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Reexamining intrapartum glucose control in patients with diabetes and risk of neonatal hypoglycemia

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Abstract

Objective: Compare the incidence of hypoglycemia in neonates born to patients with diabetes, based on last maternal glucose before delivery.

Study Design: Cohort of singleton births from individuals with pregestational and gestational diabetes (GDM) from 2017 to 2019.

Results: We included 853 deliveries. Maternal hyperglycemia before delivery was associated with 1.8-fold greater risk of neonatal hypoglycemia (glucose <45 mg/dL) in patients with GDM on medication (adjusted risk ratio (aRR): 1.8; 95% CI: 1.1–2.7), compared with euglycemia. This association was not seen in diet-controlled GDM (0.5; 0.23–1.1), nor in Type 1 (1.1; 0.88–1.4), or Type 2 pregestational diabetes (1.1; 0.61–1.9). Further, pregestational diabetes, compared to GDM, regardless of intrapartum maternal glucose control, was associated with neonatal hypoglycemia and NICU admission.

Conclusion: Maternal hyperglycemia before delivery only carried a higher risk of neonatal hypoglycemia in those with GDM on medications. Other interventions to reduce neonatal hypoglycemia are needed.

Introduction

Pregestational (Type 1 diabetes mellitus and Type 2 diabetes mellitus) and gestational diabetes mellitus (GDM) can result in medically complicated pregnancies and have a prevalence of 1–2% and 14%, respectively.[1,2] While pregestational diabetes precedes

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pregnancy, GDM is defined by insulin resistance diagnosed during pregnancy as a result of the release of human placental lactogen. Pregnant women with pregestational diabetes have increased risks of miscarriage, polyhydramnios, preeclampsia, progression of microvascular disease, kidney disease, and operative delivery, while neonates of these women are at elevated risk of being large for gestational age or small for gestational age; metabolic derangements, such as neonatal hypoglycemia, hyperbilirubinemia, polycythemia, hypocalcemia; facial nerve and brachial plexus injury secondary to the increased risk of birth trauma or injury; and perinatal mortality.[3–6] Tight intrapartum glycemic monitoring and control in women with diabetes is postulated to decrease the risk of fetal acidemia, neonatal hypoglycemia, and neonatal intensive care unit (NICU) admission; however, minimal evidence exists to support this relationship.[7,8] The optimal frequency of glucose monitoring during labor that is required to maintain target glucose levels has not been established, and current guidelines for glucose monitoring in labor are based on data for ideal blood glucose levels in pregnant people with Type 1 diabetes mellitus (T1DM).[9] Intrapartum glucose control guidelines for Type 2 diabetes mellitus (T2DM) and GDM are extrapolated largely from studies in T1DM, and their efficacy for improving neonatal outcomes in other populations remains untested.[10] The American College of Obstetricians and Gynecologists (ACOG) recommends the use of a continuous insulin infusion to maintain blood glucose levels at 100 mg/dL, however, the protocol has not been universally adopted and does not account for the varying degrees of insulin requirement from patient to patient.[11] Due to the lack of a standardized protocol, other academic medical centers have developed protocols to improve the consistency of management of diabetes intrapartum and postpartum and allow for individualization of care based on specific glycemic control requirements for each patient. A formal protocol for managing insulin infusion during labor developed at Northwestern Memorial Hospital showed that while there was an improvement in maternal glucose control, interestingly, there was an in increase in frequency of neonatal hypoglycemia.[12] This further supports the idea that strict intrapartum maternal glucose control may not be the only factor related to decreasing the incidence of neonatal hypoglycemia.

Elevated maternal intrapartum glucose has been associated with neonatal hypoglycemia primarily in pregestational diabetes.[8] However, a randomized controlled trial of women with GDM demonstrated that tight maternal glucose control intrapartum did not result in a lower incidence of neonatal hypoglycemia in the first 24 hours of life.[13] Significant time and effort is placed in regular glucose monitoring intrapartum in all diabetes types, when these resources could be apportioned to other aspects of care. Similarly, a better understanding of the relationship between maternal intrapartum glycemic control and neonatal hypoglycemia in pregestational diabetes and GDM is critical to improving newborn outcomes. We hypothesize that strict intrapartum glycemic control may not be the key driver in preventing neonatal hypoglycemia. The primary objective of this study was to evaluate the incidences of neonatal hypoglycemia and NICU admission in patients with immediate pre-delivery maternal hyperglycemia compared with patients with normal capillary glucose and to determine whether this relationship differed by maternal diabetes type.

