Profile of Pregnant Women with Gestational Diabetes Mellitus at Increased Risk for Large for Gestational Age Newborns

Perfil de gestantes com Diabetes Mellitus Gestacional com maior risco para recém-nascidos grandes para a idade gestacional

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Abstract

Objective Gestational diabetes mellitus (GDM) is associated with a higher risk of perinatal morbidity and mortality, and its main complication is the occurrence of large for gestational age (LGA) newborns. The present study aims to characterize pregnant women with GDM and to identify factors associated with the occurrence of LGA newborns in this population.

Methods A cross-sectional study was performed based on medical records of women whose prenatal care and delivery were performed at the Maternal and Child Unit of the Hospital Universitário of the Universidade Federal do Maranhão, state of Maranhão, Brazil. A total of 116 pregnant women diagnosed with GDM were included according to the criteria of the International Association of Diabetes and Pregnancy Study Groups (IADPSG).

Results The variables associated with LGA newborns after multivariate analysis were: obesity prior to pregnancy (OR = 11.6; 95% CI: 1.40–95.9), previous macrosomia (OR = 34.7; 95% CI: 4.08–295.3), high blood glucose levels in the 3rd trimester (OR = 2,67; 95% CI: 1.01–7.12) and combined change in the oral glucose tolerance test (OGTT) (fasting + postdextrose) (OR = 3.53; 95% CI: 1.25–14.2) = 1.17–10.6). Otherwise, insufficient weight gain during pregnancy reduced the risk for LGA newborns (OR = 0.04; 95% CI: 0.01–0.32).

Conclusion Obesity prior to pregnancy, previous macrosomia, high blood glucose levels in the 3rd trimester, and combined change in the OGTT were independent predictive factors for LGA newborns in pregnant women with GDM.

Keywords
- gestational diabetes mellitus
- oral glucose tolerance test
- large for gestational age

Resumo

Objetivo Diabetes mellitus gestacional (DMG) está associado a um maior risco de morbidade e mortalidade perinatais, e sua principal complicação é a ocorrência de

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recém-nascidos grandes para idade gestacional (GIG). O presente estudo visa caracterizar as gestantes com DMG e identificar fatores associados à ocorrência de recém-nascidos GIG nesta população.

Métodos Estudo transversal realizado a partir da coleta de dados de prontuário de mulheres cujo acompanhamento pré-natal e parto foram realizados na Unidade Materno-Infantil do Hospital Universitário da Universidade Federal do Maranhão, MA, Brasil. Foram incluídas 116 gestantes diagnosticadas com DMG pelo critério do International Association of Diabetes and Pregnancy Study Groups (IADPSG).

Resultados As variáveis associadas à GIG após análise multivariada foram: obesidade pré-gestacional (OR= 11,6; IC 95%: 1,40–95,9), macrossomia anterior (OR = 34,7; IC 95%: 4,08–295,3), glicemia em jejum elevada no 3° trimestre (OR = 2,67; IC 95%: 1,01–7,12) e alteração combinada no teste de tolerância oral à glicose (jejum + pós-dextrose) (OR= 3,53; IC 95%: 1,17–10,6). Ganho de peso inferior reduziu o risco para GIG (OR= 0,04; IC 95%: 0,01–0,32).

Conclusão Obesidade anterior à gestação, macrossomia prévia, níveis elevados de glicose no sangue no 3° trimestre e alteração combinada no TOTG foram fatores preditivos independentes para os recém-nascidos GIG em gestantes com DMG.

Palavras-chave
- diabetes mellitus gestacional
- teste oral de tolerância à glucose
- grande para idade gestacional

Introduction

Gestational diabetes mellitus (GDM) is classically defined as glucose intolerance resulting in hyperglycemia of variable intensity, with onset or first recognition during pregnancy, which may or may not persist after childbirth.[1]

