

Risk of obstetric and neonatal morbidity in gestational diabetes in a single institution

A retrospective, observational study

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Abstract

Gestational diabetes mellitus (GDM) is defined as a carbohydrate intolerance with onset or first recognition occurring during pregnancy and GDM could be risk factor for various maternal fetal complications. This study aimed to investigate risks of maternal and neonatal outcomes according to GDM and normal glucose tolerance. This retrospective, observational study included singleton pregnant women who had received a 50-g oral glucose challenge test in 2nd trimester of gestation and gave birth at National Health Insurance Service Ilsan Hospital. Maternal and neonatal complications were compared between GDM and non-GDM groups. Among the 682 women, 56 were diagnosed with GDM and 626 were non-GDM group. Maternal age was older and prepregnant body mass index was higher in GDM. The rate of cesarean delivery, preeclampsia, and transfusion was similar; however, the incidence of preterm birth was higher in GDM. Multivariate analysis, however, showed that GDM was independent risk factor only for preterm birth in <37 weeks (adjusted odds ratio, 2.25; 95% confidence interval, 1.16–4.36). Regarding neonatal morbidities, APGAR score <7 at 5 minutes and the rate of macrosomia were similar; however, the rates of neonatal intensive care unit (NICU) admission, large for gestational age (LGA), and intubation were higher in GDM. Multivariate analysis, however, showed that GDM was not independent risk factor for LGA, NICU admission, and intubation rate. Compared with the non-GDM group, GDM was associated with an increased likelihood of preterm birth <37 weeks, however, did not increase cesarean delivery, postpartum hemorrhage, LGA, and NICU admission rate. This study showed that the majority of women with GDM delivered with similar maternal and neonatal outcomes in non-GDM women.

Abbreviations: BMI = body mass index, GDM = gestational diabetes mellitus, GIGT = gestational impaired glucose tolerance, IOM = Institute of Medicine, LGA = large for gestational age, NICU = neonatal intensive care unit, OGCT = oral glucose challenge test.

Keywords: gestational diabetes, gestational weight gain, newborn infant, obstetric delivery, pregnancy outcome

1. Introduction

Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance first diagnosed during pregnancy.^[1,2] Even though the majority of GDM resolves in postpartum, GDM can serve as a significant risk factor for type 2 diabetes later in life.^[3–5]

During pregnancy, GDM is associated with many critical obstetrical complications. Insulin resistance in GDM patients is associated with development of gestational hypertension and preeclampsia.^[6–9] Furthermore, suboptimal glucose control in GDM patients has been reported to increase risk of stillbirth.^[10] Per neonatal morbidity, randomized trials have consistently demonstrated that maternal hyperglycemia significantly increases the

likelihood of having large for gestational age (LGA) or macrosomic infants.^[11–14] Macrosomia could further aggravate adverse neonatal outcomes such as shoulder dystocia and its associated complications including brachial plexus injuries, clavicle fractures, and neonatal depressions. Such fetal weight gain is associated with an increased risk of operative deliveries.^[15,16]

To prepare for such cases, obstetricians have been previously advised to pay attention to maternal weight changes during pregnancy. Previous retrospective cohort study demonstrated that pregnant women with appropriate body weights were likely to have optimal pregnancy outcomes, whereas women with excessive weight gain during pregnancy were associated with a significantly increased risk of having an LGA infant, preterm birth, and cesarean delivery.^[17]

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Informed consent was waived because of the retrospective study design.

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are publicly available.

The study was approved by the National Health Insurance Service Ilsan Hospital Institutional Review Board (#NHIMC 2020-03-083) and performed in accordance with the principles of the Declaration of Helsinki.