Materials and Methods

This study was a retrospective cohort study of live births complicated by maternal pregestational diabetes or GDM at a single academic teaching hospital in Boston, Massachusetts. We assumed that around 16% of women will have pre-delivery hyperglycemia, yielding an allocation ratio of 0.2 for maternal hyperglycemia to euglycemia. A prior study found that whether or not patients with GDM were randomized to treatment or usual prenatal care, around 15% of neonates had hypoglycemia at birth.[14] Thus, using a two-sided alpha of 0.05, in order to achieve 85% power to detect a 12% difference in neonatal hypoglycemia (from 15% to 27%), we needed to evaluate a total of 832 live births.

Our study population included all singleton pregnancies that resulted in a live birth from January 2017 to June 2019 with a diagnosis of GDM or pregestational diabetes. Patients with multifetal gestations, intrauterine fetal demise, and pre-viable birth (prior to 24 weeks gestational age) were excluded. Patients were identified using billing ICD-10 codes, and the clinical diagnosis was confirmed by review of the medical records. GDM was diagnosed based on the Carpenter-Coustan criteria (two or more elevated values on the 100-gram 3-hour oral glucose tolerance test) or a 50-gram 1-hour oral glucose tolerance test ≥200 mg/dL. GDM controlled with diet and lifestyle changes alone was classified as diet-controlled GDM, whereas GDM requiring medication (insulin or glyburide) was classified as GDM on medication. The diagnosis of pregestational diabetes (T1DM and T2DM) was established by an elevated hemoglobin A1c ≥6.5%, as defined by the American Diabetes Association, or by history of diabetes diagnosis or treatment prior to pregnancy.

At our hospital, pregnancies complicated by GDM on medications or pregestational diabetes were managed with capillary glucose monitoring every 2 to 4 hours in early labor and every 1 to 2 hours in active labor with a goal of maintaining glucose between 80–110 mg/dL. Capillary glucose is monitored every 4 hours until delivery for diet-controlled GDM, and more frequently if elevated. Intravenous (IV) insulin was initiated for patients with T1DM after they were in active labor or had discontinued oral intake. For patients with GDM and T2DM, IV insulin was initiated when the maternal capillary glucose was >110 mg/dL over at least 2 consecutive occasions.

Maternal hyperglycemia was defined as an elevated maternal capillary glucose >110 mg/dL in the last blood glucose measurement prior to delivery. Despite the protocol mentioned above, the time between the glucose measurement and delivery ranged from minutes to up to 4 hours. Maternal euglycemia was defined as maternal capillary glucose ≤110 mg/dL. Patient demographics, delivery outcomes, intrapartum treatment, and neonatal clinical information were abstracted from the electronic medical record. The primary outcome was neonatal hypoglycemia, defined as capillary glucose <45 mg/dL within the first hour of life. Secondary outcomes included neonatal hypoglycemia 2 to 24 hours after birth and NICU admission, irrespective of indication for NICU admission. At our hospital, all neonates born to women with diabetes undergo a glucose check within one hour after birth. Depending on the initial glucose, not all infants had subsequent glucose measurements. Secondary analyses included evaluating outcomes between each diabetes type and between pregestational diabetes and GDM subgroups. During the study period, infant capillary

glucose <45 mg/dL was the threshold for immediate intervention (initiation of breast- or bottle-feeding) but did not automatically necessitate NICU admission. The neonate was admitted to the NICU if these interventions were ineffective at raising the infant glucose and/or if the neonate was symptomatic. There were no protocol changes during this study period.

Descriptive data were presented as the median and interquartile range (IQR) or n (%). Proportions were compared using a Chi-square or Fisher's exact test for categorical variables. Risk ratios (RR) and 95% confidence intervals (CI) were calculated using modified Poisson regression with an unstructured correlation matrix, accounting for multiple pregnancies per woman. Potential confounders were identified *a priori* based on review of the literature and included maternal age, race/ethnicity, body mass index (BMI), use of IV insulin, diabetes type, and insurance status. All tests were two sided, and P-values <0.05 were considered statistically significant. Data were analyzed using SAS 9.4 (SAS Institute Inc., Cary, NC).

A post hoc analysis was performed using the same cohort to determine the effect of maternal diabetes type on neonatal outcomes independent of immediate maternal pre-delivery glucose level. Exposure was defined by categories of diabetes: pregestational and gestational diabetes. Further subgroup analysis separating the cohort into four subgroups (diet-controlled GDM, GDM on medication, T1DM, and T2DM) was performed using diet-controlled GDM as the reference group, as they most closely represent normal glucose metabolism of all 4 groups.

This study was determined to be exempt human subjects research by the institutional review board at Beth Israel Deaconess Medical Center (Protocol 2019P000208).

