23.3) | 20.1 (19.1–21.8) | \(<0.01\) |
| Nulliparity | 23 (49.0) | 150 (57.7) | 0.26 |
| Type of fertility treatment | 24 (51.1) | 91 (35.6) | 0.05 |
| Ovulation cycle tracking | 1 (4.1) | 2 (2.2) | 0.57 |
| Ovulation induction | 3 (12.5) | 19 (20.9) | 0.57 |
| AIH | 3 (12.5) | 16 (17.6) | 0.57 |
| IVF or ICSI | 17 (70.8) | 54 (59.3) | 0.57 |
| Smoking | 7 (15.2) | 29 (11.6) | 0.47 |
| Alcohol consumption | 10 (22.2) | 51 (20.5) | 0.84 |
| Preexisting hypertension | 6 (12.8) | 28 (10.8) | 0.62 |
| Chorionicity | — | — | — |
| Dichorionic | 14 (29.8) | 98 (37.8) | 0.59 |
| Monochorionic | 33 (70.2) | 158 (61.0) | — |
| Unidentified | 0 (0.0) | 3 (1.2) | — |
| 50-g GCT 1-h glucose (mg/dL) | 124.5 (79.8–154.8) | 119 (103–135.3) | 0.85 |
| Gestational weeks at OGTT (weeks) | 14.5 (13–25.3) | 18.9 (14–25) | \(<0.05\) |
| 75-g OGTT results | — | — | — |
| Fasting glucose (mg/dL) | 91 (84–94) | 82 (78–85) | \(<0.01\) |
| 1-h glucose (mg/dL) | 166 (143–189) | 124 (106–139) | \(<0.01\) |
| 2-h glucose (mg/dL) | 153 (132–164) | 114 (102–124) | \(<0.01\) |
| Nutritional guidance | 46 (97.9) | — | — |
| Insulin therapy | 4 (8.5) | — | — |
| SMBG implemented | 6 (12.7) | — | — |

Values are presented as mean (interquartile range) or numbers (%). Statistics are shown as \( p \)-values.

GDM, gestational diabetes mellitus; BMI, body mass index; AIH, artificial insemination by husband; IVF, *in vitro* fertilization; ICSI, intracytoplasmic sperm injection; SMBG, self-monitoring of blood glucose.
Four (8.5%) women with GDM were treated with insulin. SMBG was implemented for all four patients in the insulin group and two patients in the diet group. Glycemic control during pregnancy was good, with glycoalbumin levels below 15.8% in all patients in both the insulin and diet groups. There was no difference in weight gain between the insulin and diet groups throughout pregnancy. Nutritional guidance was provided to 46/47 patients with GDM, and the frequency of nutritional guidance sessions during pregnancy varied from one to six.

**Outcomes of study population**

Pregnancy and neonatal outcomes of twin pregnancies with and without GDM are presented in Table 2. There were 86 live births from 47 twin pregnancies with GDM, while there were 502 live births from 260 non-GDM twin pregnancies. The median weight gain throughout pregnancy was +8.0 kg in the GDM group and +11.8 kg in the non-GDM group, with less weight gain in the GDM group (p < 0.01); however, other delivery outcomes were similar for both mothers and neonates in the GDM and non-GDM groups. Similar results were observed for the outcomes adjusted for age and pre-pregnancy BMI (Table 3).

**Discussion**

Our study demonstrated that twin pregnancies with GDM were more common in older pregnant women with a higher pre-pregnancy BMI. Additionally, although 8.5% of pregnant women with twin pregnancies complicated by GDM were treated with insulin, they also tended to have severe caloric restrictions despite the twin pregnancies. There was no difference in delivery outcomes between the GDM and non-GDM groups.

In this study, the GDM group was older and had a higher BMI, which is consistent with previous reports. There were no significant differences in the other background factors between the GDM and non-GDM groups. In twin pregnancies, the high placental weight and high secretion of human placental lactogen increase insulin resistance and predispose pregnant women to GDM [23]. Furthermore, it has been reported that the degree of glucose intolerance in twin pregnancies is the same as that in singleton pregnancies due to increased fetal glucose consumption [24, 25] and maternal basal metabolic rate [25]. The incidence of GDM in twin pregnancies in our study (15.3%) was similar to that in singleton pregnancies in our hospital (13%) (p = 0.26) [26].

The percentage of patients receiving insulin therapy in singleton pregnancies at perinatal centers in Japan has been reported to be around 31–35% [24, 27, 28], while the percentage of patients receiving insulin therapy in twin pregnancies was reported to be 12.1% [29], 18.1% [30], 26.1% [31], and 45% [24]. The insulin introduction rate in twin pregnancies among GDM cases was 8.5% in this study, which was not different from the insulin introduction rate in singleton pregnancies with GDM in our hospital (8.6%) (p > 0.99) [26]. However, the insulin introduction rate in this study was lower than that in previous reports of twin pregnancies with GDM. This was because both women with twin pregnancies or singleton pregnancies were provided the same nutritional guidance; the caloric intakes were all within the range of 1,500–2,100 kcal. Therefore, it is possible that the caloric requirements of twin pregnancies were not sufficient and that 43/47 (91.4%) cases were controlled by diet alone. In fact, weight gain was lower in pregnant women with GDM (+8.0 kg) than in those without GDM (+11.8 kg).

