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Maternal and Neonatal Outcomes in Korean Women with Type 1 and Type 2 Diabetes

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Background: The purpose of this study was to evaluate maternal and neonatal outcomes in Korean women with type 1 diabetes and type 2 diabetes.
Methods: We performed a retrospective survey of 163 pregnancies in women with type 1 diabetes (n=13) and type 2 diabetes (n=150) treated from 2003 to 2010 at Cheil General Hospital & Women's Healthcare Center, Korea. We compared maternal characteristics as well as maternal and neonatal outcomes between groups.
Results: Differences in glycosylated hemoglobin between type 1 and type 2 diabetes were not significant. Birth weight (3,501±689.6 g vs. 3,366±531.4 g) and rate of major congenital malformations (7.7% vs. 5.6%) were not significantly different. However, women with type 1 diabetes had higher rates of preeclampsia (38.5% vs. 8.2%, P=0.006), large for gestational age (LGA; 46.2% vs. 20.4%, P=0.004), macrosomia (38.5% vs. 13.4%, P=0.032), and admission for neonatal care (41.7% vs. 14.8%, P=0.03) than women with type 2 diabetes.
Conclusion: Maternal and neonatal outcomes for women with type 1 diabetes were poorer than for women with type 2 diabetes, especially preeclampsia, LGA, macrosomia and admission to the neonatal intensive care unit.

Keywords: Pregnancy outcome; Type 1 diabetes; Type 2 diabetes

INTRODUCTION

Type 2 diabetes is the most common form of diabetes in women of reproductive age in developed countries, and its increasing prevalence in this group seems likely to continue to rise [1]. Between 2002 and 2003 the proportion of type 2 diabetes in pregnancy ranged from 13.3% to 44.5%, with a mean prevalence of 27.6% throughout the United Kingdom [2].

Pregnant women with type 1 and type 2 diabetes are associated with high risk of adverse outcomes including stillbirth, perinatal mortality, congenital anomaly, macrosomia, and caesarean section [3,4]. In addition, women with diabetes are at a 2- to 3-fold increased risk of giving birth to infants with major congenital malformations compared with women in the general population [2,4]. Type 2 diabetes is thought of as lower risk than type 1 diabetes, and this is also true in relation to diabetes in pregnancy. However, recent studies report poorer outcomes in women with type 2 diabetes [5-8], and published data suggest outcomes similar to those of type 1 diabetic women [9,10].

There have been no reports describing maternal and neonatal outcomes for women with type 1 and type 2 diabetes in Korea. Therefore, the aim of this study was to compare maternal and neonatal outcomes in Korean women with type 1 and type 2 diabetes.

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METHODS

We performed a retrospective complete enumeration of 163 pregnancies in women with pre-gestational diabetes mellitus using medical records from 2003 to 2010 treated at Cheil General Hospital & Women's Healthcare Center, Korea. The subjects included 13 women with type 1 diabetes and 150 with type 2 diabetes. We compared their maternal characteristics as well as maternal and neonatal outcomes. Women with gestational diabetes were excluded from our study. This study was approved by the Ethics Committee of the Institutional Review Board of Cheil General Hospital & Women's Healthcare Center, Seoul, Korea.

Outcome measures

Miscarriage was defined as the spontaneous ending of pregnancy before 20 weeks. Due to the increased risks associated with twin pregnancy, pregnancy and perinatal morbidity analyses were performed only in singleton pregnancies. Preterm delivery was defined as delivery before 37 weeks and early preterm delivery was defined as delivery before 34 weeks. Stillbirth was defined as fetal death after 24 weeks and neonatal death as death of a live-born infant before 28 days of age. For singleton infants, large for gestational age (LGA) was defined as birth weight ≥90th centile and small for gestational age as birth weight ≤10th centile. Macrosomia was defined as birth weight greater than 4,000 g, regardless of gestational age. Major congenital malformations were classified according to the European Surveillance of Congenital Anomalies (EUROCAT) system [11].

Data collection

Pre-gestational diabetes was defined as type 1 or type 2 diabetes diagnosed before pregnancy. Maternal pre-pregnancy height and weight were obtained by self-reported questionnaire and used to calculate body mass index. Glycosylated hemoglobin (HbA1c) levels were determined by the Variant II HbA1c program (BioRad, Hercules, CA, USA) and the mean value was calculated for each trimester to account for measurements at varying gestational ages.