Results

During the study period, 1133 deliveries were identified as having GDM or pregestational diabetes using ICD10 codes. After excluding those whose diagnosis could not be clinically confirmed and those that did not meet inclusion criteria, 853 deliveries from 844 people met inclusion criteria (Fig 1). The prevalence of pregestational diabetes was 20.4%, of which 58.6% had T1DM. Prior to delivery, 18% of patients had hyperglycemia. Baseline characteristics are presented in Table 1. Among patients with GDM, the group with maternal hyperglycemia was more likely to self-identify as non-white compared to patients with euglycemia. The median gestational age at time of delivery was lower for pregestational diabetes (37.7 weeks; IQR: 36.7–38.6) compared to GDM (39 weeks, IQR: 37.9–39.7). For those with pregestational diabetes, time from last maternal glucose to delivery was lower (median 45–50 min from delivery) compared to those with GDM (84–90 min) as anticipated based on our hospital guidelines for intrapartum glucose monitoring. For both GDM and pregestational diabetes, IV insulin was used more frequently in patients with maternal hyperglycemia compared to euglycemia. However, 76.4% of patients with pregestational diabetes and hyperglycemia required IV insulin intrapartum compared to 10.0% of patients with GDM and hyperglycemia. Patients with pregestational diabetes were more likely to

have a large for gestational age infant compared to patients with GDM (25.3% versus 10.3%) and were less likely to have a vaginal delivery (29.3% versus 61.4%).

The primary outcome of neonatal hypoglycemia within one hour of delivery was observed in 41.6% of neonates born to patients with immediate pre-delivery hyperglycemia compared to 28.9% of neonates born to patients who were euglycemic (RR: 1.4; 95% CI: 1.2–1.8). However, after adjusting for age, race/ethnicity, insurance status, BMI, IV insulin use, and diabetes type, this difference was not significant (RR: 1.1; 95% CI: 0.88 – 1.4; Fig 2). Incidence of neonatal hypoglycemia 2 to 24 hours after delivery did not differ based on maternal pre-delivery glycemic control (Table 2), and this remained true after adjusting for confounders (Fig 2). While patients with hyperglycemia were significantly more likely to have a neonate admitted to the NICU (29.2%) compared with patients with euglycemia (16.9%), this difference was attenuated and no longer significant in adjusted models (RR: 1.3; 95% CI: 0.95 – 1.2; Fig 2).

We then performed a subgroup analysis to evaluate whether the relationship of maternal hyperglycemia and neonatal hypoglycemia or NICU admission was modified by the type of maternal diabetes. When comparing outcomes based on pre-delivery glycemic control, we found that maternal hyperglycemia was only associated with an increased risk for neonatal hypoglycemia at 1 hour of life in patients with GDM on medication (Table 2). Among patients with GDM on medication, this translated to a 1.6-fold increased risk of neonatal hypoglycemia for patients with pre-delivery maternal hyperglycemia compared with those with euglycemia. This relationship held in the adjusted model (adjusted RR: 1.8; 95% CI: 1.1 – 2.7).

We observed that even among patients with pre-delivery maternal euglycemia, the incidence of neonatal hypoglycemia at 1 hour of life was higher in patients with pregestational diabetes (73.8% in T1DM and 42.3% in T2DM) compared to patients with GDM (14.3% in diet-controlled GDM and 40.5% in GDM on medication, Table 2). This observation, combined with our results demonstrating that the relationship between maternal hyperglycemia and neonatal hypoglycemia is strongly modified by diabetes type, led us to perform a post-hoc analysis focusing our attention on diabetes type as the exposure (rather than pre-delivery glycemic control) and subsequent neonatal outcomes. We found that the risk of neonatal hypoglycemia at 1 hour after birth was strongly influenced by type of maternal diabetes, with a 2.2-fold adjusted risk among patients with pregestational diabetes (95% CI 1.8 – 2.6) compared to patients with GDM (Table 3). NICU admission also was more common in pregestational diabetes compared to GDM (adjusted RR: 2.4; 95% CI: 1.8 – 3.1). We then used T1DM, T2DM, and GDM on medications as separate exposures with diet-controlled GDM as the reference group, as those patients most closely resemble healthy pregnancy physiology. We found that T1DM was associated with significantly increased risks for neonatal hypoglycemia at 1 hour of life and 2–24h of life and for NICU admission compared with infants born to women with diet-controlled GDM (Table 3). T2DM also was associated with an increased risk for neonatal hypoglycemia at 1 hour and NICU admission.

