

Glucose control among women with gestational diabetes and early offspring's growth

María Socorro Parra-Cabrera, MPH, ScD,^(1,3) Erika Marlen Hurtado-Salgado, MSc, ScD,^(1,3)
Eric Monterrubio-Flores, MSc, ScD,⁽²⁾ Ignacio Méndez-Gómez-Humarán, MSc, ScD,⁽³⁾
Lea Aurora Cupul-Uicab, MSc, ScD.⁽¹⁾

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Abstract

Objective. To assess the association between glucose control during pregnancy and infant's growth. **Materials and methods.** Prospective study of 130 women with gestational diabetes mellitus (GDM) followed up to three months after birth. Infant's growth was assessed as weight-for-age (WfA), weight-for-length (WfL), and length-for-age (LfA) z-scores. The association of adequate vs. inadequate glucose control with infant's growth was evaluated using linear mixed models.

Results. Overall, glucose control during pregnancy was not associated with WfA ($\alpha\beta = 0.089$; 95%CI: -0.248,0.426), WfL ($\alpha\beta = 0.006$; 95%CI: -0.280,0.291), and LfA ($\alpha\beta = 0.136$; 95%CI: -0.157,0.429). We observed heterogeneity of effects by gestational age; infants with adequate control compared to inadequate had reduced WfA if they were born at ≥ 39 weeks.

Conclusion. Glucose control of women with GDM might have little impact on their early offspring's growth; however, gestational age might be relevant in terms of heterogeneity of effects. Future studies to confirm the latter findings are required.

Keywords: gestational diabetes mellitus; glucose control; infant's growth; offspring; prospective study

Resumen

Objetivo. Evaluar la asociación del control de glucosa en el embarazo con el crecimiento infantil. **Material y métodos.** Estudio prospectivo de 130 mujeres con diabetes gestacional (DG) y sus productos. Crecimiento infantil determinado como puntuaciones-z de peso para la edad (PE), peso para la longitud (PL) y longitud para la edad (LE). La asociación del control adecuado (vs. inadecuado) de glucosa y crecimiento se evaluó con modelos lineales mixtos. **Resultados.** El control de glucosa no se asoció con PE ($\beta\alpha = 0.089$; IC95%: -0.248,0.426), PL ($\beta\alpha = 0.006$; IC95%: -0.280,0.291) y LE ($\beta\alpha = 0.136$; IC95%: -0.157,0.429). Se observó heterogeneidad de efectos por edad gestacional; aquellos con control adecuado comparado con inadecuado tuvieron PE reducido si nacieron a las ≥ 39 semanas. **Conclusión.** El control de glucosa en mujeres con DG parece tener poco impacto en el crecimiento temprano de sus hijos; sin embargo, la edad gestacional parece ser relevante. Se requieren estudios para confirmar estos hallazgos.

Palabras clave: diabetes mellitus gestacional; control de glucosa; crecimiento infantil; hijos; estudio prospectivo

* Both authors contributed equally.

- (1) Center for Population Health Research, National Institute of Public Health. Cuernavaca, Morelos, Mexico.
- (2) Center for Nutrition and Health Research, National Institute of Public Health. Cuernavaca, Morelos, Mexico.
- (3) Center for Research in Mathematics AC Aguascalientes. Aguascalientes, Mexico.

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Corresponding author: Aurora Cupul-Uicab. Center for Population Health Research, National Institute of Public Health.
Av. Universidad 655, col. Santa María Ahuacatlán. 62100 Cuernavaca, Morelos, Mexico.
email: lea.cupul@insp.mx

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Gestational Diabetes Mellitus (GDM) is metabolic disorder characterized by glucose intolerance that develops first in pregnancy, regardless whether such alteration persists after delivery;^{1,2} this condition is usually diagnosed in the second and third trimester of pregnancy.² Pancreatic β cell response is decreased or delayed in pregnancies complicated with GDM, resulting in diminished insulin secretion and subsequent hyperglycemia.^{3,4} Maternal hyperglycemia in pregnancy leads to fetal hyperglycemia because glucose easily crosses the placental barrier.⁵ A surplus of glucose transfer to the fetus promotes the release of insulin by the fetal pancreas; persistent maternal hyperglycemia favors fetal hyperinsulinemia, hyperplasia of pancreatic β cells, and high insulin-like growth factors. Fetal insulin-like growth factors promote the synthesis of protein, lipid, and glycogen, which triggers high fetal growth rate and macrosomia.^{5,6}

