

## Perinatal Outcome in Newborns of Women with Gestational Diabetes Mellitus

Bora Baysal<sup>1\*</sup> and Ozgur Oner<sup>2</sup>

<sup>1</sup>Department of Neonatology, Usak University School of Medicine, Usak, Turkey.

<sup>2</sup>Department of Obstetrics and Gynecology, Usak University School of Medicine, Usak, Turkey.

### \*Correspondence:

Dr. Bora Baysal, Department of Neonatology, Usak University School of Medicine, Usak, Turkey.

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### ABSTRACT

**Objective:** This study was planned to determine the perinatal outcomes of the newborns of term pregnant women who were diagnosed with GDM and decided to have cesarean delivery.

**Materials and Methods:** Thirty-five pregnant patients diagnosed with GDM were included in the study. The control group consisted of 35 patients who did not have any pregnancy-related disease and were decided to deliver with elective cesarean section. All participants were screened with a 50-g GCT at 24-28 weeks of gestation. Pregnant women with meeting the following laboratory criteria were accepted as GDM. If the serum glucose level was greater than 140 mg/dL on the 50-g GCT, a 100-g OGTT was applied. Diagnosis of GDM was confirmed if 2 of the blood glucose test results were above the following levels: fasting serum glucose  $\geq$  92 mg/dL and/or 1-hour glycemia  $\geq$  180 mg/dL, and/or 2-hour glycemia  $\geq$  153 mg/dL. Perinatal outcome between GDM subjects and control group was compared. All participants in GDM and control groups underwent cesarean delivery. Primary outcome measures included gestational birthweight, gestational age at delivery, stillbirth and neonatal death, minor and major birth defects.

**Results:** While neonatal hypoglycemia was detected in 4 cases in the GDM group, it was found in one case in the control group. No stillbirth was detected in either the GDM group or the control group. While neonatal death was detected in one case in the GDM group, no neonatal death was observed in the control group. While mild preeclampsia was detected in one case in the GDM group, it was not found in the control group. Birth weeks and birth weights of the cases in both groups were recorded similarly. While 8 babies of 2500 grams or less were born in GDM cases, all of the cases in the control group were over 2500 grams. While prematurity was detected in two babies in the GDM group, no prematurity was reported in the control group. Neonatal intensive care needs were seen in three babies in the GDM group, and there were no infants in need of intensive care in the control group.

**Conclusions:** There is a slight increase in low birth weight, prematurity and intensive care unit needs of babies born to mothers with GDM.

### Keywords

GDM, Perinatal outcome, Stillbirth, Prematurity.

### Introduction

Although the consequences of gestational diabetes mellitus (GDM) have been recognised for a long time, the association between GDM and perinatal and maternal outcome was not definitively reported before the publication of the

Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study [1,2]. Likewise, recent well designed study by France demonstrated that caesarean section, pre-eclampsia/eclampsia, macrosomia, respiratory distress, birth trauma and cardiac malformations were increased in women with GDM compared with the healthy pregnant women [3]. Interestingly the risk of mortality and morbidity were higher in GDM women with insulin-treated than those with diet-treated GDM [3-5].

The main reasons for the unclear maternal and perinatal data on GDM can be listed as follows. (i) Some of the cases diagnosed with GDM had hyperglycemia problem before pregnancy, (ii) The first diagnosis of Type 2 diabetes was made during pregnancy and these patients were accepted as GDM, (iii) The effects of obesity-related problems of maternal obese cases on perinatal outcome are due to GDM and (iv) evaluating each group of patients as if they were a single patient group in the study group. Including GDM cases receiving insulin therapy and diet therapy within the same group of patients is another important problem [1-5]. For these reasons, GDM cases who received insulin treatment were excluded from the study in this study. This study was planned to determine the perinatal outcomes of the newborns of term pregnant women who were diagnosed with GDM and decided to have cesarean delivery.