Statistical analysis

Statistical analysis was performed with SPSS version 21.0 (IBM Co., Armonk, NY, USA). Analyses were performed using the chi-square test or Fisher exact test for categorical variables and independent *t*-tests for continuous variables. A $P<0.05$ was considered statistically significant.

RESULTS

During the 8-year study period, 163 pregnancies were enrolled. Among the 163 pregnancies, 13 (8.0%) were complicated by type 1 diabetes and 150 (92.0%) by type 2 diabetes. Maternal characteristics, diabetes status and pregnancy preparation data are shown in Table 1. Details of pregnancies and neonatal outcomes for 163 singleton pregnancies are shown in Tables 2 and 3.

Maternal characteristics by type of diabetes

The maternal age at delivery of women with type 1 diabetes was lower than women with type 2 diabetes (31.5±2.6 years vs. 34.0±4.2 years, $P=0.004$). Women with type 2 diabetes were, as expected, older ($P=0.004$), heavier ($P<0.001$), and shorter duration of diabetes ($P=0.012$) than women with type 1 diabetes (Table 1).

Table 1. Maternal characteristics according to type of diabetes ($n=163$)

Characteristic	Type 1 diabetes	Type 2 diabetes	*P* value
Number	13	150	
Maternal age, yr	31.5±2.6	34.0±4.2	0.004
Gestational age at delivery, wk	38.4±1.6	38.6±1.6	0.602
Pre-gestational BMI, kg/m^2	19.3±2.6	25.7±4.4	<0.001
Age of diagnosis of DM, yr	25.0±7.6	30.0±5.6	0.003
Diabetes duration, yr	6.5±7.6	3.7±4.2	0.012
Parity			
Primipara	7 (53.8)	70 (46.7)	0.416
Multipara	6 (46.2)	80 (53.3)	0.416
DM family history	1 (7.7)	105 (70.0)	<0.001[a]
Antidiabetic therapy before conception			
Diet	0	52 (34.7)	0.011[a]
Insulin	13 (100.0)	30 (20.0)	<0.001
Oral agent	0	68 (45.3)	0.001[a]
Gestational age at booking, wk	9.68±6.8	10.25±6.5	0.775
Booked before 8/40	5 (38.5)	76 (50.7)	0.795[a]

Values are presented as mean±standard deviation or number (%).
BMI, body mass index; DM, diabetes mellitus.
[a]Fisher exact test.

Table 2. Maternal outcomes according to type of diabetes (n=163)

	Type 1 diabetes	Type 2 diabetes	*P* value
Number	13	150	
Miscarriage	0	6 (4.0)	0.602[a]
Termination of pregnancy	0	2 (1.4)	0.846[a]
Method of delivery			0.188
Vaginal delivery	6 (46.2)	38 (26.8)	0.124
Induction	0	1 (0.7)	0.916[a]
Repeated C/S	1 (7.7)	51 (35.9)	0.032[a]
Primary C/S	6 (46.2)	52 (36.6)	0.497
Pre-eclampsia[b]	5 (38.5)	12 (8.2)	0.006[a]
Preterm delivery (n=144)			
Preterm delivery <37 wk	3 (23.1)	12 (13.7)	0.088[a]
Early preterm delivery <34 wk	0	2 (1.4)	0.667[a]

Values are presented as number (%).
C/S, cesarean section.
[a]Fisher exact test, [b]Missing data.

Table 3. Neonatal outcomes according to type of diabetes (n=155)