Gestational diabetes mellitus is usually diagnosed through provocative tests using glucose loads. In 2010, the International Association of Diabetes and Pregnancy Study Groups (IADPSG) suggested a new diagnostic criteria based on the 75 g oral glucose tolerance test (75-g OGTT) – performed between 24 and 28 weeks of gestation, with plasma glucose measured at baseline (fasting), after 1 hour, and after 2 hours, wherein one altered measurement (fasting plasma glucose $\geq$ 92 mg/dL; 1 hour $\geq$ 180 mg/dL; 2 hour $\geq$ 153 mg/dL) is sufficient for the diagnosis of GDM.[2] The American Diabetes Association (ADA) endorsed this diagnostic criteria in 2011, and 2 years later, the World Health Organization (WHO) revised and updated this criteria and introduced the recommendations of the IADPSG.[3,4] Currently, the Brazilian Society of Diabetes and the Brazilian Federation of Gynecology and Obstetrics Associations, similar to the ADA and the WHO, use the same criteria for the diagnosis of GDM.[5]

The prevalence of GDM is quite variable, depending on the population under study and on the diagnostic criteria. According to the IADPSG criteria, the prevalence of GDM significantly increased by up to between 15 and 20%.[2] In addition to being related to changes in the diagnostic criteria, this increase is also related to the increasing prevalence of obesity (body mass index [BMI] $\geq$ 30 kg/m^2), which itself is a risk factor for the onset of GDM.[6] The risk of developing GDM is estimated to be 2, 4, and 8 times greater in overweight, obese, and morbidly obese women, respectively, than in women of healthy weight.[7] Thus, the higher the degree of maternal obesity, the greater the risk of developing GDM, primarily because of insulin resistance.[7,8]

Gestational diabetes mellitus is associated with a high risk of perinatal morbidity and mortality, and the main complication is macrosomia or large for gestational age (LGA) fetuses.[9] Macrosomia is defined as birth weight > 4,000 g; however, this definition fails to consider gestational age (GA). Large for gestational age corresponds to birth weight $\geq$ 90th percentile for the corresponding GA.[10]

Fetal macrosomia is clinically relevant because it poses risks both for the mother as well as for the fetus. Maternal complications are often related to fetal-pelvic disproportion, prolonged labor, soft-tissue lacerations, high rates of cesarean section, postpartum hemorrhage, and placental retentions arising from uterine atony.[9] It is also associated with perinatal morbidity and mortality; the fetal injuries most commonly associated with macrosomia and shoulder dystocia are fracture of the clavicle and damage to the nerves of the brachial plexus, which can produce Erb paralysis.[11]

The literature features substantial variations in factors that increase the probability of macrosomia with respect to the extent of the association between risk factors and excessive birth weight, with the true role of the several factors involved in the genesis of this complication remaining undefined. Fetal macrosomia is related to advanced maternal age, maternal diabetes and glucose intolerance, post-term pregnancy, excessive weight and obesity prior to pregnancy, male fetus, multiparity, excessive weight gain (EWG) during pregnancy, parental height, and an obstetric history of macrosomia.[12,13]

The most common and well-described pathogenic mechanism of accelerated fetal growth is related to maternal diabetes mellitus. In maternal hyperglycemia, excess glucose crosses the placenta and reaches the fetal circulation, thereby stimulating fetal insulin secretion. Hyperinsulinemia and excess glucose *in utero* favors insulin-sensitive tissue hypertrophy, promoting accelerated growth that may lead to macrosomia.[14]

To characterize the profile of pregnant women with GDM who are at a higher risk of presenting complications caused by excessive fetal growth, the present study seeks to identify risk factors associated with LGA newborns in this population.

Methods

A cross-sectional study was conducted at the Maternal and Child Unit of the Hospital Universitário of the Universidade Federal do Maranhão, state of Maranhão, Brazil, using information from medical records. The research protocol was approved in advance by the local Research Ethics Committee (opinion number: 1451033).

The present study included pregnant women with GDM diagnosed by OGTT using the IADPSG criteria, whose monitoring and delivery had taken place at the HUMI between January 2015 and December 2017. The exclusion criteria were: pregnant women with plasma glucose $\geq$ 126 mg/dl during the 1st trimester; previous diagnosis of chronic hypertension and collagen diseases; human immunodeficiency virus, hepatitis B or hepatitis C infection; newborns hospitalized in a neonatal intensive care unit (ICU); fetal malformation; and twin pregnancies. The data were collected from maternal and neonatal electronic medical records.