Discussion

In our large cohort of patients with diabetes in pregnancy, we found an increased risk of neonatal hypoglycemia in neonates born to women with diabetes and pre-delivery maternal hyperglycemia. However, strict intrapartum maternal glycemic control appeared to be associated with a reduced risk of neonatal hypoglycemia only in patients with GDM on medication, but not for other diabetes subtypes. The finding that intrapartum maternal glucose control was only associated with GDM on medications suggests greater fetal sensitivity to transient maternal glucose elevation in the context of GDM in contrast to pregestational diabetes, in which fetal endocrine responses may be dominated by more chronic maternal metabolic exposures; future investigation into the physiologic mechanisms are necessary. Neonatal hypoglycemia and NICU admission appeared to be more common in patients with T1DM and T2DM, and pre-delivery maternal glucose control did not appear to alter this risk. Pregestational diabetes (compared to GDM) seemed to be the key driver of neonatal adverse outcome (24 hour neonatal hyperglycemia rates and NICU admission).

A large, systematic review that included 23 studies from 1978 to 2016 drew similar conclusions—that the relationship between intrapartum glucose and neonatal hypoglycemia was inconsistent.[8] This was likely due to major limitations including temporal and institutional heterogeneity in intrapartum glucose management, definitions of neonatal hypoglycemia, and patient demographics. Another Canadian retrospective cohort study of diabetes in pregnancy also concluded that there was no significant association between glycemic control and neonatal hypoglycemia, but did not separately analyze diet-controlled GDM and on medication.[15] The patients in the Canadian study were younger and had a lower BMI than our cohort.

Tight glucose control in labor aims to prevent the rise in fetal insulin in response to maternal hyperglycemia, with the goal of decreasing the risk of neonatal hypoglycemia.[7,15] The strict intrapartum glucose management adopted by our institution and similar hospitals across the country was extrapolated from standard management of patients with T1DM. Our study found that elevated maternal glucose immediately prior to delivery was associated with an 80% increase in the risk of neonatal hypoglycemia at 1 hour of life only in the subgroup of women with GDM on medication, supporting the importance of adhering to strict glucose control prior to delivery for this subgroup. Neither prolonged hypoglycemia from 2–24 hour of life nor increases in NICU admission were observed, likely due to effective response to initial hypoglycemia with early corrective action. Tight maternal glucose control increases physician and nursing resource utilization on the labor and delivery unit, introduces the risk of overtreatment and maternal hypoglycemia, and increases maternal anxiety, without proven neonatal benefits in all patients.

Diabetes type had a large impact on neonatal outcome, suggesting that there are likely other (potentially chronic) mechanisms that play a role in neonatal glucose outcomes for pregnant patients with pregestational diabetes. For the other subgroups of maternal diabetes (Table 3), immediate pre-delivery glucose control was only associated with risk of adverse neonatal outcome in GDM on medication; however, the presence of maternal pregestational diabetes (rather than GDM) had a significant association with increased rates of hypoglycemia and

NICU admission. Strategies other than strict intrapartum glucose control to reduce adverse neonatal outcomes are necessary.

Future studies are necessary to determine the evidence-based glucose target range that strikes a balance between needless strict maternal glucose control and neonatal safety. The consensus-based guidelines recommended by ACOG (target goal of 70–100 mg/dL)[1,2] and the Endocrine Society Clinical Practice Guidelines (target goal of 72–126 mg/dL)[16] have not been reliably demonstrated to reduce adverse neonatal outcomes. While some studies have clearly shown worse neonatal outcomes with maternal pre-delivery glucose values of 140–180 mg/dL, the evidence-based threshold for maternal glucose that limits neonatal risk remains undefined. A recent randomized controlled trial evaluating a very stringent maternal glucose control (100 mg/dL) algorithm for patients with GDM demonstrated no difference in neonatal hypoglycemia rates. This study had a different threshold for defining neonatal hypoglycemia (<40 mg/dL in the first 24 hour of life), utilized two very different maternal treatment algorithms than at our institute, and was underpowered to evaluate outcomes such as NICU admission or major neonatal morbidity or mortality. In the future, large-scale studies that utilize more summative measures of intrapartum glucose or continuous glucose monitoring in labor may assist in defining optimal maternal target glucose ranges by diabetes type that optimize neonatal health. This could potentially be modeled using existing clinical datasets.

This study has several strengths. To our knowledge, it is the largest retrospective cohort study of pregnant women with diabetes in the United States that examines intrapartum glycemic control. At our institute, all infants born to mothers with diabetes uniformly get glucose evaluated within 1 hour of birth regardless of diabetes type (with only 2–3% of missing data for our primary outcome); thus, minimizing the risk of sampling bias. In addition at our hospital, GDM is primarily managed using insulin and not glyburide (a sulfonylurea), which can increase the risk of neonatal hypoglycemia. We had only two people in this study on glyburide, so this is not anticipated to affect the interpretation of the results. Compared to other large studies, it is contemporary; has in-depth maternal, neonatal and delivery characterization; and has representation of all four diabetes types. This allowed us to better examine the effect of intrapartum maternal glucose control on neonatal hypoglycemia within multiple diabetes subtypes using multivariable analysis. Similarly, Dude *et al.* found that strict intrapartum glucose control resulted in an increased frequency of neonatal hypoglycemia.[12] Lastly, our study draws from a diverse population with a large community referral base, which improves generalizability over prior studies.