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Besides complications associated with macrosomia, neonates of pregnancies complicated by GDM have been reported to be at increased risk of multiple, often transient, complications (e.g., hypoglycemia, hyperbilirubinemia, respiratory distress, and/or cardiomyopathy).^[18,19]

Despite such established complications of GDM, it is important to note that women with mild gestational diabetes have similar malformation rates with general nondiabetic obstetric population,^[20] and GDM patients who achieve euglycemia with nutritional therapy alone (i.e., class A1 GDM do not have the aforementioned pregnancy complications nor increased risk of stillbirth).^[21] GDM is becoming more common worldwide, with the prevalence of 6% to 7% in the United States; with westernization of diet in South Korea, similar rate of 5.6% is observed.^[1,22-24] In South Korea, pregnant women – except for those previously diagnosed with diabetes – undergo GDM screening with a 50-g oral glucose challenge test (OGCT) between 24 and 28 weeks of gestation. If screening results were ≥ 140 mg/dL, a 100-g oral glucose tolerance test (OGTT) was performed for the confirmatory diagnosis of GDM.

This study aimed to investigate maternal and neonatal outcomes according to GDM and normal glucose tolerance in a single institution.

2. Materials and Methods

This study was an observational, retrospective study conducted at the National Health Insurance Service Ilsan Hospital in the Republic of Korea between January 1, 2012 and December 31, 2019. The study was approved by National Health Insurance Service Ilsan Hospital's institutional review board (approval number; NHIMC 2020-03-083). The need for informed consent was waived due to the retrospective design of this study. All women who had received a 50-g OGCT between 24 and 28 weeks of gestation and delivered at the National Health Insurance Ilsan Hospital were considered for participation in this study. The following inclusion criteria were excluded: multiple pregnancies, preexisting diabetes mellitus or hypertension, and women with autoimmune diseases or major fetal anomalies requiring postpartum urgent care (such as hydrocephalus or major cardiac disease). From EMR, maternal age, gestational age at birth, maternal weight before pregnancy and just before delivery, and hemoglobin level change before and after delivery to assess blood loss during delivery were obtained. To evaluate maternal outcomes, the preterm birth rate, cesarean delivery rate, incidence of preeclampsia, and maternal weight gain during pregnancy were evaluated. To evaluate neonatal outcomes and morbidities, our group investigated neonatal birth weight, 1- and 5-minute APGAR scores, neonatal intensive care unit (NICU) admission rate, meconium status, and neonatal intubation status were obtained. Length of hospitalization longer than 6 days as abnormal. In addition, we investigated known neonatal complications of GDM, which are LGA, fetal skull fracture, and brain damage. LGA was defined according to papers of Doubilet et al.^[25] All diagnoses were based on the International Classification of Disease, 10th revision codes, and relevant procedure codes. Cerebral hemorrhage (P10x), other birth injuries to skull (P131), intracranial hemorrhage (P52), and neonatal cerebral ischemia (P91) are considered as brain damages. Weeks of gestation were determined by obstetricians using the earliest ultrasonography examinations or calculated from the first date of last menstruation period.^[26] If the gestational age obtained from ultrasonography examinations differed from those obtained using the first date of mothers' last menstrual period by >7 days, gestational age by ultrasonography was used. GDM screening was performed between 24 and 28 weeks of gestation in women without previous history of glucose intolerance. If this 50-g screening test was >140 mg/dL of plasma glucose concentration, diagnostic 100-g, 3-hour

OGTT was performed. For the 50-g screening, the plasma glucose level was measured 1 hour after 50-g oral glucose loading regardless of the time of the day or the time of the last meal. In case of the 100-g OGTT, 3-hour OGTT was performed after overnight fasting. The proposed criteria for the interpretation of the diagnostic 100-g OGTT are 95 mg/dL at fasting, 180 mg/dL at 1 hour, 155 mg/dL at 2 hour, and 140 mg/dL at 3 hour: two or more abnormal values are required for a positive diagnosis of GDM.^[27,28]

The gestational impaired glucose tolerance (GIGT) group was defined as those who had abnormal 50-g OGCT but normal 100-g. We hypothesized that this group would have different outcomes than those with a normal 50-g OGCT and those with abnormal 100-g OGTT.

Student *t* test was used for the analysis of continuous values in two groups and the χ^2 test or Fisher's exact test for categorical values. Independent predictors for maternal and neonatal complications were determined by multivariate analysis using a logistic regression model. All *P*-values were 2-tailed, and *P* < .05 was defined to be statistically significant. All analyses were performed using the Statistical Package for Social Sciences version 23.0 (SPSS Inc., Chicago, IL).

