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MAYARA SILVA DOS SANTOS

FATORES PREDITIVOS DO PESO AO NASCER DE RECÉM-NASCIDOS DE MULHERES ADULTAS COM DIABETES MELLITUS PRÉ-GESTACIONAL

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Artigo apresentado ao Programa de Residência Multiprofissional em Saúde Perinatal da Maternidade Escola da Universidade Federal do Rio de Janeiro/UFRJ, como parte dos requisitos necessários à obtenção do título de Especialista Multiprofissional com ênfase em Nutrição na Saúde Perinatal.

Orientadora: Dra. Cláudia Saunders
Coorientadora: Me. Luciana da Cunha Bernardes Argenta

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UNIVERSIDADE FEDERAL DO RIO DE JANEIRO

CENTRO DE CIÊNCIAS DA SAÚDE

MATERNIDADE-ESCOLA

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FATORES PREDITIVOS PARA PESO AO NASCER DE RECÉM-NASCIDOS DE MÃES COM DIABETES MELLITUS TIPO 1 E TIPO 2

Artigo apresentado ao Programa de Residência Multiprofissional em Saúde Perinatal da Maternidade-Escola da Universidade Federal do Rio de Janeiro/UFRJ, como parte dos requisitos necessários à obtenção do título de Especialista Multiprofissional com ênfase em Nutrição na Saúde Perinatal.

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Cláudia Saunders

Dra. Cláudia Saunders – Presidente da banca

Luciana da Cunha Bernardes Argenta

Me. Luciana da Cunha Bernardes Argenta – Coorientador

Letícia Barbosa Gabriel da Silva

Me. Letícia Barbosa Gabriel da Silva - 1° Examinador

Natércia da Silva Rebello

Me. Natércia da Silva Rebello - 2° Examinador

INTRODUÇÃO

Atualmente é bem estabelecido na literatura a associação entre Diabetes Mellitus (DM) e o excesso de peso, principalmente relacionado ao DM tipo 2. As taxas de indivíduos com DM tipo 2 cresceram concomitantemente às taxas de excesso de peso na população. A ampliação da prevalência de DM nas últimas décadas e o impacto desse aumento no incremento da frequência de DM pré-gestacional de mulheres em idade fértil evidencia a importância de se evitar as consequências em curto prazo para mulheres com DM pré-gestacional, como cesárea de emergência e pré-eclâmpsia, e danos de curto e longo prazo para seus filhos, como maior risco de nascerem grandes para a idade gestacional, prematuridade, DM tipo 1 no início da infância, menor quociente de inteligência, transtornos do espectro autista e sobrepeso e obesidade em fase pré-escolar.

Sabe-se que o peso ao nascer é um preditor de comorbidades que exerce influência sobre a saúde do recém-nascido desde o período perinatal até a fase adulta, influenciando no maior risco de sobrepeso ou obesidade na infância, risco de DM tipo 1 e tipo 2 na infância e adolescência e aumento do risco de doenças cardiovasculares em adultos.

Os fatores modificáveis associados ao peso ao nascer são descritos na literatura, porém há carência de estudos em gestantes com DM pré-gestacional. A identificação dentre esses fatores, os modificáveis ainda no período inicial da gestação, é de grande importância, já que o feto dessas mães é exposto desde a fecundação a um ambiente uterino metabolicamente distinto quando comparado ao de gestantes sem comorbidades. Logo, faz-se necessário identificar esses fatores a fim de implementar medidas de intervenção na assistência pré-natal, e assim propiciar melhores resultados perinatais.

Nesta perspectiva, o estudo teve como objetivo identificar os fatores preditivos de peso ao nascer de recém-nascidos de mulheres adultas com DM pré-gestacional atendidas em uma maternidade pública do Rio de Janeiro.