GDM is a public health problem due to its adverse health effects on the mothers and their offspring.¹ Women who develop GDM are at a higher risk of preeclampsia, polyhydramnios, primary caesarean delivery, and trauma due to fetal macrosomia; in the long-term they are at increased risk of having type 2 DM (T2D) and cardiovascular disease.^{3,4} While offspring are at a higher risk of developing perinatal complications including preterm birth, congenital malformations, respiratory distress syndrome, metabolic disturbances, and neonatal death.^{3,4,6} Common complications of the newborn are macrosomia and being born large for gestational age (LGA);^{4,6} a higher percent of body fat mass had also been reported among them.^{3,7} On the long-term, offspring exposed to maternal GDM are more likely to develop T2D and obesity later in life.^{3,6}

The estimated global prevalence of GDM for 2021 was 14.2%; the highest prevalence was reported for Middle East and North Africa (30.2%), whereas South and Central America (14.2%) had a slightly higher prevalence than North America and the Caribbean (11.7%); higher prevalence of GDM was reported among high-(14.4%) and low-income (14.7%) countries than among middle-income (9.9%).⁸ Whereas the estimated incidence of GDM for Mexico in 2023 was 26.6%.⁹ Yet, the prevalence of GDM continue to raise parallelly with the obesity pandemic, potentially affecting countries with a higher prevalence of obesity among women (41% in 2020-2023) such as Mexico.¹⁰

An adequate control of maternal hyperglycemia with changes in diet and physical activity during pregnancy might decrease the risk of some of the GDM adverse health consequences in the offspring¹¹ and reduced the need for pharmacological treatment in the mother.⁴ However, little is known about other factors that could

impact the early growth of GDM-exposed infants, rapid weight gain in infants had been linked to a higher risk of being overweight or obese later in life.¹² Identifying modifiable factors related to early growth of children exposed to maternal GDM might be relevant to reduce the potential long-term adverse outcomes among them and to raise awareness among women of childbearing age and health professionals. Thus, we aimed to assess the effect of maternal glucose control during the late second and third trimester of pregnancy on the growth of the infants born to women with GDM.

Materials and methods

We analyzed data from the cohort "Healthy Pregnancy Means Future", which enrolled 155 pregnant women without pregestational diabetes from the Mexican Ministry of Health Women's hospital in the state of Morelos in August, 2015-May, 2018.¹³ For this observational study, were eligible women aged 18-45 years with a diagnosis of GDM according to the American Diabetes Association criteria.² A total of 8 900 women in their late second and third trimester of pregnancy from 12 healthcare centers of the Ministry of Health from Morelos state were screened for GDM, 158 of them were confirmed to have GDM at the Women's hospital, all of whom were invited to participate with a participation rate of 90.5% (figure S1).¹⁴ Those who accepted were followed up to three months of age of their infants with a follow-up rate of 95.1% ($n=136$). Infants' anthropometric measurements were taken at birth and thereafter monthly during the follow-up period to assess their growth. Infants with birthweight <2 kg ($n=5$) and one who died at birth ($n=1$) were considered ineligible, leaving 130 infants with at least one anthropometric measurement after birth for the analysis. There were 497 observations nested within 130 infants, most contributed with three measurements ($n=114$). The study protocol was approved by the Research Ethics Committee at the National Institute of Public Health of Mexico (ID: 1292, CI-112-2015), and was performed in line with the principles of the Declarations of Helsinki; all women gave their written informed consent before participating in the study.

Glucose control during pregnancy

As part of the study, all women were invited to follow the guidelines of the medical nutrition therapy (MNT) up to delivery to control their glucose during pregnancy. The ascertainment of glucose was based on the pregnant woman's postprandial capillary levels measured every six hours daily during the late second and third trimester of pregnancy using glucometers provided by

the study (ACCU-CHEK® *Softclix*). Women recorded their glucose values on diaries delivered to the medical personnel at each appointment; the median number of reports delivered was three (range 1-5), 58.5% delivered three or more reports and only 10% delivered only one report. Glucose control was defined based on the percentage of daily postprandial glucose levels (mg/dL) as recorded by the woman in their dairies. Those with >80% of their daily glucose values <125 mg/dL were considered as having adequate and those with ≤80% as having inadequate glucose control. The only treatment indicated besides MNT was insulin. The median age of gestation at the first medical appointment to assess their glucose was 28 weeks, the 25th and 75th percentiles were 27.0 and 29.1, respectively.