3. Results

A total of 2535 women who delivered at the National Health Insurance Service Ilsan Hospital between January 1, 2012 and December 31, 2019 were recruited for this study. A total of 1727 pregnant women who did not receive the 50-g OGTT were excluded, leaving a total of 808 women received 50-g OGCT test. Of them, 82 women with twin pregnancies, 32 women with preexisting hypertension, 8 women with autoimmune diseases, and 4 women with major fetal anomalies were further excluded, leaving final 682 women in this study (Fig. 1).

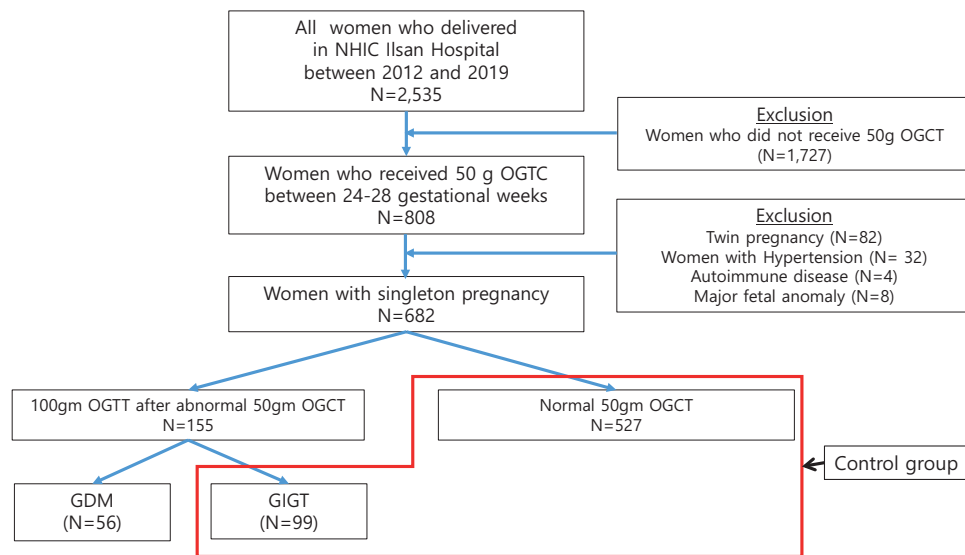
Among the participants, 155 women had a 50-g OGTT of ≥ 140 mg/dL, and 56 were diagnosed with GDM after the 100-g OGTT. The remaining 99 women were diagnosed with GIGT. A total of 527 women with glucose level <140 mg/dL after 50-g OGCT were labeled as the non-GDM group (Fig. 1).

Among the 56 GDM patients, 47 were of the GDM A1 type whose fasting glucose levels were <105 mg/dL, and only 8 required insulin for glucose control.

The patients' demographics according to their gestational glucose tolerance status are shown in Table 1. Among the 682 participants, 56 were diagnosed with GDM, and 626 were control group. GDM patients were older (35.2 ± 4.5 vs 33.5 ± 4.5 years old; *P* = .006) and delivered earlier (37.1 ± 2.4 vs 38.0 ± 1.9 weeks; *P* = .001) (Table 1). Prepregnant body mass index (BMI) and rates of obesity – defined as BMI > 25 – were higher in GDM group (24.3 ± 5.4 vs 21.9 ± 3.4 kg/m²; 42.9% vs 16.6%; all *P* < .001) (Table 1). Intrauterine fetal death in GDM group was 0 and 3 in non-GDM group. The BMI at term, maternal height, and the proportion of multiparity were similar between the two groups (Table 1). All values of maternal characteristics of the GIGT group were between those of the GDM and those of group with glucose level < 140 mg/dL after 50-g OGCT.

The comparisons of maternal outcomes according to GDM are shown in Table 2. The incidences of cesarean delivery and preeclampsia were similar between the two groups (50.0% vs 38.7%, 3.6% vs 1.4%, respectively; all *P* > .05). The incidence of preterm birth was higher in the GDM group than in the non-GDM group (8.9% vs 2.6%, in <34 weeks, *P* = .023; 28.6% vs 11.8%, in <37 weeks, *P* = .001) (Table 2).