## Materials and Methods

Thirty-five patients with GDM who had no history of clinical chorioamnionitis and preterm premature rupture of membranes and who were decided to have cesarean delivery were included in the study. All pregnant participants were screened with a 50-g GCT at 24-28 weeks of gestation. Pregnant women with meeting the following laboratory criteria were accepted as GDM. If the serum glucose level was greater than 140 mg/dL on the 50-g GCT, a 100-g OGTT was applied. Diagnosis of GDM was confirmed if 2 of the blood glucose test results were above the following levels: fasting serum glucose  $\geq 92$  mg/dL and/or 1-hour glycemia  $\geq 180$  mg/dL, and/or 2-hour glycemia  $\geq 153$  mg/dL. Thirty-five term pregnant women who were decided to have cesarean section due to maternal and perinatal reasons were included as control. Pregnant women in the GDM group were selected among those with single pregnancy. Cases with multiple pregnancy were excluded from the study. Gestational age was determined based on the date of the woman's last menstrual period and the prenatal ultrasound examination at the first 14 weeks of pregnancy. Patients with a history of preterm delivery, placenta previa or ablatio placenta, those with a history of diabetes mellitus or those who had a C/S decision due to preeclampsia or eclampsia were not included in the study. Cases with normal vaginal delivery, gestational hypertension or chronic hypertension were not included in the study. Patients who were given insulin therapy because of GDM or diabetes mellitus or systemic inflammatory disease and a history of recurrent urinary infections were also excluded from the study.

Outcome measures included clinical pregnancy, miscarriage, live birth, birth weight, gestational age at delivery, stillbirth and neonatal death. Maternal events occurring during pregnancy such as preeclampsia, eclampsia, gestational hypertension, and cesarean delivery were recorded. Preterm delivery, minor and major birth defects, fetal growth restriction, and the need for intensive care unit were also recorded from database. Perinatal outcome between GDM subjects and control group was compared. The definitions of the primary outcome measures we evaluated in the study are as follows; minor/major birth defects defined as a physical defect present at birth. Stillbirth defined as a baby born with no signs of life at or beyond 24 weeks' gestation and neonatal death defined as death of the baby in the first 28 days of life. Preterm birth was defined

as birth at a gestational age  $< 32$  weeks, and fetal growth restriction was defined as a birth weight under the third percentile. This study was conducted in accordance with the Declaration of Helsinki.

## Statistical analysis

The total mean of two groups compared based on the Mann-Whitney test with the effect size of 40%, power of 90% and 0.05 type 1 error, was found to be at least 68 patients. The results of Kolmogorov test show that not all quantitative variables have a normal distribution. Mann-Whitney test is used to examine the relationship between quantitative variables in the two Groups. Chi-square test and Fisher's exact test are used to examine qualitative variables.  $p$ -value  $\leq 0.05$  was considered significant. Statistical Package for Social Sciences version 26.0 (SPSS Inc., Chicago, IL, USA) was used to perform data analysis.

## Results

While neonatal hypoglycemia was detected in 4 cases in the GDM group, it was found in one case in the control group. No stillbirth was detected in either the GDM group or the control group. While neonatal death was detected in one case in the GDM group, no neonatal death was observed in the control group. The baby who died had a congenital cardiac anomaly. While mild preeclampsia was detected in one case in the GDM group, it was not found in the control group. Birth weeks and birth weights of the cases in both groups were recorded similarly. Although the birth weights of the babies in the control group were slightly higher than that of the GDM group, the difference was not significant. While eight babies of 2500 grams or less were born in GDM cases, all of the cases in the control group were over 2500 grams. While prematurity was detected in two babies in the GDM group, no prematurity was reported in the control group. Neonatal intensive care needs were seen in three babies in the GDM group, and there were no infants in need of intensive care in the control group. While coarctation was found in one baby with GDM cases, no minor or major birth defects were found in the control group (Table 1).