In 2009, the Institute of Medicine (IOM) released gestational weight gain (GWG) guidelines, including those for pregnant women with twins [32]. Specifically, the optimal GWG is 16.8–24.5 kg for women with a normal BMI (18.5–24.9 kg/m²), 14.1–22.7 kg for overweight women (BMI: 25.0–29.9 kg/m²), and 11.3–19.1 kg for obese women (BMI: ≥30 kg/m²). In our study, only 3 out of 43 (7.0%) women with a pre-pregnancy BMI ≥18.5 kg/m² reached the recommended GWG. Among non-GDM women with a BMI ≥18.5 kg/m², only 28 out of 215 (13.0%) reached the IOM-recommended weight gain for twin pregnancies for each pre-pregnancy BMI (p = 0.439). None of the women gained more than the recommended IOM weight.

In Japanese twin pregnancies, Suzuki [33] found that the GWG of women with normal pre-pregnancy BMI and a good perinatal outcome was 13.9 ± 3.4 kg. Shimura et al. [34] reported that the GWG of women who gave birth to both twins with a weight appropriate for gestational age was 13.6 kg, suggesting that the optimal GWG for Japanese pregnant women with twins may be lower than that described in the IOM guidelines. However, since both of these two studies involved Japanese twin pregnancies without gestational diabetes, the optimal GWG for Japanese twin pregnancies with GDM has not been investigated in the past. It is necessary to examine the optimal GWG and the recommended caloric intake for women with GDM having twin pregnancies.

Several studies have reported no difference in delivery outcomes between twin pregnancies with and without GDM [10, 13, 30, 35]. Our study concurs with these previous studies. This is because twin pregnancies are high-risk pregnancies and are subject to careful gestational and delivery management [18]. Prenatal care (PNC) is recognized as a means of monitoring maternal and fetal...
health, leading to safe and healthy pregnancies, safe births, and healthy newborns [36]. In our hospital, prenatal checkups were performed every 2 weeks for twin pregnancies with or without GDM, and weekly checkups were performed in the second trimester. It was not clear whether the increased number of PNCs in twin pregnancies reduced the probability of risk in cases of GDM complications. However, it could have been useful for assessing maternal and fetal health status and the accessibility of essential health services of appropriate quality.

| Table 2 | Newborn and delivery outcomes of twin pregnancies with and without GDM |
|---------|--------------------------------------------------------------------------------|
|         | Twin pregnancies with GDM \((n = 47)\) | Twin pregnancies without GDM \((n = 260)\) | \(p\)-value |
| GA at delivery (weeks) | 37 (35–37) | 37 (35–37) | 0.64 |
| Preterm delivery <37 weeks | 23 (48.9) | 121 (46.5) | 0.87 |
| Mode of delivery | — | — | 0.78 |
| Scheduled cesarean delivery | 21 (44.7) | 116 (44.6) | |
| Vaginal delivery | 6 (12.7) | 26 (10.0) | |
| Emergency cesarean delivery | 20 (42.6) | 118 (45.4) | |
| Number of live births | — | — | 0.08 |
| 2 | 41 (87.2) | 245 (94.2) | |
| 1 | 4 (8.5) | 12 (4.6) | |
| 0 | 2 (4.2) | 3 (1.2) | |
| Gestational weight gain (kg) | 8 (5.9–12.3) | 11.8 (9–15) | <0.01 |
| Total placenta weight (g) | 880 (650–1,046) | 913 (795–1,021) | 0.45 |
| Neonatal sex | — | — | 0.50 |
| Male/male | 23 (48.9) | 106 (40.8) | |
| Male/female | 5 (10.6) | 43 (16.5) | |
| Female/female | 19 (40.4) | 111 (42.7) | |
| Newborns of mother with GDM \((n = 86)\) | Newborns of mother without GDM \((n = 502)\) | \(p\)-value |
| Birth weight (g) | 2,322 (2,005.5–2,593.5) | 2,288 (2,003–2,538) | 0.57 |
| SGA | 24 (27.3) | 151 (30.5) | 0.72 |
| AGA | 63 (71.6) | 333 (62.8) | |
| LGA | 1 (1.1) | 11 (2.2) | |
| Apgar score at 1 min | 8 (8–8) | 9 (9–9) | 0.66 |
| Apgar score at 5 min | 8 (8–8) | 9 (9–9) | 0.81 |
| Apgar score of <7 at 5 min | 9 (10.2) | 42 (8.4) | 0.54 |
| Admission to NICU | 31 (36.1) | 153 (30.5) | 0.32 |
| Neonatal blood glucose level <40 mg/dL | 16 (18.8) | 108 (21.5) | 0.15 |
| Neonatal hyperbilirubinemia | 16 (18.8) | 84 (16.7) | 0.64 |
| Respiratory distress syndrome | 5 (5.9) | 30 (6.0) | 1.00 |
| RDS + TTN | 8 (9.4) | 65 (13.0) | 0.48 |
| Early neonatal deaths | 2 (2.3) | 3 (0.60) | 0.16 |
| Congenital anomaly | 7 (8.2) | 22 (4.4) | 0.17 |