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PREDICTIVE FACTORS OF WEIGHT AT BIRTH OF NEWBORNS OF ADULT WOMEN WITH PREGESTATIONAL DIABETES MELLITUS - A RETROSPECTIVE OBSERVATIONAL STUDY

Mayara Silva dos Santos [a], Luciana da Cunha Bernardes Argenta [b], Letícia Barbosa Gabriel da Silva [b,c], Karina dos Santos [b,c], Lenita Zajdenverg [b], Erlaine de Souza Gomes [c], Mariana Campos de Moraes [c], Cláudia Saunders [a,b,c]

[a] Multiprofessional Residency Program in Perinatal Health, Maternidade Escola, Universidade Federal do Rio de Janeiro (UFRJ), Rua das Laranjeiras, 180, Laranjeiras, CEP 22240-003 Rio de Janeiro, RJ, Brazil.

[b] Maternidade Escola, Universidade Federal do Rio de Janeiro (UFRJ), Rua das Laranjeiras, 180, Laranjeiras, CEP 22240-003 Rio de Janeiro, RJ, Brazil.

[c] Instituto de Nutrição Josué de Castro, Centro de Ciências da Saúde, Universidade Federal do Rio de Janeiro (UFRJ), Av. Carlos Chagas Filho, 373, bl. J 2°, andar, Cidade Universitária, CEP 21941.590 Rio de Janeiro, RJ, Brazil.

Corresponding author:
Mayara Silva dos Santos
Maternidade Escola
Universidade Federal do Rio de Janeiro
Rua das Laranjeiras, 180, Laranjeiras, Rio de Janeiro, RJ, 22240-003, Brazil.
Phone: 55 (21) 99114-6578
E-mail: mayarasantos0794@gmail.com; mayarassants1@gmail.com.

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PREDICTIVE FACTORS OF WEIGHT AT BIRTH OF NEWBORNS OF ADULT WOMEN WITH PREGESTATIONAL DIABETES MELLITUS - A RETROSPECTIVE OBSERVATIONAL STUDY

ABSTRACT

Aims: To identify predictive factors of birth weight (BW) of newborns of women with pregestational diabetes mellitus (DM).

Methods: Retrospective observational study with data from pregnant women who started prenatal nutritional monitoring up to 28 weeks, single pregnancy, and BW information. Quantitative variables were analyzed, and mean and standard deviation (SD) measures were calculated. Predictive factors were identified using multivariate linear regression.

Results: Eighty-six pregnant women were analyzed, 50% were diagnosed with type 1 DM, 46.5% with type 2 DM, and 3.5% with unclassified DM; 41% were mixed black and white, 35.6% had overweight and 33.3% had pregestational obesity. The mean BW was 3313.9g (SD=696.08). The predictive factors identified were: in the model I -gestational weight gain (GWG) at the 3rd trimester (ß=60.42; p=0.04), and gestational age at delivery (ß=194.03; p<0.001); in model II - gestational weight gain (GWG) at the 3rd trimester (ß=58.73; p=0.04), and gestational age at delivery (ß=226.55; p<0.001); in model III -time of diagnosis of DM (ß=28.52; p=0.01, gestational weight gain (GWG) at the 3rd trimester (ß=68.86; p=0.02), and gestational age at delivery (ß=232.99; p<0.001); adjusted by time of diagnosis of DM and 1rd, 2nd, and 3rd trimester.

Conclusion: The results indicate that weight gain in the 3rd trimester and gestational age at delivery explain the BW of newborns of women with pregestational DM. The results contribute to the review of the prenatal routines of this group of pregnant women, as they are modifiable variables.

Keywords: Pregestational Diabetes Mellitus; Birth Weight; Gestational Weight Gain; Prenatal Care.