The variables studied were the following: maternal age in whole years, categorized as $<$ 35 years old or $>$ 35 years old; maternal height in centimeters; prepregnancy BMI estimated using the Quetelet index and classified according to the Food and Agriculture Organization (FAO)/WHO criteria; gestational weight gain (WG) estimated by the difference between maternal weight at delivery and the usual weight prior to the pregnancy reported at the 1st prenatal visit.[15,16] Weight gain was classified according to the Institute of Medicine (IOM) criteria as insufficient (IWG), appropriate (AWG) and EWG.[17] The investigation also included the following: a family history of diabetes among first-degree relatives; obstetric history, including parity, previous pregnancy with macrosomia, and a previous history of GDM; OGTT values upon diagnosis; and blood sugar levels throughout the 3rd trimester, using the arithmetic mean of capillary blood glucose levels while fasting and 2 hours after breakfast, routinely measured at every visit.

The studied characteristics of the newborns were the following: birthweight, gender, type of delivery, and GA. Birthweight was corrected for GA based on the recent recommendations suggested by the Intergrowth study, and it was used to analyze the calculated percentile values with the aid of this tool.[18] Based on calculated percentile values, the newborns were classified as small for gestational age (SGA, weight $<$ 10th percentile), appropriate for gestational age (AGA, 10th percentile $<$ weight $<$ 90th percentile), or LGA (weight $>$ 90th percentile).[10] Macrosomia was defined as birth weight $\geq$ 4,000 g, regardless of the GA.[10]

Data were processed using the software PASW Statistics for Windows, Version 18.0 (SPSS Inc., Chicago, IL, USA). Initially, a descriptive statistical analysis was performed by estimating frequency, mean, and standard deviation (SD). The normality of quantitative variables was tested using the Lilliefors test. Subsequently, analysis of variance (ANOVA) with the post-hoc Tukey test was used for the comparative analysis of numerical variables. The distribution of categorical variables was analyzed using the chi-squared test or the Fisher exact test. Odds ratio (OR) and 95% confidence intervals (CIs) were used to assess the association with the LGA outcome. A multivariate logistic regression model was built to estimate the ORs adjusted for variables presenting *a p-value* $<$ 0.10 in the bivariate analysis. Variables related to glycemia parameters were not adjusted to avoid multicollinearity. In addition, receiver operating characteristic (ROC) curves were analyzed to estimate the area under the curve (AUC), and a 95% CI was established to predict LGA newborns using OGTT levels (at 0, 60, and 120 minutes). The significance level adopted for all of the analyses was of 5%.

Results

In total, 116 pregnant women with GDM were included in the present study. The mean age was 32.7 $\pm$ 6.4 (range: 18–44) years old; 41.1% of the women had a family history of diabetes among their first-degree relatives, and 25% were multiparous. The mean GA at delivery was 38.1 $\pm$ 1.5 weeks, with a cesarean section rate of 75%. The overall occurrence of LGA newborns was of 25.9%.

With regard to prepregnancy BMI, 28% (32/116), 31% (35/116), and 43% (49/116) of the women had normal weight, were overweight, and were obese, respectively. Considering the IOM recommendations for WG during pregnancy, $\sim$ 35% of the pregnant women had EWG, with a similar percentage being observed for WG in each prepregnancy BMI category (►**Table 1**). Large for gestational age newborns were more frequent in overweight and obese women. Macrosomia was only more frequent in the group of mothers who were obese before pregnancy (►**Table 2**). Only four women had SGA newborns and, of these, only one had insufficient WG during pregnancy.

The mean GA when OGTT was conducted was 25 weeks. At the time of the test, $\sim$ 13% of the diagnoses were because of changes only in fasting plasma glucose, and 50.9% were because of changes in both fasting and post-dextrose load. The mean fasting plasma glucose level at the time of the test was higher in the group of pregnant women who were overweight and obese prior to the pregnancy (►**Table 1**).