Our study has a few limitations. It was designed to evaluate the exposure of recent intrapartum glucose control, but we did not have information on more chronic markers of glucose control, such as maternal hemoglobin A1c throughout pregnancy. The maternal capillary glucose values used in this study were the most recent glucose values available prior to delivery. Our exposure definition may be identifying a very transient exposure to maternal hyperglycemia since the this group was unlikely to have been exposed to prolonged periods of profound hyperglycemia due to the frequency of glucose monitoring intrapartum and corrective insulin use at our hospital. In addition, despite institution protocol that pregnancies are monitored every 1–2 hours in active labor, a portion of our glucose

measurements were more than 2 hours prior to delivery. Those in the euglycemia group were more likely to have a longer time between last glucose measurement and delivery compared to the hyperglycemia group. It is possible that those with glucose measurements more than two hours prior to delivery had hyperglycemia that we missed. In that case, we would expect that our results would be biased towards the null, and the true association more extreme than what we reported. Another limitation in this study is that our sample size was not large enough to draw conclusions regarding infrequent neonatal outcomes such as seizures or mortality. Further, the definition of neonatal hypoglycemia has changed over time even in our own institution and there is no accepted national standard.[12] Definitions used in prior studies ranged from <30 mg/dL to ≤48 mg/dL with or without symptoms, or need for intravenous glucose treatment,[17,18] which makes it more difficult to compare our results with those from different studies.

Immediate pre-delivery maternal hyperglycemia >110 mg/dL was associated with a 1.8-fold risk of neonatal hypoglycemia at 1 hour of birth only in the subgroup of women with GDM on medication. We did not see this associating in women with pregestational diabetes or diet-controlled GDM. Pregestational diabetes was associated with twice the risk of neonatal hypoglycemia and twice the risk of NICU admission compared to women with GDM. This illustrates the need to identify if a more lenient target for intrapartum glucose can safely be considered and to identity other modifiable factors of neonatal hypoglycemia in women with pregestational diabetes.

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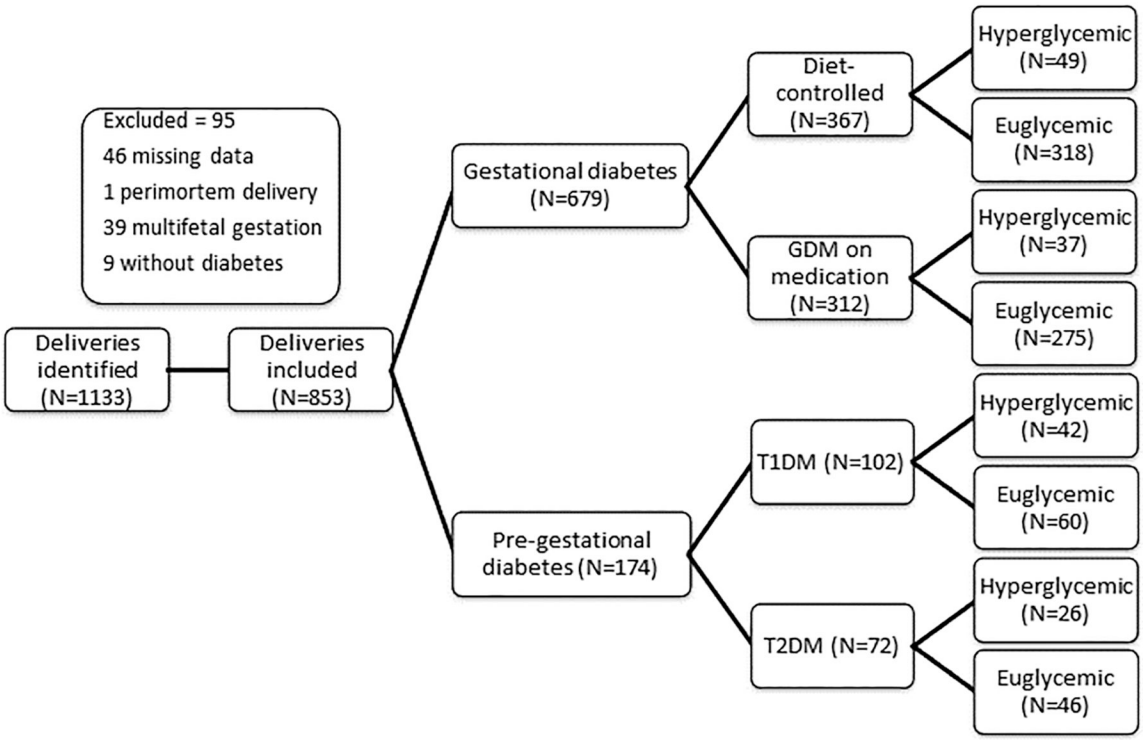