Infants' growth measures

The infant's recumbent length (cm) and weight (g) were measured at birth, at one, two, and three months after birth following standardized techniques by specially trained health personnel. Recumbent length was measured using infant stadimeters with a precision of 1mm; weight was measured with the children without clothes or diapers using pediatric scales (BAME brand) with a precision of 10g (for weights up to 20k), the scales were calibrated weekly. Markers of infant growth were age and sex-specific *z-scores* of *weight-for-age*, *weight-for-length*, and *length-for-age* calculated from birth to three months of age using the World Health Organization (WHO) growth standard reference population.¹⁵

Covariates

Relevant covariates were obtained from questionnaires filled in at recruitment. Parity was reported as the number of offspring born alive and/or stillborn before the index pregnancy, those whose firstborn was the index infant were considered primiparas. Education was reported as the highest number of years of formal education attained, and a history of diabetes was reported as having a first-degree relative with a T2D diagnosis. Women's height (mt) was measured at enrollment and pre-pregnancy weight (kg) was self-reported. Pre-pregnancy BMI (kg/m²) was calculated using self-reported pre-pregnancy weight and was categorized using the WHO cut-off points to define normal BMI (18.5-24.9), overweight (25.0-29.9), and obesity (≥30.0).¹⁶ Physical activity was reported as minutes per week performing various activities such as walking, cycling, and household chores; those doing >30 minutes at least 3-times per week were considered as active.

Gestational age (GA, weeks) at birth was ascertained using the last menstrual period and the sex of the infants was coded as girl or boy. Pregnancy complications such as preeclampsia, gestational hypertension, child's macrosomia, other health-related complications (*i.e.*, premature rupture of membranes, hemorrhage, sepsis, and preterm birth), and complications related to the delivery (*i.e.*, lack of dilation, prior C-section, unplanned C-section, low or high fetal heart beath, and fetal respiratory distress) were obtained from hospital records.

Statistical analysis

We present medians with interquartile ranges (IQR) for numerical variables and frequencies (absolute and relative) for categorical variables to describe the characteristics of the participants according to their glucose control in pregnancy. Comparisons between adequate and inadequate glucose control groups were assessed using Kruskal-Wallis for continuous variables and Pearson's Chi² or Fisher's exact tests for categorical variables. Adjusted linear mixed models with random intercepts were fitted to estimate the average change in the infant's *z-scores* of *weight-for-age*, *weight-for-length*, and *length-for-age* from birth up to three months for those with adequate glucose control compared to those with inadequate control. The minimal set of confounders for adjustment was identified using directed acyclic graphs¹⁷ and included maternal age, parity, pre-pregnant BMI (kg/m²), education, and infants' sex. Given the size of our sample, we adjusted for pre-pregnant BMI as continuous rather than categorical to favor precision.

Heterogeneity of effect by GA at birth (<39 weeks vs. ≥39 weeks) was explored in fully adjusted models by introducing a multiplicative term (*e.g.*, glucose control*GA); due to the small sample size, the median of GA (39 weeks) was defined as cut-off point to have balanced groups for this test. Similarly, we assessed heterogeneity of effects by infants' age (months) in fully adjusted models. We defined a *p-interaction* <0.10 *a priori* as indicative of relevant heterogeneity; only GA showed evidence of heterogeneity with this criterion, thus, we also present results stratified on GA. Linear predictions of each outcome, from birth to three months, for glucose control groups before and after stratifying on GA were also conducted; for this analysis, maternal age and pre-pregnant BMI were centered at the mean for interpretation purposes. As a sensitivity analysis, we also explored heterogeneity of effects using GA as a continuous variable to assess the robustness of our findings. All statistical analyses were conducted using

Stata (version 15.1, release 2020; StataCorp, College Station, TX, USA).