1. INTRODUCTION

According to the International Diabetes Federation (IDF, 2021), the worldwide prevalence of individuals aged between 20 and 79 years with Diabetes Mellitus (DM) was 10.5% in 2021, with a projection for the year 2045 of 12.2% [1]. In addition, 16.7% of newborns worldwide were born from mothers affected by hyperglycemia during pregnancy, considering pregnant women aged between 20 and 49 years, and the prevalence of pregestational DM in pregnant women aged 10.6% of DM cases during pregnancy [2]. In 2019, the National Health Survey of Brazil described that 15.9% of adults over 18 years of age reported a diagnosis of DM [3]. In another national study also from 2019, it was shown that women have a higher prevalence of DM when compared to men (7.8% vs. 7.1%, respectively) and there was an inverse association with the level of education [4].

The association between type 2 DM and excess weight is well established in the literature, increasing the risk as the body mass index (BMI) increases [5, 6]. The rates of individuals with type 2 DM increased concomitantly with the rates of overweight and obesity in the population. In Brazil, the prevalence of obesity in adults jumped 72% between 2006 and 2019, from 11.8% to 20.3%, respectively, and among women, 74.6% are overweight or obese (53.9% and 20.7%, respectively) [4].

The increase in the prevalence of DM in recent decades and the impact of this increase in the frequency of pregestational DM in women of childbearing age [7] highlights the importance of avoiding short-term consequences for women with pregestational DM, such as cesarean section. and preeclampsia, and short-term and long-term harm to their children, such as the increased risk of large-for-gestational-age (LGA) newborns, prematurity [8], increased risk of type 1 DM in early childhood [9], lower IQ, higher risk of autism spectrum disorders [10] and higher risk of overweight and obesity in preschool-age [11].

It is known that birth weight (BW) is a predictor of comorbidities that influences the health of the newborn from the perinatal period to adulthood [12], such as for overweight or obesity in childhood [13], risk types 1 and 2 DM in childhood and adolescence [14; 15] and increased risk of cardiovascular disease in adults [16].

A study that analyzed the effects of maternal blood glucose on the BW of the children of 472 women without DM found that the duration of pregnancy, gender of the newborn, pregestational BMI, and gestational weight gain (GWG) influenced this outcome, being impaired glucose tolerance (defined as altered fasting or post-oral glucose tolerance test result) is also an independent factor on BW [17]. Hu et al. when investigating the association of BW and DM in adults, found that both low weight (BW < 2,500 g) and macrosomia (BW > 4,000 g) are associated with the risk of type 2 DM in adulthood in women [18], demonstrating the contribution to the intergenerational perpetuation of the disease if birth weight is not controlled.

Some variables, such as GPG or maternal blood glucose, can be modified with early prenatal care, supported by a multidisciplinary team, including nutritional monitoring. Thus, obstetric and perinatal outcomes can be favored [19], reducing low birth weight [20]. In pregnant women with gestational diabetes mellitus (GDM), obesity, or hypertension, the adoption of a healthy diet can influence modifiable factors such as glycemic control, the incidence of preeclampsia, and birth weight-related factors such as fetal macrosomia and LGA [21].

Lemaitre et al. in a retrospective study of French pregnant women with type 1 DM, showed that levels of glycated hemoglobin in the 1st. trimester >6.5% were associated with a greater chance of the combined outcome - prematurity large for gestational age (LGA), small for gestational age (SGA), or cesarean delivery (OR 2.81; 95% CI 1.01-7, 86) and an increased rate of LGA (OR 2.20; 95% CI 1.01-4.78). Reinforcing the importance of glycemic control in early pregnancy to optimize perinatal outcomes and reduce the risk of LGA [22].

The modifiable factors associated with BW are described in the literature, but there is a lack of studies on pregnant women with pregestational DM. From this perspective, the study aimed to identify the predictive factors of BW in newborns of adult women with pregestational DM treated at a public maternity hospital in Rio de Janeiro.

2. MATERIAL AND METHODS

2.1. Study design

This is an observational, prospective study, nested within a randomized clinical trial (Rebec - RBR-4tbgv6), carried out with data from pregnant women and their children attended at a public maternity hospital in Rio de Janeiro, Rio de Janeiro - Brazil, in the period of November/2016 to March/2020.

