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Original Article

Evaluation of pregnancies complicated by diabetes in terms of fetal and neonatal outcomes

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Abstract

Objective: To compare fetal and neonatal outcomes among pregnant women with different degrees of glucose intolerance and glycemic control.

Methods: This prospective study included 223 pregnant women who delivered at Ümraniye Training and Research Hospital between 2010 and 2011, together with their newborns. Participants were classified into five groups: normoglycemic women (Group 1), women with one abnormal value on the 100-g oral glucose tolerance test (OGTT) (Group 2), women with gestational diabetes mellitus (GDM) and adequate glycemic control (Group 3), women with GDM and inadequate glycemic control (Group 4), and women with pregestational diabetes mellitus (Group 5). Fetal and neonatal outcomes were compared among the groups.

Results: Gestational age at delivery was significantly lower in Group 4 than in the other groups ($p<0.05$). Mean birth weight was significantly higher in Group 5 than in Groups 1, 2, and 3 ($p<0.05$), whereas the 1-minute Apgar score was significantly lower in Group 5 than in these groups ($p<0.05$). The frequencies of low birth weight, prematurity, macrosomia, polyhydramnios, stillbirth, neonatal intensive care unit admission, and neonatal hypoglycemia differed significantly among the groups, with adverse outcomes generally occurring more frequently in Groups 4 and 5.

Conclusion: Different degrees of glucose intolerance and glycemic control during pregnancy were associated with differences in fetal and neonatal outcomes. Adverse outcomes were more frequently observed among women with inadequately controlled GDM and those with pregestational diabetes.

Keywords: Gestational diabetes mellitus, glucose intolerance, high-risk pregnancy, neonatal outcomes, pregestational diabetes.

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INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as glucose intolerance first recognized during pregnancy. Diabetes diagnosed before pregnancy is classified as pregestational diabetes mellitus (PGDM) (1). The prevalence of diabetes during pregnancy has increased worldwide in parallel with rising rates of obesity and advanced maternal age. Approximately 6–9% of pregnancies are complicated by diabetes, with GDM accounting for the majority of cases. The reported prevalence of GDM ranges from 5% to 15%, depending on the population studied and the diagnostic criteria used (1,2). Pregnancies complicated by diabetes are associated with an increased frequency of adverse fetal and neonatal outcomes, including preterm delivery, macrosomia, fetal growth abnormalities, stillbirth, neonatal respiratory complications, and neonatal hypoglycemia, as well as higher rates of cesarean delivery (3,4). The frequency of these outcomes may vary according to the degree of maternal glucose intolerance and glycemic control.

The aim of this study was to compare fetal and neonatal outcomes among pregnant women with different degrees of glucose intolerance and glycemic control.

MATERIALS AND METHODS

Ethical approval

The study was approved by the Ethics Committee of Ümraniye Training and Research Hospital on March 10, 2010 (approval no. 2010/13). The study was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants before inclusion in the study.

Study design and participants

This prospective study was conducted in the Department of Obstetrics and Gynecology of Ümraniye Training and Research Hospital during an 11-month period between 2010 and 2011. A total of 223 pregnant women who were followed in the outpatient or delivery units and subsequently delivered at our hospital, together with their newborns, were included in the study. Written informed consent was obtained from all participants. Women with chronic hypertension or elevated blood pressure during the first trimester, those using medications that could affect glucose metabolism, and those with multiple pregnancies were excluded. The participants were classified into five groups according to glucose tolerance, diabetes status, and glycemic control: Group 1 (Normoglycemic group): This group included 85 women with a 50-g glucose challenge test result >140 mg/dL but no abnormal values on the subsequent 100-g oral glucose tolerance test (OGTT). Group 2 (One abnormal OGTT value): This group included 44 women with a 50-g glucose challenge test result >140 mg/dL and one abnormal value on the subsequent 100-g OGTT. Group 3 (GDM with adequate glycemic control): This group included 52 women diagnosed with gestational diabetes mellitus (GDM) based on two or more abnormal values on the 100-g OGTT or a 50-g glucose challenge test result ≥180 mg/dL. These women were managed with diet and/or insulin as required and achieved adequate glycemic control during follow-up. Adequate glycemic control was defined as a fasting blood glucose level <95 mg/dL and a 1-hour postprandial blood glucose level <140 mg/dL. Group 4 (GDM with inadequate glycemic control): This group included 24 women diagnosed with GDM who did not achieve the specified glycemic targets during follow-up. Inadequate glycemic control was defined as failure to maintain a fasting blood glucose level

<95 mg/dL and/or a 1-hour postprandial blood glucose level <140 mg/dL. Group 5 (Pregestational diabetes mellitus): This group included 18 women with pregestational diabetes mellitus (PGDM), irrespective of the level of glycemic control during pregnancy. The Carpenter–Coustan criteria were used for the diagnosis of GDM (1,2).