Hemoglobin level change and the rate of blood transfusion were associated with intrapartum bleeding, and no significant difference between two groups was observed (Table 2). Maternal weight gain during pregnancy was lower in the GDM group than in the non-GDM group (8.4 ± 4.8 vs 12.2 ± 4.5 kg; *P* < .001) (Table 2). Like maternal characteristics, all values of



OGCT, oral glucose challenge test; GDM, gestational diabetes; GIGT; Gestational Impaired glucose tolerance

Figure 1. Final sample of women available for the analysis. OGCT = oral glucose challenge test; GDM = gestational diabetes; GIGT = gestational impaired glucose tolerance.

maternal outcomes in the GIGT group were between those of the GDM and non-GDM group, which was not different from that in normal non-GDM group.

Additionally, there were significant differences in hemoglobin A1c and fasting glucose between the GDM group and the non-GDM group ($5.6 \pm 0.7\%$ vs $4.9 \pm 1.1\%$, $88.8 \pm 18.2\text{mg/dL}$ vs $79.8 \pm 6.2\text{mg/dL}$, respectively; all $P < .001$) (Table 2).

Regarding neonatal morbidities, the rates of NICU admission and LGA were higher in the GDM group than in the non-GDM group (35.7% vs 22.0% , $P = .030$, 12.5% vs 5.1% , $P = .033$, respectively) (Table 3). The averages of the 1- and 5-minute APGAR scores were lower in the GDM group with statistical significance (6.4 ± 1.7 vs 6.8 ± 1.1 , $P = .035$, 7.8 ± 1.5 vs 8.1 ± 1.1 , $P = .038$, respectively); however, rate of APGAR score <7 at 5 minutes was similar between the two groups (7.1% vs 3.5% ; $P = .260$) (Table 3). Also, there was no significant difference between fetal birth weight nor prevalence of macrosomia, defined as fetal weight >3500 or 4000g . Rate of meconium-stained amniotic fluid was also similar between the groups (Table 3).

Severe neonatal complications associated with GDM are shown in Table 3. The incidence of neonatal brain damage and clavicle fracture were either absent or very rare and did not differ between the two groups. Respiratory distress syndrome,

hyaline membrane disease, and transient tachypnea were considered as birth asphyxia and were not different between the two groups (Table 4). The incidence of intubation rate was higher in the GDM group (10.7% vs 3.5% ; $P = .021$); however, the prolonged neonatal length of stay of longer than 6 days was similar between the two groups (26.8% vs 16.8% ; $P = .067$) (Table 4). The rate of surfactant use did not differ between the two groups (7.1% vs 2.9% ; $P = .092$) (Table 4).

In the final logistic regression model, multivariate analysis showed that GDM was risk factor only for preterm birth <37 weeks (adjusted odds ratio, 2.25; 95% confidence interval, 1.16–4.36), however, GDM was not risk factor for preterm birth <34 weeks, LGA, NICU admission and intubation rate (Table 5).

4. Discussion

This study demonstrated that GDM patients were older, have higher prepregnancy BMI, and were more likely to have increased preterm birth <37 weeks. GDM patients were not more likely to have increased cesarean delivery rate, preeclampsia, APGAR score <7 at 5 minutes, and neonatal length of stay >6 days.

Table 1
Patients' general characteristics according to gestational glucose tolerance status

	GDM (n = 56)	Control (n = 626)	Significance
Age (years old)	35.2 ± 4.5	33.5 ± 4.5	0.006*
Gestational weeks at birth (wk)	37.1 ± 2.4	38.0 (1.9)	0.001*
50-gm OGCT (g/dL)	171.1 ± 26.5	117.3 ± 23.3	$<0.001^*$
Maternal height (cm)	160.6 ± 5.8	161.5 ± 5.2	0.271
Prepregnant BMI (kg/m ²)	24.3 ± 5.4	21.9 ± 3.4	$<0.001^*$
BMI at term (kg/m ²)	27.7 ± 5.4	26.6 ± 3.4	0.071
BMI > 25 before pregnancy	24 (42.9)	104 (16.6)	$<0.001^*$
Multiparity	30 (53.6)	374 (59.7)	0.368

Values are presented as the mean ± standard deviation or n (%).