Figure 1. Participant Allocation

GDM= gestational diabetes, T1DM= Type 1 diabetes mellitus; T2DM= Type 2 diabetes mellitus. Maternal euglycemia was defined as capillary glucose ≤110 mg/dL and hyperglycemia was defined as glucose >110 mg/dL.

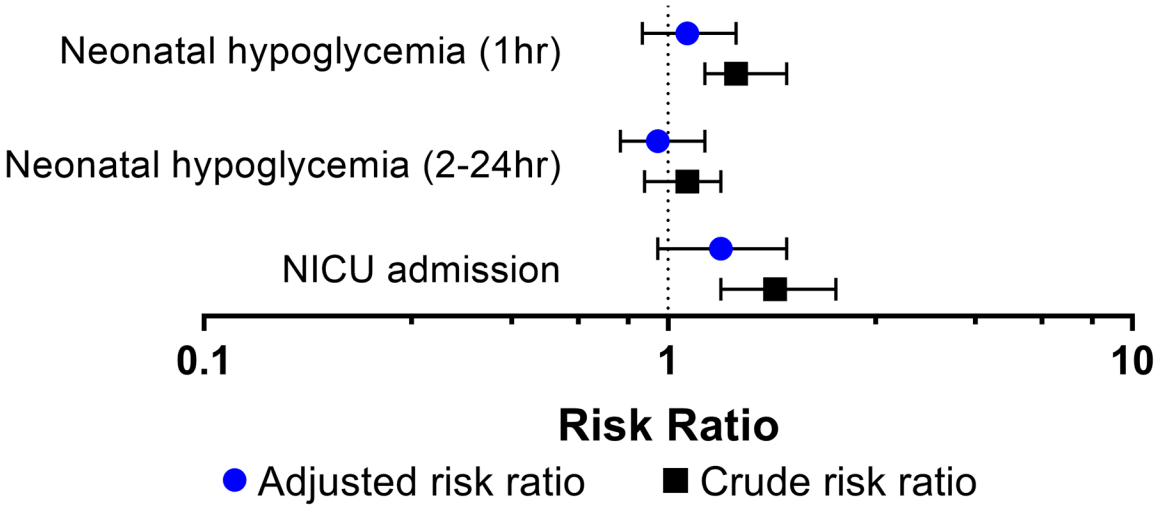

Figure 2. Risk of neonatal outcomes among women with pre-delivery hyperglycemia compared with euglycemia

Risk of neonatal hypoglycemia (<45 mg/dL) within 1 hour and within 2–24 hours from birth, and neonatal intensive care unit (NICU) admission for infants in the setting of maternal hyperglycemia >110 mg/dL compared to euglycemia are displayed as both crude risk ratio (black square) with 95% confidence intervals (bars) and adjusted risk ratio (blue circles) with 95% confidence intervals (bars) adjusted for maternal age, race/ethnicity, insurance status, BMI, and IV insulin use.

Table 1.

Baseline characteristics by type of diabetes and capillary glucose level immediately before delivery