2.2. Ethical Issues

The present study used data from the research "Effect of the DASH Diet on the Perinatal Outcome of Pregnant Women with Diabetes Mellitus" (Rebec-RBR-4tbgv6), a controlled clinical trial to test the adapted DASH Diet on the perinatal outcome of Brazilian adult pregnant women with DM. The larger study was approved by the Research Ethics Committee (CEP) of Maternity School/UFRJ on 07/31/15 (CAAE 47335515.0.0000.5275).

Likewise, the present study was approved by the Ethics and Research Committee of Maternity School/UFRJ on 11/17/2021 (CAAE 52970921.6.0000.5275).

2.3. Eligibility Criteria

Inclusion criteria were: adult pregnant women (age >18 years at conception), diagnosis of pregestational DM (Types 1 and 2 or unclassified), singleton pregnancy, prenatal care at the maternity unit studied beginning at gestational age (GA) < 28 weeks (diagnosed by ultrasound), non-smokers, non-users of alcoholic beverages and with the availability of information on birth weight in medical records. Exclusion criteria were: diagnosis of other chronic diseases (except obesity) and women with DM complications, such as diabetic retinopathy and nephropathy.

2.4. Data collection and definition of variables

Data were obtained from medical records. In the original study, all pregnant women were followed up during prenatal care by a multidisciplinary team (physicians, psychologists, nurses, and nutritionists). During the consultations, a complete nutritional assessment was carried out and an individualized food plan was developed, based on nutritional needs and the recommended GWG schedule at each stage of pregnancy, according to pregestational BMI (IOM, 2009) [23].

In the nutritional assessment, pregestational weight (kg) was considered as referring to the maximum period of two months before conception or obtained up to the 14th gestational week. Height (m) was measured at the first prenatal consultation and gestational weight (kg) was measured at all prenatal consultations, using a Filizola® scale and a stadiometer attached to the scale. The measurements were taken by trained professionals [24]. For the classification of pregestational BMI, the following cutoff points were used: low weight (<18.5 kg/m²), adequate (18.5-24.99 kg/m²), overweight (25-29.99 kg/m²), m²) and obesity (≥30.0 kg/m^2) [25]. To assess the adequacy of the total GWG, the total gain ranges of 12.5–18 kg for underweight BMI, 11.5–16 kg for adequate BMI, 7–11.5 kg for overweight BMI, and 5-9 were considered. kg for obesity BMI [23].

Fasting glucose < 95 mg/dL, 1h postprandial < 140 mg/dL, and 2h postprandial < 120 mg/dL were considered as parameters for assessing glycemic control and average values per quarter were considered.

For the analysis of newborn data, weights <2500 g were classified as having low birth weight (LBW) and fetal macrosomia when the weight was ≥4000 g [26]. The GA at birth was evaluated according to ultrasonography in the first trimester, and the newborns were classified as preterm (<37 weeks), the term (37-42 weeks), and post-term (>42 weeks) [27]. The classification of weight for GA at birth (by gender) was performed considering as small for gestational age (SGA) BW < Z-score -2 for gestational age; suitable for gestational age (AGA) between Z-score -2 and +2; and large for gestational age (LGA) >Z-score +2 according to the INTERGROWTH-21st curves [28].

2.5. Variables analyzed

The dependent variable was BW in grams (considering the first weight measured shortly after birth, measured by a pediatrician using a pediatric Welmy infant scale®).

The independent variables and variables analyzed for sample characterization were: maternal age (years), pregestational BMI (kg/m^2) - considering pregestational weight (kg) and height (m),- number of pregnancies, abortions, and deliveries, number of prenatal care consultations and prenatal nutritional assistance, gestational age at the first prenatal consultation (weeks of gestation), time of DM diagnosis (years), type of delivery, maternal and fetal complications, skin color, marital status, occupation, education level, sanitation conditions in the housing (garbage collection, piped water, sewage network), and number of people in the family. As for the newborns, the characterization variables collected at delivery were: sex, conditions at birth, complications, gestational age at delivery, head circumference, length, and Apgar score. As for the type of pregestational DM, the variables were DM Type 1, DM Type 2, and unclassified DM.