Statistical analysis

Statistical analyses were performed using NCSS 2007 and PASS 2008 Statistical Software (Utah, USA). Continuous variables were summarized as mean ± standard deviation and, where appropriate, median values, whereas categorical variables were presented as numbers and percentages. For comparisons among the five groups, one-way analysis of variance (ANOVA) was used for normally distributed continuous variables, followed by the Tukey honestly significant difference (HSD) test for post-hoc pairwise comparisons when the overall test was statistically significant. The Kruskal–Wallis test was used for continuous variables that did not meet parametric assumptions, followed by the Mann–Whitney U test for pairwise comparisons when appropriate. Categorical variables were compared using the chi-square test. For contingency tables with small expected cell counts, an exact test with Monte Carlo simulation was used as appropriate. All tests were two-sided, and a p-value <0.05 was considered statistically significant.

RESULTS

A total of 223 pregnant women and their newborns were included in the study. Maternal age differed significantly among the five groups (p<0.01). Women in Groups 1 and 2 were significantly younger than those in Groups 3, 4, and 5. Gravidity also differed significantly among the groups (p<0.05). Pairwise comparisons showed that gravidity was significantly lower in Group 1 than in Groups 3, 4, and 5 (p=0.026, p=0.034, and p=0.009, respectively) and significantly lower in Group 2 than in Group 5 (p=0.029). Parity differed significantly among the groups (p<0.05), with lower values in Groups 1 and 2 than in Groups 3, 4, and 5 (Table 1).

Table 1. Demographic characteristics of the study groups

Variable	Group 1 (n=85)	Group 2 (n=44)	Group 3 (n=52)	Group 4 (n=24)	Group 5 (n=18)	p
Age (years) mean±SD	28.65±5.28	28.06±5.93	31.88±5.61	32.21±5.57	33.50±7.47	0.001**
Gravidity mean±SD	2.47±1.68	2.43±1.42	2.86±1.34	3.16±2.03	3.05±0.99	0.015*
Parity mean±SD	2.16±1.14	2.09±1.19	2.59±1.22	2.83±1.57	2.71±1.04	0.010*

Abbreviaton: *Kruskal–Wallis test. SD, standard deviation. *p<0.05;* **p<0.01.

Gestational age at delivery differed significantly among the groups (p<0.01). Post-hoc comparisons showed that gestational age at delivery was significantly lower in Group 4 than in the other groups. Mean birth weight also differed significantly among the groups (p<0.05), with Group 5 having a significantly higher mean birth weight than Groups 1, 2, and 3 (Table 2).

Table 2. Clinical and neonatal characteristics of the study groups

Variable	Group 1 (n=85)	Group 2 (n=44)	Group 3 (n=52)	Group 4 (n=24)	Group 5 (n=18)	p
Gestational age at delivery (weeks), mean±SD	39.26±1.35	38.99±1.94	38.94±1.24	37.71±2.79	38.94±1.21	0.003**
Birth weight (g), mean±SD	3277.8±456.1	3262.9±647.8	3298.8±560.7	3312.1±1037.0	3786.1±750.2	0.033*
1-minute Apgar score, mean±SD	8.76±1.12	8.54±1.57	8.75±0.73	7.87±1.22	7.05±2.86	0.001**
Presentation anomaly, n (%)	2 (2.4)	4 (9.1)	4 (7.7)	4 (16.7)	2 (11.1)	0.141
Cesarean delivery, n (%)	29 (34.1)	22 (50.0)	25 (48.1)	16 (66.7)	11 (61.1)	0.027*
Vaginal delivery, n (%)	56 (65.9)	22 (50.0)	27 (51.9)	8 (33.3)	7 (38.9)	
1-minute Apgar score <7 n (%)	4 (4.7)	3 (6.8)	3 (5.8)	5 (20.8)	4 (22.2)	0.032*
1-minute Apgar score ≥7 n (%)	81 (95.3)	41 (93.2)	49 (94.2)	19 (79.2)	14 (77.8)	

Abbreviations: *One-way ANOVA was used for continuous variables, and the chi-square test was used for categorical variables, as appropriate. SD, standard deviation. *p<0.05;* **p<0.01.