Characteristic	Type 1 diabetes	Type 2 diabetes	*P* value
Number	13	142	
Neonatal weight, g	3,501.5±689.6	3,366.3±531.4	0.394
Neonatal birth weight centiles			
LGA ≥90th centile	6 (46.2)	29 (20.4)	0.044
SGA ≤10th centile	2 (15.4)	12 (8.5)	0.332[a]
Macrosomia	5 (38.5)	19 (13.4)	0.032[a]
Neonatal complication			
Asphyxia, TTN, RDS, MAS	6 (46.2)	59 (41.8)	0.492
Hyper bilirubinemia, jaundice	3 (23.1)	46 (32.6)	0.357[a]
Hypocalcaemia	1 (7.7)	3 (2.1)	0.300[a]
Hypoglycemia	0	8 (5.7)	0.485[a]
Polycythemia[b]	0/10	1/109 (0.9)	0.916[a]
Cardiac hypertrophy, heart failure[b]	0/13	1/141 (0.7)	0.916[a]
Malformation	1 (7.7)	8 (5.6)	0.515[a]
Birth injury	0	4 (2.8)	0.702[a]
Admission of neonatal care	5 (41.7)	19 (14.8)	0.030[a]

Values are presented as mean±standard deviation or number (%).
LGA, large for gestational age; SGA, small for gestational age; TTN, transient tachypnea of newborn; RDS, respiratory distress syndrome; MAS, meconium aspiration syndrome.
[a]Fisher exact test, [b]Missing data.

Table 4. HbA1c according to type of diabetes and pregnancy trimester (n=163)

	Type 1 diabetes	Type 2 diabetes	*P* value
Number	13	150	
HbA1c trimester, %			
1st	6.3±1.0	7.0±1.5	0.111
2nd	5.9±0.8	5.7±0.9	0.510
3rd	5.9±0.4	6.2±0.8	0.336

Values are presented as mean±standard deviation.
HbA1c, glycosylated hemoglobin.

Glycemic control according to type of diabetes during pregnancy

Glycemic control data were available for 163 pregnancies (100%) during the 1st trimester, 2nd trimester, and 3rd trimester, but the availability of pre-conception data was limited. There were no differences in 1st trimester HbA1c levels between the two groups (Table 4). Moreover, 2nd and 3rd trimester HbA1c levels were slightly decreased during pregnancy, but this was not statistically significant (Table 4).

Maternal outcomes

We investigated maternal outcomes for 163 pregnancies (100%) and 155 infants (95.1%) (Table 2). There were six miscarriages (type 2 diabetes), two terminations of pregnancies (type 2 diabetes), and 0 stillbirths among the 163 pregnancies. Women with type 1 diabetes were more likely to deliver by primary caesarean section, but this difference was not statistically significant (46.2% type 1 diabetes, 36.6% type 2 diabetes; P=0.497). Pre-eclampsia was more common in women with type 1 diabetes than with type 2 diabetes (38.5% type 1 diabetes, 8.2% type 2 diabetes; P=0.006). There were no differences between women with type 1 and type 2 diabetes in terms of preterm delivery (23.1% type 1 diabetes, 13.7% type 2 diabetes; P=0.088) or early preterm delivery (0% type 1 diabetes, 1.4% type 2 diabetes; P=0.667).

Neonatal outcomes

Neonatal birth weight was similar in both groups (mean weight

3,501.5±689.6 g vs. 3,366.3±531.4 g, P=0.394). Children of women with type 1 diabetes were more likely to be LGA (46.2% type 1 diabetes, 20.4% type 2 diabetes; P=0.044). Women with type 1 and type 2 diabetes were equally likely to have babies that were small for gestational age (15.4% type 1 diabetes, 8.5% type 2 diabetes; P=0.332). Women with type 1 diabetes were more likely to have macrosomic infants (birth weight >4,000 g) than women with type 2 diabetes (38.5% type 1 diabetes, 13.4% type 2 diabetes; P=0.032). Major malformations were identified in nine infants (5.8%; 7.7% type 1 diabetes, 5.6% type 2 diabetes; P=0.515). There was one heart anomaly (7.7%) among infant of women with type 1 diabetes and four instances of caudal regression, three of heart anomaly and one of anal anomaly in infant of women with type 2 diabetes. There were nine (5.8%) serious adverse pregnancy outcomes (major malformation, stillbirth, neonatal death). It was no significant difference between women with type 1 and type 2 diabetes. Birth injury was identified in four infants (2.8%; 0% type 1 diabetes, 2.8% type 2 diabetes; P=0.702). There was one of cranial injury, one of peripheral injury, and two of clavicle fracture in children of women with type 2 diabetes. Overall, 24 singleton infants (15.4%) were admitted to the neonatal intensive care unit. Infant of women with type 1 diabetes (41.7% type 1 diabetes, 14.8% type 2 diabetes; P=0.03) were more likely to be admitted for neonatal care.