With regard to treatment, $\sim$ 43% of the pregnant women received only insulin as a medical therapy during pregnancy. Blood glucose levels were monitored during the 3rd trimester, and the mean fasting blood glucose level was higher in the group of women who were obese prior to the pregnancy (►**Table 1**).

The percentage of LGA newborns was statistically higher among women with overweight, with obesity, with a previous history of macrosomia, with high mean fasting blood glucose in the 3rd trimester, with changes in 3 OGTT measurements, and with a combined change in the OGTT (fasting + after dextrose load). In women with IWG during pregnancy, the percentage of LGA newborns was statistically lower. After the multivariate analysis, the following factors were associated with LGA newborns: obesity (OR = 11.6; 95% CI: 1.40–95.9), previous macrosomia (OR = 34.7; 95% CI: 4.08–295.3), high

Table 1 Description of maternal and obstetric data according to pre-gestational body mass index

Variables	Total $n = 116$	Pre-gestational BMI			*p-value*
		Normal $n = 32$	Overweight $n = 35$	Obesity $n = 49$	
Age (years old)	32.7 ± 6.4	30.9 ± 7.1	33.6 ± 5.4	33.2 ± 6.3	0.158
Height(cm)	156 ± 6	156 ± 7	155 ± 5	157 ± 5	0.178
Multiparous (%)	25.0%	12.5%	20.0%	36.7%	0.101
Weigth gain (kg)	9.5 ± 6.9	12.9 ± 5.3	9.5 ± 6.4	7.3 ± 7.4**	0.001*
Categories of weigth gain (%)					0.731
Insufficient	33.6%	40.6%	37.1%	26.5%	
Appropriate	31.0%	28.1%	28.6%	34.7%	
Excessive	35.4%	31.3%	34.3%	38.8%	
OGTT values (mg/dl)					
Fasting	95.6 ± 14.6	89.6 ± 12.0	98.2 ± 16.9**	97.6 ± 13.3**	0.021*
60 minutes	187.8 ± 34.5	184.7 ± 31.0	198.1 ± 42.2	183.0 ± 30.1	0.202
120 minutes	172.1 ± 35.1	160.4 ± 31.3	185.8 ± 36.4**	169.7 ± 33.7	0.009*
Number of points changed in OGTT (%)					0.255
1 point	37.1%	53.1%	28.6%	32.6%	
2 points	37.9%	31.3%	42.8%	38.8%	
3 points	25.0%	15.6%	28.6%	28.6%	
Categories changed in OGTT					0.084
Only fasting	12.9%	18.7%	5.7%	14.3%	
Only after dextrose load	36.2%	50.0%	34.3%	28.6%	
Fasting and after dextrose load	50.9%	31.3%	60.0%	57.1%	
Insulin therapy (%)	43.1%	28.1%	54.3%	44.9%	0.091
Mean fasting blood glucose during 3rd trimester (mg/dl)	90.8 ± 15.3	85.1 ± 12.0	91.8 ± 17.1	93.8 ± 15.2**	0.048*
Delivery (%)					0.991
Normal	25.0%	25.0%	25.7%	24.5%	
Cesarean	75.0%	75.0%	74.3%	75.5%	

Abbreviations: BMI, body mass index; OGTT, oral glucose tolerance test.
* Statistically significant differences among BMI categories ($p < 0.05$). ** Statistically significant difference compared with the normal BMI group ($p < 0.05$).

Table 2 Description of newborn data according to pregestational maternal body mass index

Variables	Total $n = 116$	Pregestational BMI			*p-value*
		Normal $n = 32$	Overweight $n = 35$	Obesity $n = 49$	
Gender (%)					0.538
Male	47.4%	53.1%	40.0%	49.0%	
Female	52.6%	46.9%	60.0%	51.0%	
Post-term pregnancy (%)	12.9%	15.6%	8.5%	14.3%	0.645
GA at birth (weeks)	38.1 ± 1.5	38.3 ± 1.3	37.5 ± 1.9	38.2 ± 1.1	0.072
Weight at birth(g)	3342 ± 534	3092 ± 348	3319 ± 592	3523 ± 530**	0.001*
Macrossomia (%)	11.2%	0%	14.3%	16.3%**	0.037*
LGA (%)	25.9%	3.1%	28.6%**	38.8%**	0.001*

Abbreviations: BMI, body mass index; GA, gestational age; LGA, large for gestational age.
* Statistically significant differences among BMI categories ($p < 0.05$).
** Statistically significant differences compared with the normal BMI group ($p < 0.05$).