No statistically significant difference was observed among the groups in the frequency of fetal presentation anomalies (p>0.05). The 1-minute Apgar score differed significantly among the groups (p<0.01). Group 5 had significantly lower 1-minute Apgar scores than Groups 1, 2, and 3 (p=0.001 for each comparison), and Group 4 had a significantly lower score than Group 1 (p=0.044). The frequency of a 1-minute Apgar score <7 also differed significantly among the groups (p<0.05), with higher rates observed in Groups 4 and 5 (Table 2). Mode of delivery differed significantly among the groups (p<0.05). Vaginal delivery was more frequent in Group 1, whereas cesarean delivery was more frequent in Groups 4 and 5 (Table 2). Cesarean section indications also differed significantly among the groups (p<0.05). Previous cesarean section was a more frequent indication in Groups 1, 2, and 3, whereas macrosomia was more frequent as an indication in Groups 4 and 5 (Table 3).

Table 3. Indications for cesarean delivery according to study group

Indication	Group 1	Group 2	Group 3	Group 4	Group 5	p
Severe preeclampsia, n (%)	0	1 (4.5)	0	1 (6.3)	1 (9.1)	0.012*
Previous cesarean section, n (%)	17 (58.6)	9 (40.9)	16 (64.0)	1 (6.3)	5 (45.4)	
Fetal distress, n (%)	3 (10.3)	2 (9.1)	2 (8.0)	3 (18.8)	1 (9.1)	
Macrosomia, n (%)	1 (3.4)	4 (18.2)	4 (16.0)	7 (43.8)	3 (27.2)	
Presentation anomaly, n (%)	2 (6.9)	4 (18.2)	3 (12.0)	4 (25.0)	1 (9.1)	
Other, n (%)	6 (20.7)	2 (9.1)	0	0	0	

**Exact test with Monte Carlo simulation. p<0.05.*

The frequency of low birth weight differed significantly among the groups (p<0.05), with higher rates observed in Groups 4 and 5. Significant differences were also observed among the groups in the frequencies of prematurity, macrosomia, polyhydramnios, neonatal intensive care unit admission, and neonatal hypoglycemia (all p<0.01), with these adverse outcomes occurring more frequently in Groups 4 and 5. Stillbirth also differed significantly among the groups (p<0.05), with the highest rate observed in Group 5 (Table 4).

Table 4. Fetal and neonatal outcomes according to study group

Outcome	Group 1 (n=85)	Group 2 (n=44)	Group 3 (n=52)	Group 4 (n=24)	Group 5 (n=18)	p
Low birth weight n (%)	4 (4.7)	3 (6.8)	3 (5.8)	6 (25.0)	2 (11.1)	0.020*
Prematurity n (%)	2 (2.4)	3 (6.8)	3 (5.8)	6 (25.0)	2 (11.1)	0.006**
Macrosomia n (%)	1 (1.2)	5 (11.4)	5 (9.6)	9 (37.5)	7 (38.9)	0.001**
Polyhydramnios n (%)	1 (1.2)	2 (4.5)	6 (11.5)	13 (54.2)	10 (55.6)	0.001**
Stillbirth n (%)	1 (1.2)	1 (2.3)	0	0	2 (11.1)	0.033*
NICU admission n (%)	5 (5.9)	5 (11.4)	6 (11.5)	10 (41.7)	5 (27.8)	0.001**
Neonatal hypoglycemia n (%)	0	1 (2.3)	2 (3.8)	11 (45.8)	4 (22.2)	0.001**

Abbreviation: *NICU, neonatal intensive care unit. Chi-square test. *p<0.05;* **p<0.01.*