	Gestational diabetes		Pregestational diabetes	
	Maternal hyperglycemia n=86	**Maternal euglycemia n=593**	**Maternal hyperglycemia n=68**	**Maternal euglycemia n=106**
Maternal age (years)	34.7 (31.9 – 37.7)	34.3 (31.2 – 37.5)	33.8 (30.2 – 37.2)	33.7 (31.2 – 37.9)
BMI at delivery (kg/m^2)	31.1 (27.9 – 36.5)	31.2 (27.2 – 36.5)	32.4 (29.0 – 37.0)	34.2 (29.9 – 39.1)
Race/ethnicity				
White	14 (16.3)	208 (35.1)	38 (55.9)	51 (48.1)
Black	14 (16.3)	57 (9.6)	7 (10.3)	16 (15.1)
Hispanic	7 (8.1)	27 (4.6)	3 (4.4)	7 (6.6)
Asian	20 (23.3)	138 (23.3)	5 (7.4)	9 (8.5)
Other/unknown	31 (36.0)	163 (27.5)	15 (22.1)	23 (21.7)
Insurance type				
Public	28 (32.6)	172 (29.0)	14 (20.6)	29 (27.4)
Private/other	58 (67.4)	421 (71.0)	54 (79.4)	77 (72.6)
Marital status				
Married	46 (53.5)	388 (65.4)	45 (66.2)	70 (66.0)
Single	21 (24.4)	127 (21.4)	15 (22.1)	29 (27.4)
Other	2 (2.3)	8 (1.3)	0 (0.0)	2 (1.9)
Unknown	17 (19.7)	70 (11.8)	8 (11.8)	5 (4.7)
Nulliparity	41 (47.7)	271 (45.7)	36 (52.9)	42 (39.6)
Diabetes diagnosis				
Diet-controlled GDM	49 (57.0)	318 (53.6)	-	
GDM on medication	37 (43.0)	275 (46.4)	-	
Type 1 Diabetes	-	-	42 (61.8)	60 (56.6)
Type 2 Diabetes	-	-	26 (38.2)	46 (43.4)
Blood glucose measurements	118 (114 – 126)	86 (77 – 96)	127 (119 – 142)	90 (82 – 99)
Time from glucose measurement to delivery (minutes)	83.5 (44.8 – 131.6)	89.6 (53.0 – 140.0)	44.5 (22.6 – 56.2)	49.8 (22.8 – 86.6)
Mode of delivery				
Spontaneous vaginal	67 (77.9)	350 (59.0)	22 (32.4)	29 (27.4)
Operative vaginal	2 (2.3)	21 (3.5)	3 (4.4)	0 (0.0)
Cesarean	17 (19.8)	222 (37.4)	43 (63.2)	77 (72.6)
Gestational age at delivery (weeks)	39.0 (37.4 – 39.7)	39.0 (38.0 – 39.7)	37.9 (36.9 – 38.4)	37.6 (36.4 – 38.7)
Intravenous insulin use	9 (10.5)	13 (2.2)	52 (76.5)	70 (66.0)
Chorioamnionitis	9 (10.5)	56 (9.4)	3 (4.4)	5 (4.7)
Apgar ≤7 at 1 minute	17 (19.8)	92 (15.5)	19 (27.9)	30 (29.3)
Apgar ≤7 at 5 minutes	9 (10.5)	16 (2.7)	5 (7.4)	10 (9.4)

	Gestational diabetes		Pregestational diabetes	
	Maternal hyperglycemia n=86	**Maternal euglycemia n=593**	**Maternal hyperglycemia n=68**	**Maternal euglycemia n=106**
Birth weight (grams)	3168 (2855 – 3505)	3280 (2930 – 3670)	3350 (2790 – 3925)	3495 (3015 – 3825)
Small for gestational age	7 (8.1)	68 (11.5)	6 (8.8)	7 (6.7)
Large for gestational age	8 (9.3)	62 (10.5)	18 (26.5)	26 (24.5)

Data presented as median (interquartile range) or n (column %)

BMI= body mass index

GDM= gestational diabetes

Maternal euglycemia was defined as capillary glucose ≤110 mg/dL and maternal hyperglycemia was defined as glucose >110 mg/dL.

Table 2:

Risk of neonatal outcomes among women with pre-delivery hyperglycemia compared with euglycemia stratified by maternal diabetes type