Table 3 Crude and adjusted odds ratios of developing large for gestational age offspring

Variables	LGA (Percentil >90)				
	%	Crude OR (95% CI)	*p-value*	Adjusted OR (95% CI)	*p-value*
Previous macrossomia					
No	17.5	Ref.		Ref.	
Yes	92.3	56.7 (6.92–463.8)	< 0.001*	34.7 (4.08–295.3)	0.001*
Pregestational BMI					
Normal	3.1	Ref.		Ref.	
Overweight	28.6	12.4 (1.48–103.5)	0.006*	6.53 (0.62–68.5)	0.117
Obesity	38.8	19.6 (2.41–155.9)	< 0.001*	11.6 (1.40–95.9)	0.023*
Categories of weigth gain					
Insufficient	7.7	0.11 (0.03–0.45)	< 0.001*	0.04 (0.01–0.32)	0.001*
Appropriate	41.7	Ref.		Ref.	
Excessive	29.3	0.57 (0.22–1.48)	0.368	0.39 (0.11–1.37)	0.142
Number of points changed in OGTT (%)					
1 point	16.3	Ref.		Ref.	
2 points	27.3	1.92 (0.67–5.49)	0.327	1.05 (0.29–3.75)	0.932
3 points	37.9	3.14 (1.04–9.47)	0.037*	1.86 (0.38–9.03)	0.440
Categories changed in OGTT					
Only fasting	13.3	0.92 (0.16–5.16)	1.000	1.11 (0.16–7.38)	0.912
Only after dextrose load	14.3	Ref.		Ref.	
Fasting and after dextrose load	37.3	3.56 (1.29–9.82)	0.020*	3.53 (1.17–10.60)	0.024*
Mean fasting blood glucose during 3rd trimester (mg/dl).					
> 95 mg/dL	41.7	3.07 (1.25–7.53)	0.022*	2.67 (1.01–7.12)	0.048*
< 95 mg/dL	18.8	Ref.		Ref.	

Abbreviations: BMI, body mass index; CI, confidence interval; LGA, large for gestational age; OGTT, oral glucose tolerance test; OR, odds ratio.
* Statistically significant differences in the prevalence of LGA ($p < 0.05$). Adjustment of the OR for pregestational BMI variables, previous macrosomia, weight gain categories, mean fasting blood glucose during the 3rd trimester, number of altered points and categories of OGTT.

mean fasting blood glucose in the 3rd trimester (OR = 4.23; 95% CI: 1.25–14.2), and combined change in the OGTT (fasting + after the dextrose load) (OR = 3.53; 95% CI: 1.17–10.6). Insufficient WG reduced the risk for LGA newborns even after adjustment (OR = 0.04; 95% CI: 0.01–0.32) (►**Table 3**).

The prediction of the occurrence of LGA newborns was estimated using plasma glucose values from the OGTT at 0, 60, and 120 minutes (►**Fig. 1**). The data show an area under the curve (AUC) of 0.647 (0.552–0.735) at 0 minutes, of 0.525 (0.413–0.634) at 60 minutes, and of 0.661 (0.567–0.747) at 120 minutes, thus demonstrating that at 0 and 120 minutes were the times that best predicted the occurrence of LGA newborns ($p < 0.05$).