Results

Overall, women were young (29 y); a little more than half (52.3%) were primiparas, had <10y or formal education (54.6% [14.6+40.0]), reported doing >30 minutes of physical activities at least three times per week (53.1%), and had pregnancy or delivery complications (50.8%); the majority had BMI indicative of overweight or obesity before pregnancy (70.8%) and had a first degree relative with T2D (73.9%) (table I). The most common complications were macrosomia

(13.9%), gestational hypertension (5.4%), preeclampsia (3.9%), and others related to the delivery (24.6%). The median age of gestation at delivery was 39.0 weeks (IQR, 2.0), a little more than half of the infants were males (51.5%), and few required being cared for at the NICU (10.1%). Most of the woman maintained an adequate glucose control during pregnancy (76.9%) and very few were treated with insulin (9.2%). The characteristics of the mothers and their infants did not differ among those with adequate versus inadequate glucose control, except for GA at birth, those with inadequate control delivered their infants a little earlier (38.5 weeks; IQR, 2.5) than those with adequate control (39.1 weeks; IQR, 2.0).

Table I
CHARACTERISTICS OF MOTHERS AND THEIR INFANTS ACCORDING TO GLUCOSE CONTROL AFTER DIAGNOSIS OF GESTATIONAL DIABETES. MORELOS, MEXICO 2015-2018

Characteristics	Overall (n= 130)	Inadequate glucose control* (n= 30)	Adequate glucose control* (n= 100)	p-value [‡]
	n (%; 95%CI) Median [IQR]	% or Median [IQR]	% or Median [IQR]	
Mothers				
Age (years)	29.0 [8.0]	27.5 [8.0]	29.0 [8.5]	0.64
Education (years)				0.61
<7.0	19 (14.6; 9.5,21.9)	20.0	13.0	
7.0-9.0	52 (40.0; 31.8,48.7)	36.7	41.0	
10.0+	59 (45.4; 36.9,54.0)	43.3	46.0	
Married or has a partner				0.23
No	11 (8.5; 4.7,14.7)	3.3	10.0	
Yes	119 (91.5; 85.2,95.2)	96.7	90.0	
Physical activity				0.39
No	61 (46.9; 38.4,55.5)	40.0	49.0	
Yes	69 (53.1; 44.4,61.5)	60.0	51.0	
Pregestational BMI (kg/m ²)				0.72
<25.00	38 (29.2; 21.9,37.6)	23.3	31.0	
25.00-29.99	56 (43.1; 34.7,51.7)	46.7	42.0	
30.00+	36 (27.7; 20.6,36.1)	30.0	27.0	
Primiparous				0.12
No	62 (47.7; 39.1,56.3)	60.0	44.0	
Yes	68 (52.3; 43.6,60.8)	40.0	56.0	
Pre-pregnant weight (kg)	65 [18.0]	66 [18.0]	65 [19.0]	0.76
First-degree relative with T2D				0.14
No	34 (26.2; 19.2,34.4)	36.7	23.0	
Yes	96 (73.9; 65.5,80.7)	63.3	77.0	
Delivered by C-section				0.87
No	46 (35.4; 27.5,44.0)	36.7	35.0	
Yes	84 (64.6; 55.9,72.4)	63.3	65.0	

(continues...)

(continuation)

Pregnancy complications				0.71
None	64 (49.2; 40.6,57.8)	43.3	51.0	
Preeclampsia	5 (3.9; 1.5,8.9)	6.7	3.0	
Gestational hypertension	7 (5.4; 2.5,10.9)	3.3	6.0	
Macrosomia	18 (13.9; 8.8,20.9)	16.7	13.0	
Other health-related complications [§]	4 (3.1; 1.1,7.9)	0.0	4.0	
Related to the delivery [#]	32 (24.6; 17.9,32.8)	30.0	23.0	
Required insulin				
No	118 (90.8; 0.84,4,94.7)	83.3	93.0	0.11
Yes	12 (9.2; 5.3,15.6)	16.7	7.0	
Gestational age at birth (wk)	39.0 [2.0]	38.5 [2.5]	39.1 [2.0]	0.04
Sex				0.54
Female	63 (48.5; 39.9,57.1)	53.3	47.0	
Male	67 (51.5; 42.9,60.1)	46.7	53.0	
Required attention at the NICU at birth				0.18
No	116 (89.9; 83.3,94.1)	83.3	91.9	
Yes	13 (10.1; 5.9,16.6)	16.7	8.1	

BMI: body mass index; IQR: interquartile range; NICU: neonatal intensive care unit; T2D: type 2 diabetes.

* Adequate glucose control was defined as having >80% of their daily values of glucose <125 mg/dL (considered as controlled) as recorded in dairies throughout the follow-up.

‡ P-values from Pearson's Chi2 or Fisher's exact tests for proportions and Wilcoxon rank-sum for continuous or discrete variables comparing those with poor and good glucose control.