	Maternal hyperglycemia >110mg/dL		Maternal euglycemia ≤110 mg/dL	
	N (%)	Crude RR (95% CI) Adjusted RR (95% CI)	N (%)	Crude RR (95% CI) Adjusted RR (95% CI)
All diabetes types	*n=154*		*n=699*	
Neonatal hypoglycemia (1 hour)	64 (41.6)	1.4 (1.2 – 1.8) 1.1 (0.88 – 1.4)†	202 (28.9)	Reference Reference
Neonatal hypoglycemia (2–24 hours)	69 (44.8)	1.1 (0.89 – 1.3) 0.95 (0.79 – 1.2)†	297 (42.5)	Reference Reference
Admission to Neonatal Intensive care unit	45 (29.2)	1.7 (1.3 – 2.3) 1.3 (0.95 – 1.8)†	118 (16.9)	Reference Reference
Gestational diabetes, diet-controlled	*n=49*		*n=318*	
Neonatal hypoglycemia (1 hour)	7 (14.3)	0.63 (0.31 – 1.3) 0.50 (0.23 – 1.1)*	75 (23.6)	Reference Reference
Neonatal hypoglycemia (2–24 hours)	13 (26.5)	0.71 (0.44 – 1.1) 0.73 (0.44 – 1.2)*	121 (38.1)	Reference Reference
Admission to Neonatal Intensive care unit	12 (24.5)	1.8 (1.03 – 3.2) 2.0 (1.1 – 3.4)*	43 (13.5)	Reference Reference
Gestational diabetes on medication	*N=37*		*N=275*	
Neonatal hypoglycemia (1 hour)	15 (40.5)	1.6 (1.1 – 2.5) 1.8 (1.1 – 2.7)*	71 (25.8)	Reference Reference
Neonatal hypoglycemia (2–24 hours)	15 (40.5)	0.94 (0.62 – 1.4) 0.97 (0.64 – 1.5)*	118 (42.9)	Reference Reference
Admission to Neonatal Intensive care unit	6 (16.2)	1.2 (0.53 – 2.6) 1.2 (0.54 – 2.5)*	38 (13.8)	Reference Reference
Type 1 Diabetes	*n=42*		*n=60*	
Neonatal hypoglycemia (1 hour)	31 (73.8)	1.1 (0.89 – 1.5) 1.1 (0.88 – 1.4)*	38 (63.3)	Reference Reference
Neonatal hypoglycemia (2–24 hours)	27 (64.3)	1.0 (0.76 – 1.3) 0.97 (0.92 – 1.02)*	39 (65.0)	Reference Reference
Admission to Neonatal Intensive care unit	20 (47.6)	1.4 (0.89 – 2.3) 1.4 (0.87 – 2.3)*	20 (33.3)	Reference Reference
Type 2 Diabetes	*n=26*		*n=46*	
Neonatal hypoglycemia (1 hour)	11 (42.3)	1.02 (0.61 – 1.7) 1.1 (0.61 – 1.9)*	18 (39.1)	Reference Reference
Neonatal hypoglycemia (2–24 hours)	14 (53.8)	1.00 (0.998 – 1.00) 1.2 (0.77 – 2.0)*	19 (41.3)	Reference Reference
Admission to Neonatal Intensive care unit	7 (26.9)	0.74 (0.36 – 1.5) 0.65 (0.28 – 1.5)*	17 (37.0)	Reference Reference

Data presented n (%), risk ratio (RR), and 95% confidence interval (CI)

Neonatal hypoglycemia defined as capillary glucose <45 mg/dL.

*Adjusted for maternal age, race/ethnicity, body mass index, IV insulin, and insurance status

[†]Adjusted for maternal age, race/ethnicity, body mass index, IV insulin, insurance status, and diabetes type

Table 3.

Risk of neonatal outcomes for patients with Type 1 diabetes mellitus, Type 2 diabetes mellitus, gestational diabetes mellitus diet-controlled, and gestational diabetes mellitus on medication

	Gestational Diabetes	Pregestational Diabetes	Gestational Diabetes				Pregestational Diabetes			
	n=679	n=174	Diet-controlled n=367		On medication n=312		Type 1 n=102		Type 2 n=72	
	RR (95% CI) aRR (95% CI)*	RR (95% CI) aRR (95% CI)*	N (%)	RR (95% CI) aRR (95% CI)*	N (%)	RR (95% CI) aRR (95% CI)*	N (%)	RR (95% CI) aRR (95% CI)*	N (%)	RR (95% CI) aRR (95% CI)*
Neonatal hypoglycemia (1 hour)	Reference Reference	2.3 (1.9–2.8) 2.2 (1.8–2.6)	82 (22.3)	Reference Reference	86 (27.6)	1.2 (0.95–1.6) 1.1 (0.85–1.5)	69 (67.6)	3.0 (2.4–3.8) 3.0 (2.3–3.9)	29 (40.3)	1.9 (1.3–2.6) 1.5 (1.1–2.2)
Neonatal hypoglycemia (2–24 hours)	Reference Reference	1.5 (1.3–1.7) 1.3 (1.1–1.6)	134 (36.5)	Reference Reference	133 (42.6)	1.1 (0.92–1.4) 1.05 (0.86–1.3)	66 (64.7)	1.8 (1.5–2.2) 1.5 (1.2–1.9)	33 (45.8)	1.2 (0.93–1.6) 1.2 (0.85–1.6)
Admission to NICU	Reference Reference	2.5 (1.9–3.3) 2.4 (1.8–3.1)	55 (15.0)	Reference Reference	44 (14.1)	0.94 (0.65–1.4) 0.87 (0.60–1.3)	40 (39.2)	2.6 (1.9–3.7) 2.8 (1.9–4.1)	24 (33.3)	2.2 (1.5–3.4) 1.7 (1.1–2.6)

Neonatal hypoglycemia defined as capillary glucose <45 mg/dL.

NICU= neonatal intensive care unit.

Data presented as n (%), crude (cRR) and adjusted risk ratio (aRR) and 95% confidence interval (CI).

*Adjusted for maternal age, race, body mass index, and insurance status.