Values are presented as mean (interquartile range) or numbers (%). GDM, gestational diabetes mellitus; GA, gestational age; SGA, small for gestational age (newborn with birth weight of <10\textsuperscript{th} percentile for GA); AGA, appropriate for gestational age (newborn with birth weight between 10\textsuperscript{th} and 90\textsuperscript{th} percentile for GA); LGA, large for gestational age (newborn with birth weight of >90\textsuperscript{th} percentile for GA); RDS, respiratory distress syndrome; TTN, transient tachypnea of the newborn; NICU, neonatal intensive care unit; Early neonatal deaths, Deaths of newborns within 1 week.
The unique feature of our study is the clarification of the characteristics for GDM, gestational and delivery outcomes, and the clinical course of GDM in Japanese twin pregnancies. There are a few previous studies on risk factors and gestational and delivery outcomes of twin pregnancies with GDM; however, most of these studies included patients mostly from Western countries [10-13, 15, 16]. It has been reported that pre-pregnancy obesity [2] and excessive weight gain during pregnancy [6, 37] are risk factors for GDM. It is difficult to directly apply the reported clinical course in those countries to twin pregnancies with GDM in the Japanese population because Asian women develop GDM even in the absence of GDM risk factors, such as pre-pregnancy obesity and weight gain [38]. Therefore, the present study, which analyzed twin pregnancies with GDM in Japanese women, is clinically meaningful.

Our study has several limitations. First, this was a retrospective study. Therefore, data on the insulin level and C-peptide immunoreactivity were not collected at the time of the 75-g OGTT. As a result, we could not evaluate diabetes-related indices such as insulin secretion capacity and resistance. Second, we did not follow-up on the actual dietary habits of pregnant women after nutritional guidance was provided to them. Third, SMBG measurement was rarely used for glucose management during pregnancy. This is because insurance coverage in Japan for SMBG measurement in insulin-free GDM was not available until March 2016. Since this study included twins who were delivered after 22 weeks and 0 days of gestation from January 1, 2011 to December 31, 2016, and the rate of insulin uptake in twins in this study was 8.5%, it is expected that the number of patients who were diagnosed with GDM and underwent SMBG measurement was small. Fourth, we are not certain whether it is better to increase the caloric intake in twin pregnancies with GDM. We consider that the low-calorie diet prescribed during nutritional guidance may have led to poor weight gain. However, increasing the caloric intake may increase the number of cases in which the glycemic control might worsen or insulin might be required, which may affect the delivery outcome. Additionally, attention should be paid to excessive weight gain.

In conclusion, pregnant women with twins complicated by GDM were older, had a higher pre-pregnancy BMI, and did not have different delivery outcomes, when compared to pregnant women with twins without GDM. However, there was less weight gain throughout gestation in the twin pregnancies with GDM. For the management of twin pregnancies with GDM, it is necessary to pay attention not only to the blood glucose levels but also to the weight of the patient. Future studies should examine the optimal GWG for Japanese twin pregnancies with GDM.

| Table 3 Logistic regression-adjusted outcomes of twin pregnancies with GDM |
|-------------------------------|----------------|-----------------|
| **Preterm delivery of <37 weeks** | 0.85 (0.54–1.35) | 0.50 |
| **Death of one or more of the twins** | 2.83 (0.98–8.16) | 0.05 |
| **Emergency cesarean delivery** | 0.92 (0.58–1.47) | 0.73 |
| **SGA** | 0.82 (0.48–1.39) | 0.46 |
| **LGA** | 0.78 (0.09–6.38) | 0.81 |
| **Apgar score of <7 at 5 min** | 1.51 (0.68–3.37) | 0.31 |
| **Admission to NICU** | 1.39 (0.84–2.30) | 0.20 |
| **Neonatal blood glucose level <40 mg/dL** | 0.90 (0.49–1.66) | 0.75 |
| **Neonatal hyperbilirubinemia** | 1.54 (0.82–2.88) | 0.17 |
| **Respiratory distress syndrome** | 1.37 (0.50–3.85) | 0.53 |
| **RDS + TTN** | 0.80 (0.36–1.78) | 0.58 |
| **Early neonatal deaths** | 3.65 (0.54–24.6) | 0.18 |
| **Congenital anomaly** | 0.59 (0.23–1.50) | 0.27 |

* Adjusted for age and pre-pregnancy body mass index.

GDM, gestational diabetes mellitus; OR, odds ratio; CI, confidence interval; SGA, small for gestational age (newborn with birth weight of <10th percentile for gestational age); AGA, appropriate for gestational age (newborn with birth weight between 10th and 90th percentile for gestational age); LGA, large for gestational age (newborn with birth weight of >90th percentile for gestational age); RDS, respiratory distress syndrome; TTN, transient tachypnea of the newborn; Early neonatal deaths, Deaths of newborns within 1 week.
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Disclosure

None of the authors has any potential conflicts of interest associated with this research.

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