§ Includes premature rupture of membranes, hemorrhage, sepsis, and preterm delivery.

Includes lack of dilation, prior C-section, unplanned C-section, low or high fetal beath, fetal respiratory distress.

The average birthweight of the infants was 3.22kg (SD, 0.44) and length 50.32cm (SD, 1.69) (table S1).¹⁴ Overall, infants were born below the average *weight-for-age* (-0.18; SD, 0.94) and *weight-for-length* (-0.76; SD, 1.30), but above the average *length-for-age* (0.42; SD, 0.91) of the WHO growth reference population.¹⁸ There was a steady increase in weight and length from birth to three months; no crude differences by adequate and inadequate glucose control were observed (table S1).¹⁴

After adjusting for confounders, infants whose mothers had adequate glucose control during pregnancy had on average a slightly higher growth ($\alpha\beta$ from 0.006 to 0.136) over the study period compared to those with inadequate glucose control, however, such differences were not statistically significant (table II). As expected, *weight-for-age* (3mo: $\alpha\beta$ = 0.151) and *weight-for-length* (3mo: $\alpha\beta$ = 1.027) of the infants increased from birth to three months of age with a significant trend, whereas *length-for-age* (3mo: $\alpha\beta$ = -0.667) tended to decrease significantly (table S2).¹⁴

The effect of glucose control on average growth of the infants differed by GA at birth, indicating heterogeneity of effects (table II). Among those born

<39wk, *weight-for-age* ($\alpha\beta$ = 0.639; 95%CI: 0.184,1.095) and *length-for-age* ($\alpha\beta$ = 0.603; 95%CI: 0.208,0.998) were on average greater when their mothers had adequate glucose control compared to those with inadequate control. Whereas among those born at ≥ 39.0 weeks, *weight-for-age* ($\alpha\beta$ = -0.455; 95%CI: -0.909,-0.001) and *length-for-age* ($\alpha\beta$ = -0.330; 95%CI: -0.725,0.065) were on average reduced when their mothers had adequate glucose control compared to those with inadequate control. Although no relevant heterogeneity was observed for *weight-for-length*, stratified results were in the same direction but with smaller effects. Similar results were observed when we assessed heterogeneity of effects using GA as continuous variable, the effect of glucose control on infant's growth markers tended to vary at different values of GA (figure S2).¹⁴

The linear predictions from birth to three months of age are shown in figure 1 (and table S3).¹⁴ The predicted *weight-for-age* increased with age (figure 1a), but those with inadequate glucose control remained significantly below the average if they were born at <39wk and above the average if they were born at ≥ 39 wk. *Weight-for-length* showed a similar pattern regardless of GA and glucose control (figure 1b). The predicted

Table II
GROWTH OF INFANTS BORN FROM MOTHERS WITH GESTATIONAL DIABETES ACCORDING TO THEIR GLUCOSE CONTROL* DURING PREGNANCY BY GA AT BIRTH (N= 130[‡]). MORELOS, MEXICO, 2015-2018

Outcomes	Overall	GA <39.0 weeks	GA ≥39.0 weeks	p-interaction
	β [§] (95%CI)	β [§] (95%CI)	β [§] (95%CI)	
Weight-for-Age[#]				
Inadequate glucose control	0.000	0.000	0.000	<0.01
Adequate glucose control	0.089 (-0.248,0.426)	0.639 (0.184,1.095)	-0.455 (-0.909,-0.001)	
Weight-for-Length[#]				
Inadequate glucose control	0.000	0.000	0.000	0.11
Adequate glucose control	0.006 (-0.280,0.291)	0.235 (-0.162,0.631)	-0.226 (-0.625,0.174)	
Length-for-Age[#]				
Inadequate glucose control	0.000	0.000	0.000	<0.01
Adequate glucose control	0.136 (-0.157,0.429)	0.603 (0.208,0.998)	-0.330 (-0.725,0.065)	

β: adjusted coefficients; CI: confidence interval; GA: gestational age at birth.

* Adequate glucose control was defined as having >80% of their daily values of glucose <125 mg/dL (considered as controlled) as recorded in dairies throughout the follow-up.

[‡] There were 497 observations nested in 130 infants.

[§] From linear mixed models with random intercepts adjusted for maternal age, parity, pre-pregnant body mass index (kg/m²), education, infant's age at follow-up and sex.