DISCUSSION

In this prospective study, fetal and neonatal outcomes differed according to the degree of maternal glucose intolerance and glycemic control. The main findings were the higher frequencies of several adverse outcomes, including prematurity, macrosomia, polyhydramnios, NICU admission, and neonatal hypoglycemia, particularly among women with inadequately controlled GDM and those with PGDM. These findings are consistent with the established association between maternal hyperglycemia and adverse perinatal outcomes (5,6). Gestational age at delivery was significantly lower in Group 4 than in the other groups. Previous studies have reported an increased frequency of preterm delivery in pregnancies complicated by diabetes, particularly in the presence of poor glycemic control or additional maternal and fetal complications (5,6). In our study, prematurity was observed in 25.0% of women with inadequately controlled GDM compared with 2.4% in the normoglycemic group. However, because this was an observational study, these findings should be interpreted as associations rather than evidence of a causal relationship. The degree of glucose intolerance may also be relevant to perinatal risk. In our study, women with a single abnormal value on the 100-g OGTT represented a separate group from women meeting the diagnostic criteria for GDM. Recent evidence indicates that adverse perinatal and neonatal outcomes may increase with the number of abnormal OGTT values, while even a single abnormal value may not represent an entirely risk-free condition (7). These observations support consideration of glucose intolerance as a continuum rather than solely as a dichotomous condition. Polyhydramnios was significantly more frequent in Groups 4 and 5 than in the other groups. Maternal hyperglycemia has been associated with fetal hyperglycemia and increased fetal urine production, providing a plausible mechanism for the association between diabetes and polyhydramnios (8,9). In the present study, polyhydramnios occurred in 54.2% of women with inadequately controlled GDM and 55.6% of women with PGDM. These findings demonstrate a strong association within our cohort, although other maternal and fetal factors contributing to polyhydramnios cannot be excluded. The frequency of presentation anomalies did not differ significantly among the groups. In contrast, the mode of delivery differed significantly, with cesarean delivery occurring more frequently in Groups 4 and 5. Previous studies have also reported increased cesarean delivery rates among pregnancies complicated by diabetes (10–12). In our cohort, previous cesarean delivery was a frequent indication in Groups 1–3, whereas macrosomia was more frequently recorded as an indication in Groups 4 and 5. Therefore, the observed differences in delivery mode should not be attributed solely to maternal glucose status. Macrosomia is a well-recognized fetal complication associated with maternal diabetes (13–15). In our study, macrosomia occurred in 1.2% of Group 1, 11.4% of Group 2, 9.6% of Group 3, 37.5% of Group 4, and 38.9% of Group 5. Thus, the highest frequencies were observed among women with inadequately controlled GDM and those with PGDM. Previous studies have demonstrated an association between maternal glycemia and excessive fetal growth and have suggested that improved glycemic management is associated with lower rates of excessive fetal growth (16,17). The relatively lower frequency of macrosomia in women with adequately controlled GDM compared with inadequately controlled GDM in our cohort is consistent with this relationship, although the observational design does not allow a treatment effect to be established. Stillbirth remains one of the most serious adverse outcomes associated with diabetes in pregnancy (18–20). In the present study, stillbirth differed significantly among the groups and was most frequent in the PGDM group. Contemporary evidence also indicates that PGDM is associated with increased risks of stillbirth and other adverse perinatal

outcomes (20). Nevertheless, the small number of stillbirths in our study requires cautious interpretation of between-group differences. Neonatal outcomes also differed among the study groups. The 1-minute Apgar score was lower in the PGDM group, and the frequency of an Apgar score <7 was higher in Groups 4 and 5. NICU admission and neonatal hypoglycemia were also significantly more frequent in these groups. These findings are consistent with previous reports describing increased neonatal morbidity among pregnancies complicated by diabetes (21,22). Recent evidence similarly demonstrates associations between PGDM and neonatal hypoglycemia, NICU admission, low Apgar scores, and other adverse perinatal outcomes (20).

Limitations

This study has several limitations. Although the data were collected prospectively, the study was conducted at a single center and included relatively small numbers of women in some subgroups, particularly Groups 4 and 5. In addition, the groups differed in some baseline maternal characteristics, and multivariable adjustment for potential confounding factors was not performed. Therefore, the observed between-group differences cannot be attributed exclusively to the degree of glucose intolerance or glycemic control. Furthermore, diagnostic and management practices for diabetes in pregnancy have evolved since the 2010–2011 study period, which should be considered when interpreting the applicability of these findings to contemporary clinical practice. Finally, long-term neonatal and childhood outcomes were not evaluated.

CONCLUSION

Fetal and neonatal outcomes differed according to the degree of maternal glucose intolerance and glycemic control. Adverse outcomes, particularly prematurity, macrosomia, polyhydramnios, NICU admission, and neonatal hypoglycemia, were more frequently observed among women with inadequately controlled GDM and those with PGDM. These findings support an association between maternal glucose intolerance, glycemic control, and adverse perinatal outcomes; however, the observational design of the study does not permit causal conclusions.

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