DISCUSSION

We found that maternal and neonatal outcomes in women with type 1 diabetes were poorer than those of women with type 2 diabetes, especially pre-eclampsia, LGA, macrosomia and admission for neonatal care. Women with type 1 diabetes were more likely to have pre-eclampsia than women with type 2 diabetes. Pre-eclampsia is more common among women with pre-gestational diabetes than in those without diabetes, occurring four times as frequently [12]. It is possible that women with type 1 diabetes have a higher incidence of pre-eclampsia due to the longer duration of diabetes seen in these women compared to women with type 2 diabetes [13]. We observed no significant difference in the rate of primary cesarean section between women with type 1 and type 2 diabetes. However, a previous study showed that women with type 2 diabetes were at reduced risk of delivery by caesarean section [3]. We considered the similar rates of primary cesarean section observed in the present study. Although the statistics do not show meaningful difference due to the small sample size in type 1 group, it is possible a larger sample size will give rise to statistical difference in rates of primary cesarean section.

We observed no significant differences in the risk of stillbirth, neonatal death, miscarriage, termination of pregnancy, or preterm delivery between women with type 1 and type 2 diabetes. This finding is similar to that of a previous report regarding rates of miscarriage, termination of pregnancies, and preterm delivery [3]. Women with type 1 diabetes were more likely to have LGA infants and macrosomic infants than women with type 2 diabetes. This demonstrates improvement of outcome in type 2 diabetes, but confirms the increasing prevalence of LGA in type 1 diabetes that was described in a recent longitudinal Swedish study [10]. This finding suggests that more intensive prenatal care is required to improve glycemic control and perinatal outcomes in patients with type 1 diabetes. One possible solution is continuous glucose monitoring (CGM) during pregnancy, as randomized clinical trials using CGM during pregnancy demonstrated improved glycemic control and reduced frequency of LGA infants in women with type 1 and type 2 diabetes [14]. Our results in women with type 1 and 2 diabetes contradict these findings, suggesting that there was no significant difference in risk of macrosomia between women with type 1 and 2 diabetes [3]. We found no significant differences in risk of congenital malformation between the two groups. In a previous study, pregnancies in women with type 2 diabetes were no more likely than type 1 diabetes to result in malformation [3]. The Confidential Enquiry into Maternal and Child Health (CEMACH) study showed similar results in women with both types of diabetes [2]. In contrast, Roland et al. [8] found a higher rate of congenital malformations in women with type 2 diabetes. Among women with overt diabetes before conception, the risk of structural anomaly in the fetus is reported to increase 4- to 8-fold [15] compared with the 1% to 2% risk for the general population. In a cohort study of 2,359 pregnancies in women with pre-gestational diabetes, the major congenital anomaly rate was 4.6% overall, 4.8% for type 1 diabetes, and 4.3% for type 2 diabetes, more than double the expected rate. Neural tube defects were increased 4.2-fold and congenital heart disease by 3.4-fold. The association of glycemic control with congenital malformations has been consistently documented [16]. Therefore, maternal glucose was considered to be important variable.

In this study, infants of women with type 1 diabetes were more likely to be admitted for neonatal care than those of women with type 2 diabetes. The main reason for neonatal admission was respiratory disease.

The findings of this study may be difficult to generalize because

the data were collected at a single hospital. In addition, the number of women with type 1 diabetes was small and the study design was a retrospective chart review. The significance of this study is that it is the first attempt to summarize maternal and neonatal outcomes in Korean women with type 1 and type 2 diabetes using domestic data.

In summary, we found that maternal and neonatal outcomes in women with type 1 diabetes are poorer than those in women with type 2 diabetes, especially in terms of pre-eclampsia, LGA, macrosomia, and admission for neonatal care. Future multicenter studies with larger samples of type 1 diabetes patients are necessary to validate our conclusions. The results of this study demonstrate the need for hospital and regional collaboration to supply the larger cohorts required for accurate documentation of adverse pregnancy outcomes. Well-designed studies to investigate the predictors of perinatal outcome in women with pre-gestational diabetes are required.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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