[#] Z-scores based on the World Health Organization 2006 growth standards from birth to 3 months of age.

length-for-age (figure 1c) decreased with age, however, those with inadequate glucose control started below the average if they were born at <39wk and above the average if they were born at ≥39wk.

Discussion

Among Mexican women with GDM, glucose control had little impact on their offspring's growth in the first three months of life. The effect of glucose control on the infant's early growth showed heterogeneity by GA at birth. Among infants born at <39wk, adequate maternal glucose control in pregnancy resulted in higher average *weight-for-age* and *length-for-age* compared to those with inadequate control. Meanwhile, among those born at ≥39wk, adequate glucose control resulted in reduced average *weight-for-age* and *length-for-age* compared to those with inadequate control. As expected, weight markers increased with age, but *length-for-age* decreased.

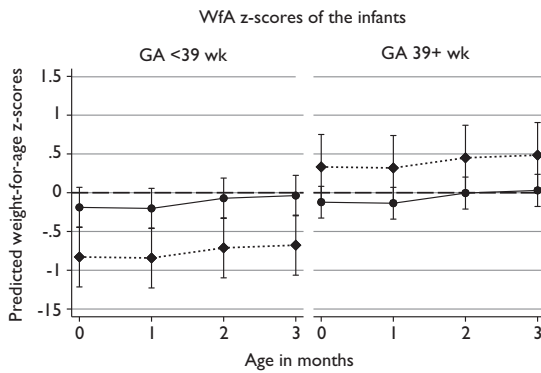
Women from our study were asked to follow the MNT guidelines from enrollment to delivery to control their glucose levels. While not directly comparable, a prior study among women with GDM from Brazil reported a lower risk of having small for GA (SGA) newborns if they receive metformin compared to diet alone, but there was a higher risk of having LGA newborns with a combination of metformin and insulin compared to diet alone.¹⁹ Thus, medical treatment alone to control

glucose levels for GDM pregnancies might not decrease the risk of having a LGA infant, which is a marker of future risk.²⁰ Recent meta-analyses^{21,22} reported lower risk of macrosomia and LGA among newborns from mothers treated with metformin relative to insulin, however, those treated with metformin were heavier as neonates and had higher BMI in mid-childhood.²¹ Thus, reaching adequate glucose control from medical treatment during pregnancy does not necessarily prevent the so-called postnatal catch-up, an important risk factor for adverse outcomes later in life.²³⁻²⁵

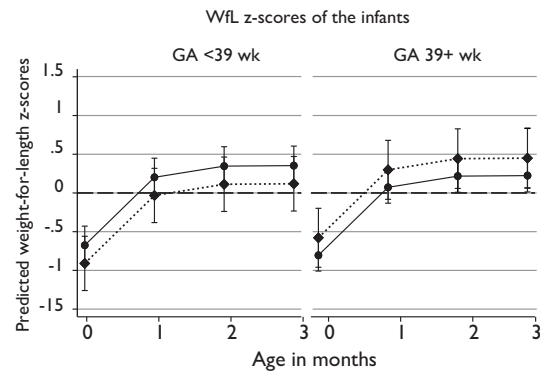
Our results showing that *weight-for-length* of the infants had a significant increase with a consistent significant decrease in *length-for-age* in the first three months of age (table S2),¹⁴ suggest that infants gained more weight than length. Such increase in *weight-for-length* in this short follow-up period cannot be disregarded, this could be a possible marker of rapid weight gain, which has been linked to a higher risk of being overweight or obese later in life.^{12,19,26} Higher zBMI among children born to GDM mothers in the first 24 months have been reported earlier,²⁷ although BMI was not assessed as an outcome in the present study, *weight-for-length* is comparable to BMI in the first 2 years of life as markers of future disease risk.²⁸

Maintaining optimal levels of blood glucose during pregnancy is relevant in terms of fetal growth and the future health of the newborn. An early study reported