BMI = body mass index; GDM = gestational diabetes mellitus; OGCT = oral glucose challenge test.

*Statistical significance.

Table 2
Comparison of maternal complications according to gestational glucose tolerance status

	GDM (n = 56)	Control (n = 626)	Significance
Cesarean delivery rate	28 (50.0)	242 (38.7)	0.096
Preeclampsia	2 (3.6%)	9 (1.4%)	0.225
Preterm delivery < 34 wks	5 (8.9%)*	16 (2.6%)*	0.023*
Preterm delivery < 37 wks	16 (28.6%)*	74 (11.8%)	0.001*
Hgb decrease after delivery	1.4 (±1.1)	1.3 (±1.1)	0.585
Transfusion	2 (3.6%)	16 (2.6%)	0.653
Weight gain during pregnancy	8.4 (±4.8)*	12.2 (±4.5)	$<0.001^{\dagger}$
Hgb A1c (%)	5.6 (±0.7)	4.9 (±1.1)	$<0.001^{\dagger}$
Fasting glucose (g/dL)	88.8 (±18.2)	79.8 (±6.2)	$<0.001^*,\dagger$

Values are presented as the mean ± standard deviation or n (%).

GDM, gestational diabetes mellitus.

*Statistical significance.

Table 3
Comparison of neonatal outcomes according to GDM

	GDM (n = 56)	Control (n = 626)	Significance
APGAR score (1 min)	6.4 ± 1.7	6.8 ± 1.1	0.035*
APGAR score (5 min)	7.8 ± 1.5	8.1 ± 1.1	0.038*
APGAR < 7 at 1 min	24 (42.9)	162 (25.9)	0.011*
APGAR < 7 at 5 min	4 (7.1)	22 (3.5)	0.260
Birth weight	2990 ± 565	3086 ± 490	0.167
NICU admission	20 (35.7)	137 (22.0)	0.030*
LGA	7 (12.5)	32 (5.1)	0.033*
Meconium aspiration	3 (5.4)	22 (3.5)	0.451
Birth weight ≥ 3500 gm	8 (14.3)	112 (17.9)	0.586
Birth weight ≥ 4000 gm	1 (1.8)	14 (2.2)	1.000

Values are presented as the mean ± standard deviation or n (%).

GDM = gestational diabetes mellitus; LGA = large for gestational age.

*Statistical significance.

Generally, the prevalence rate of GDM was 8.2% (56/682), among whom only 14.3% (8/56) were treated with insulin for glucose control. Most women with GDM achieved glycemic control only with diet, exercise, and weight control without an insulin requirement. This study showed a higher prevalence of GDM compared with previous studies conducted in South Korea.^[29] This can be attributed to the nature of our institution as an academic hospital that can accommodate high-risk pregnant women with higher average maternal age. The maternal and neonatal complications reported in this study were largely related to maternal hyperglycemia. Gardner et al^[13] reported that intensive treatment of GDM may have little effects on birth weight, birth trauma, operative delivery, or neonatal metabolic disorders. Furthermore, in contrast to historical studies, a secondary analysis of data from the Antenatal Late Preterm Steroids trial found that GDM is not associated with a clinically significant difference in neonatal respiratory outcomes.^[30]

Interestingly, weight gain during pregnancy was lower in women with GDM in this study, indicating that women with GDM are more concerned about weight gain during pregnancy. Previous retrospective cohort study has shown that women with GDM with appropriate weight gain had optimal outcomes, whereas those with excessive weight gain had significantly increased risk of having an LGA infant, preterm births, and cesarean deliveries.^[17,31] Suboptimal weight gain seemed to increase the likelihood of avoiding medical therapy for gestational diabetes and to decrease the likelihood of having an LGA neonate. However, according to the study conducted by Cheng et al,^[17] those with weight gain below the Institute of Medicine guidelines are prone to have small for gestational age neonates compared to those with proper weight gain within Institute of Medicine guidelines (7.3% vs 5.6%, $P < .001$). Hillier et al^[32] also reported that excessive maternal gestational weight gain