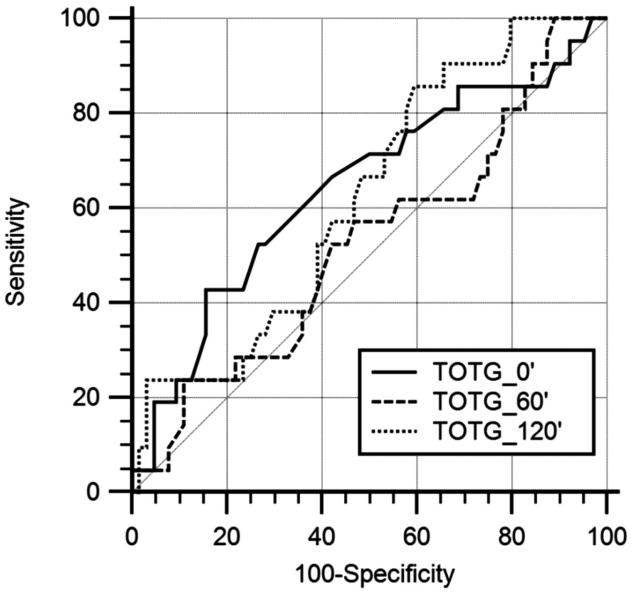

Fig. 1 ROC curve analysis of oral glucose torlerance test values 0 ', 60' and 120' for prediction of L GA.

Discussion

In the present study, the incidence of LGA newborns was of 25.9%; in the literature, this incidence varies from 15 to 45%.[19,20]

Several studies have shown the influence of prepregnancy BMI, as well as of weight gain during pregnancy, on fetal weight.[21,22] Obesity is currently one of the major public

health problems, and its prevalence has been increasing among women of reproductive age. Obesity during pregnancy is associated with an increased risk of gestational hypertension, preeclampsia, fetal macrosomia, and with the need for cesarean section, in addition to the risk of developing GDM.[23] Among Brazilian pregnant women, a BMI $>$ 25 kg/m^2 was related to an increased risk of fetal macrosomia and GDM.[13]

Excessive birthweight is more frequent among obese mothers, regardless of the association with diabetes.[24] Maternal obesity is associated with reduced sensitivity to insulin and consequential hyperinsulinemia, which, incremented by high levels of triglycerides, favor excessive fetal growth, regardless of plasma glucose levels.[8] Some authors state that maternal obesity is the leading factor for the occurrence of LGA newborns. Black et al[23] reported a 21.6% frequency of LGA newborns among overweight or obese pregnant women without GDM, a percentage that rose to 23.3% when the factors obesity and GDM were combined, whereas the frequency of LGA newborns among women with normal weight and GDM was only 2.9%.

It is estimated that between 65 and 75% of the women with GDM are also overweight or obese.[23] In our sample, 72.4% of the women with GDM were overweight or obese before the pregnancy, and the percentage of LGA newborns was higher among these women, with obesity being an independent risk factor for LGA newborns after the adjusted analysis.

The risk for LGA newborns also appears to increase when WG is considered regardless of prior BMI.[19] Miao et al[25] found a higher incidence of macrosomia among pregnant women with EWG, as did Alberico et al,[26] who observed that EWG during pregnancy was significantly associated with macrosomia, with a 2.6-fold higher risk in comparison with the recommended WG.[25,26] Mastella et al[27] found that EWG during pregnancy was an independent risk factor for LGA newborns, and that WG during the 3rd trimester was also associated with LGA newborns. In the present study, EWG was not a risk factor for the birth of LGA newborns. The limited sample and possible errors in the self-reported prepregnancy weight may have altered the amount of gained weight.

Although the IOM guidelines for gestational WG are not specific for pregnant women with GDM, they are often applied to them. It is unknown whether the IOM recommendations are appropriate for pregnant women at increased risk of adverse outcomes, or if adjusting these guidelines for women with GDM could improve perinatal outcomes.[28] It can be assumed that women with GDM require more stringent WG recommendations because of the association of EWG and hyperglycemia and their potentially additive effects that lead to adverse outcomes, such as LGA newborns.[28]

Miao et al[25] found that IWG decreased the risk for LGA newborns. This study also showed that WG below that recommended by the IOM was a protective factor for the outcome of LGA newborns, but it is necessary to consider the small sample and the limited statistical power of this analysis.

Additionally, Mastella et al[27] found that both AWG and IWG decreased the risk for LGA newborns in pregnant women with GDM. On the other hand, Vesco et al[28] noted that WG below recommendations decreases LGA newborns, but increases the risk of SGA newborns. Futhermore, Wong et al[29] showed that \EWG was a predictive factor for LGA newborns; however, they noted that changing the IOM criteria to more stringent WG recommendations would not improve perinatal outcomes, including the percentage of macrosomic and LGA newborns.