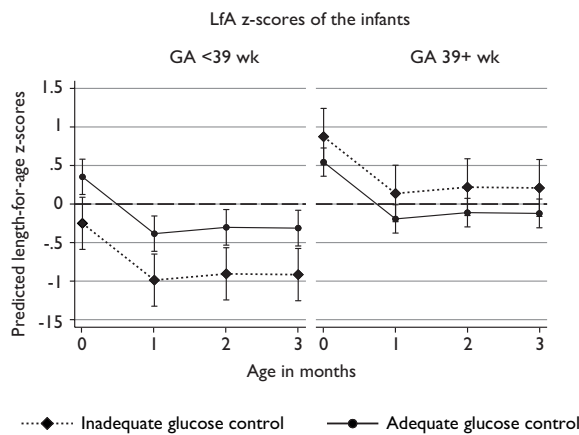
a) Infant's weight-for-age



b) Infant's weight-for-length



c) Infant's length-for-age



Linear predictions from birth to three months of age estimated from fully adjusted linear mixed models with random intercepts. Reference groups were female infants, primiparous women, <7 years of formal education, continuous variables were centered to their means (mothers age, 28.9 years; pre-pregnant BMI, 27.6 kg/m²). BMI: body mass index; GA: gestational age; LfA: length-for-age; WfA: weight-for-age; WfL: weight-for-length.

FIGURE 1. PREDICTED ANTHROPOMETRIC Z-SCORES OF INFANTS BORN FROM MOTHERS WITH GESTATIONAL DIABETES ACCORDING TO THEIR GLUCOSE CONTROL DURING PREGNANCY BY GA AT BIRTH. MORELOS, MEXICO, 2015-2018

a higher incidence of SGA infants with fasting glucose levels <86 mg/dL and a higher incidence of LGA infants with glucose >104 mg/dL,²⁶ such findings emphasize the importance of maintaining an ideal glycemic control in the management of GDM to reduce adverse perinatal outcomes. In the present study, glucose control was recorded using checkmarks when postprandial values were below the daily expected values (<125 mg/dL), thus, we did not have fasting glucose, nor the exact glucose levels to conduct similar analysis.

We observed a higher proportion of maternal and infant complications at delivery (50.8%), as expected fetal macrosomia was common (13.9%) and was higher

than the reported for Iranian infants (8.7%).²⁹ However, our estimates of macrosomia were similar to the rates (15%) reported for Spain³⁰ and at the lower end of the overall incidence (15-45%) reported for newborns from GDM mothers.³⁰ As expected, a higher proportion of women had a first-degree relative with T2D.³¹

Our analysis had some limitations. The main limitation was the small sample size, which limited the statistical power for the assessment of heterogeneity of effects, and contributed to the imprecision of our estimates. The use of the median as a cut-off point to categorize GA was not ideal, however, our results did not change substantially when we assessed heterogene-

ity of effects using GA as a continuous variable (figure S2).¹⁴ Inaccuracies when registering glucose values in the diaries could have affected our estimates due to misclassification of the exposure variable; it is likely that women might selectively registered lower glucose values than the higher ones, which may explain the higher proportion of adequate control. Although this may have occurred more often among those with a first-degree relative with T2D who might be more aware of their risks, the correlation between these variables was low ($r_{\text{Spearman}} = 0.13$). Moreover, any misclassification errors of the glucose control are likely independent of the values of the outcomes (infant's growth markers) and non-differential regarding the outcomes, because the exposure was reported before women knew their infant's outcomes. Misclassification due to random errors tends to attenuate the estimates. All women were invited to follow the MNT, few were treated with insulin, and none receive hypoglycemic drugs, therefore, we were unable to assess the independent effect of insulin on growth. Breastfeeding was not recorded in the present, thus, its effect as a potential effect modifier remains to be assessed in the present context. Lastly, our study had a very short follow-up time, thus, whether our findings persist at older ages remains unanswered.

The main strength of our study is its prospective nature; temporality is not a concern because glucose control measures preceded the assessment of the infant's growth. All anthropometry was conducted using standardized techniques by trained personnel. Screening for GDM was conducted in a large hospital specialized in pregnant women in the state of Morelos, the follow-up rate was high. Women received glucometers to measure postprandial capillary glucose levels every six hours daily during the late second and third trimester of pregnancy instead of having a single measure, this might reflect a more chronic fetal exposure to hyperinsulinemia. Our results might be generalizability only for Mexican women with GDM during pregnancy and their newborns with characteristics like those observed in our study.

Among GDM mothers, glucose control during pregnancy might not affect their offspring's growth in the first three months of life. However, GA at birth could be an important variable when assessing the effect of glucose control on the infant's early growth. Compared to inadequate glucose control, infants from mothers with adequate control showed higher average *weight-for-age* and *length-for-age* if they were born at <39wk but reduced average *weight-for-age* and *length-for-age* if they were born at ≥39wk. Our results need to be corroborated in studies with greater sample size, better measurements of glucose control, and longer follow-up.

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