**Table 1:** Perinatal outcomes of pregnant women with GDM and non-GDM controls.

	GDM (n=35)	Non-GDM control (n=35)	P value
Age	31.3 $\pm$ 1.02	32.6 $\pm$ 2.21	0.33
Parity	2.14 $\pm$ 0.33	2.94 $\pm$ 1.09	0.55
Neonatal hypoglycemia.	4	1	0.02
Stillbirth, n (%)	0	0	NA
Neonatal death, n (%)	1 (2.8%)	0	0.13
Preeclampsia/eclampsia, n (%)	1 (2.8%)	0	0.13
Birth parameters			
Gestational age (wk)	37.1 $\pm$ 0.4	37.4 $\pm$ 2.2	0.43
Birth weight (g)	2893.4 $\pm$ 302.1	2906.1 $\pm$ 413.0	0.56
Prematurity (gestational age $< 37$ week), n (%)	2 (5.71%)	0	0.04
Birth weight $< 2500$ g, n (%)	8 (22.8%)	0	0.01
Need for intensive care unit, n (%)	3 (8.57%)	0	0.04
Minor birth defects, n (%)	1 (2.8%)	0	0.13
Major birth defects, n (%)	0	0	NA

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## Discussion

Debates continue about the diagnosis and treatment of GDM during pregnancy. The answer to the question of whether diabetes diagnosis during pregnancy or hyperglycemia affects maternal and perinatal outcome negatively is not clear. We do not clearly know whether additional factors such as increased risk of obesity, high maternal age, and increased risk of urinary infection affect the early and long-term outcomes of GDM. However, in the last 50 years, a significant increase has been detected in the diagnosis of GDM, both for regular screening tests and to prevent Type 2 diabetes mellitus that may develop in the future [1-5].

The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study demonstrated that rates of birthweight and cord blood c-peptide each >95th percentile and rates of primary cesarean delivery and clinically recognized neonatal hypoglycemia increased as each OGTT value increased [6]. It is a known fact that fetuses in GDM cases are larger and heavier than non-GDM cases. The main reason for this is that high glucose levels transmitted from mother to fetus increase insulin release in the fetus and consequently increase in fetal size and weight. Therefore, it is not surprising that fetuses with higher birth weight are born in GDM cases compared to the gestational ages. Growth hormone does not have a primary role in the increase of fetal size in GDM fetuses [7,8]. The main reason for the increased cesarean incidence and shoulder dystocia in GDM cases is the presence of a large baby. However, in our study, cesarean delivery was performed in all cases in the GDM group. Because all patients had cesarean delivery in their first pregnancy. For this reason, shoulder dystocia could not be evaluated in GDM cases included in our study.

Interestingly, no increased birth weight was found in any of the patients in the GDM group. The probable reason for this is that maternal glycemic control is well done. A significant decrease in both maternal and perinatal mortality and morbidity has been reported in a pregnancy in which maternal glycemic control remains within normal limits [9,10]. On the other hand, not including GDM cases requiring insulin therapy may have led to the birth of babies with normal weight. In our study, three infants in the GDM group required intensive care unit treatment. The probable reason for this may be hypoxia that develops due to high glucose levels [11]. If hypoxia intensifies, it can lead to asphyxia and stillbirth or necessitate intensive care treatment. Hypoxia first stimulates the synthesis of erythropoietin in the fetus and then polycythemia develops. Polycythemia leads to increased erythrocyte destruction and hyperbilirubinemia, leading to a worsening of the general condition of the fetus [12]. Hyperinsulinemia, which develops due to glucose elevation, causes respiratory distress syndrome by disrupting surfactant synthesis and causes the newborn baby to be taken into intensive care [13]. All three babies we received intensive care were treated in a healthy way and discharged.

We can explain the basic mechanism of neonatal hypoglycemia detection in 4 cases in the GDM group as follows. During pregnancy, the fetus, who is accustomed to high blood sugar and

high insulin levels, has hypoglycemia attacks after birth due to the decrease in sugar and increased insulin levels [14]. We treated the clinical picture of neonatal hypoglycemia that we detected in four babies by breastfeeding the babies frequently and by blood glucose monitoring. After frequent breastfeeding, insulin levels returned to normal and neonatal hypoglycemia table improved. The net effect of hyperglycemia can be demonstrated by investigating genetic and environmental factors on GDM babies [15]. On the other hand, thanks to the studies investigating the effects of assisted reproductive techniques on GDM, the etiology of GDM will become clearer [16,17].

In conclusion, despite regular maternal glucose control and obstetric follow-ups, GDM babies have an increase in the need for neonatal intensive care as well as low birth weight and prematurity risk. For this reason, control of hyperglycemia during pregnancy should be done well regardless of diabetes diagnosis and patients should be followed up and treated in specialized centers.

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