With the increase of maternal obesity, development of lifestyle interventions may have the potential to improve adverse reproductive outcomes.[8] Wolff et al[30] showed that a simple goal-setting and support program, directed toward a dietary-induced limitation of WG in obese pregnancy, achieved very positive results, including a significant reduction in the fasting serum insulin concentration. In addition, preconceptional counseling of the overweight and obese woman, as well as lifestyle changes, may have the potential to improve adverse reproductive outcomes.[24] However, a meta-analysis that evaluated different dietary interventions in women with GDM did not observe reduction of LGA newborns among the groups studied.[31]

A previous history of macrosomia is often a risk factor for LGA newborns.[32] In the present sample, a history of macrosomia was a risk factor for LGA newborns. Heiskanen et al,[32] in a study comparing 886 pregnancies with macrosomic fetuses with 26,075 pregnancies with AGA fetuses, found a 3.1-fold higher risk of recurrence of macrosomia.[32] Nkwabong et al[33] also showed that a history of fetal macrosomia is a significant risk factor for the recurrence of macrosomia in subsequent pregnancies. Although a history of macrosomia is a nonmodifiable factor, it serves as a marker of major metabolic changes during pregnancy and, in these cases, health care providers should pay attention to potentially influential factors for excessive fetal growth that can be controlled.

With regard to blood glucose levels in the 3rd trimester, high fasting glucose level was an independent risk factor for LGA newborns. Legardeur et al[34] observed that fasting blood glucose $\geq$ 95 mg/dL doubled the risk for fetal macrosomia. Thus, adequate glycemic control throughout the pregnancy, through diet and/or insulin therapy, especially in the 3rd trimester, should be intense to reduce risks.

The occurrence of LGA newborns was significantly higher in the group of women with combined change in the OGTT (fasting + after the dextrose load), even after the multivariate analysis. Brankica et al[35] found that the combination of fasting blood glucose and blood glucose 1 hour after the glucose load in the OGTT was a predictor of occurrence of LGA newborns. Pregnant women exhibiting this combination may be considered at increased risk because of the fact that they have two distinct changes, altered fasting glucose and glucose intolerance, which suggests impairment in two different metabolic pathways associated with the disease, dysfunction of pancreatic β cells and insulin resistance.[36]

In the present study, the ROC curve analysis showed that plasma glucose 2 hours after the glucose load in the OGTT was a better predictor for LGA newborns. Silva et al have also identified high levels of plasma glucose at the 2-hour measurement in the OGTT as one of the major independent risk factors for LGA newborns.[19] Brankica et al[35] and Ouzilleau

et al[37] found high levels of fasting blood glucose to be better predictors, whereas Mello et al[38] showed that 1-hour blood glucose was the factor most closely associated with LGA newborns.[35,37,38]

Conclusion

The present study with pregnant women diagnosed with GDM showed that maternal prepregnancy obesity, history of macrosomia, combined change in the OGTT (fasting + after dextrose load), and high-fasting glycemic mean during the 3rd trimester were independent predictive factors for LGA newborns. Weight gain below that recommended by the IOM seems to be a protective factor for the occurrence of LGA newborns, and the need for specific recommendations for pregnant women with GDM may be suggested. However, more studies, with larger numbers of participants, are necessary to validate this finding. Maternal pregestational obesity and high-fasting glycemic mean in the 3rd trimester are modifiable factors, so preventive measures or therapeutic intervention can be implemented to minimize these risk factors. In general, retrospective studies present limitations related to the data obtained. Nonetheless, the present study highlights factors associated with LGA newborns of pregnant women with GDM in Brazil, which may be useful in the management of these patients during pregnancy and in preventing complications for the mothers and for the fetuses.

Collaborations

All of the authors contributed with the project and data interpretation, the writing of the article, the critical review of the intellectual content, and with the final approval of the version to be published.

Conflicts of Interests

The authors have no conflicts of interests to declare.

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