Table 4
Severe neonatal complications according to GDM

	GDM (n = 56)	Control (n = 626)	Significance
Brain damage	1 (1.8)	12 (1.9)	1.000
Clavicle fracture	0	0	
Birth asphyxia	5 (8.9)	26 (4.2)	0.167
Surfactant usage	4 (7.1)	18 (2.9)	0.092
Intubation	6 (10.7)	22 (3.5)	0.021*
Admission > 6 d	15 (26.8)	105 (16.8)	0.067

Values are presented as the mean ± standard deviation or n (%).

GDM = gestational diabetes mellitus.

*Statistical significance.

(>18 kg) may increase doubles the risk of fetal macrosomia. The good prognosis of GDM in this study is thought to be in part an appropriate amount of weight gain during pregnancy.

In the case of GIGT, regardless of the results of 100-g OGTT, obstetric complications including preeclampsia, cesarean delivery, and preterm birth tended to increase – although it was not of statistical significance – compared with those with a negative screening test for 50-g OGCT.

The differences in the NICU admission and intubation rates between the GDM and non-GDM groups are thought to be related to the increased preterm birth in the GDM group and actually multivariate analysis showed that GDM was not risk factor for NICU admission and intubation rate.

The incidence of macrosomia was not higher in GDM, and neonatal weight was similar between the two groups, which was thought to be due to the high incidence of preterm birth in GDM. Besides, LGA was not associated with GDM in multivariate analysis.

In terms of severe neonatal complications, similar outcomes were observed in brain damage, birth asphyxia, surfactant usage, and length of stay between the groups. Severe maternal complications, such as cesarean hysterectomy and uterine artery embolization after delivery, were not different between the groups.

This study has several strengths. First, we collected the data from a single institution using a uniform protocol. Therefore, it was possible to access full records, including maternal weight changes during the pregnancy period and pregravid status, and analyze the patients' information completely in a single institution through electronic medical records. Second, to the best of our knowledge, this study is the first to investigate GIGT that could impair glucose tolerance and result in adverse maternal and neonatal outcomes, unlike women with normal results in the 50-g OGCT.

However, this study had several limitations. First, the major limitation of this study included a small population size, which may not be sufficient to generalize the results. Second, the results of this study may not be also generalizable because the data used in this study were collected and processed in a single institution.

Table 5
Logistic regression analysis of maternal and neonatal complications by GDM

	Unadjusted		Adjusted*	
	OR (95% CI)	P-value	OR (95% CI)	P-value
LGA*	2.65 (1.11–6.31)	0.028	1.52 (0.597–3.89)	0.378
NICU admission*	1.97 (1.11–3.51)	0.022	1.58 (0.83–3.01)	0.163
Intubation*	3.29 (1.28–8.49)	0.014	2.04 (0.65–6.38)	0.22
Preterm delivery < 34 wk†	3.73 (1.32–10.61)	0.013	2.68 (0.88–8.16)	0.083
Preterm delivery < 37 wk†	2.98 (1.59–5.59)	0.001	2.25 (1.16–4.36)	0.016‡

CI = confidence interval; GDM = gestational diabetes; LGA = large for gestational age; NICU = Neonatal Intensive Care Unit; OR = odds ratio.

*Adjusted for maternal age, gestational age, and prepregnancy BMI.

†Adjusted for maternal age and prepregnancy BMI.

‡Statistical significance.

In conclusion, GDM was an independent risk factor in preterm birth <37 weeks and did not increase preterm birth <34 weeks, Cesarean delivery, postpartum hemorrhage, LGA, NICU admission rate, and other severe neonatal complications, though the population of this study was relatively small. This study showed that the majority of women with GDM delivered without severe adverse maternal and neonatal morbidities and women with GDM should be given accurate information regarding the risk of GDM.

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