Independent variables tested in linear regression models were selected for biological plausibility or $p<0.20$ in bivariate analysis.

2.6. Statistical treatment of data

In the exploratory data analysis of the quantitative variables, the means and standard deviation (SD) were calculated as measures of central tendency and dispersion, respectively.

Bivariate and multivariate linear regression were performed. As an inclusion criterion in the multivariate model, variables with $p<0.20$ were selected in the bivariate analysis, and for biological plausibility, $p<0.05$ was adopted as the criterion for permanence in the final model to identify the variables that predict birth weight. All analyzes were performed using SPSS statistical software for Windows version 21.0.

3. RESULTS

The initial study sample consisted of 86 pregnant women with pregestational DM, with a mean age of 30 years (SD=6.59), 43 with Type 1 DM (50%), 40 with Type 2 DM (46, 5%), and 3 with unclassified DM (3.5%).

According to the pregestational maternal nutritional status, 35.6% were overweight and 33.3% had obesity. Most women had inadequate GWG, with 46.9% above the recommendations and 13.6% below (Table 1).

Regarding sociodemographic conditions, most women had a paid job during pregnancy (64.7%; n=55), lived with a partner (83.5%; n=71), and most had 3 or fewer people in the family composition. (71.6%; n=58), completed high school (67.5%; n=58), lived in housing with adequate sanitation conditions (96.4%; n=80), had had black or mixed black and white (68.7%; n=57), had no associated comorbidities (69.2%; n=54) and had a cesarean delivery (87.7%; n=71) (Table 1).

All pregnant women used insulin during pregnancy. As for maternal complications, the most frequent were Hypertensive Syndromes of Pregnancy (22.8%; n=18), preeclampsia (15.2%; n=12), and gestational hypertension (7.6%; n=8). Regarding prenatal consultations, the pregnant women had an approximate average of 11 consultations (SD=3.97). The average number of consultations with the nutritionist was approximately 5 (SD=1.74).

The mean time of DM diagnosis in these women was 8.35 years (SD=7.00). Regarding glycemic control, 87.2%, 79%, and 66.1% of pregnant women had inadequate control in the three trimesters of pregnancy, respectively. The mean pre-pregnancy BMI was 28.20 kg/m² (SD=5.10) and the mean total GWG was 12.37 kg (SD=5.43, Table 2).

Regarding newborns, the mean BW was 3313.93g (SD=696.08), the mean gestational age at birth was 37.13 weeks (SD=1.47), the mean length was 47.47 cm (SD=3.36) and the mean head circumference was 34.19 cm (SD=2.25, Table 2). Most were born AGA (n=42, 55.3%), followed by LGA (n=27, 35.5%) and SGA (n=7, 9.2%), 21.6% (n=19) were classified as macrosomic, 10.2% (n=9) were LBW and 25.9% were preterm (Table 2).

The predictive factors identified were: in the model I -gestational weight gain (GWG) at the 3rd trimester ($ß=60.42$; $p=0.04$), and gestational age at delivery ($ß=194.03$; $p<0.001$); in model II - GWG at the 3rd trimester ($ß=58.73$; $p=0.04$), and gestational age at delivery ($ß=226.55$; $p<0.001$); in model III -time of diagnosis of DM ($ß=28.52$; $p=0.01$), GWG at the 3rd trimester ($ß=68.86$; $p=0.02$), and gestational age at delivery ($ß=232.99$; $p<0.001$). All models were fitted for the glycated hemoglobin of the 1st, 2nd, and 3rd trimesters (Table 3).

4. DISCUSSION

This study shows that the predictive variables of BW of newborns born to women with pre-gestational DM were the total GWG in the 3rd trimester and the time of diagnosis of DM, adjusted for the gestational age at delivery. These results corroborate what the scientific literature currently discusses about the perinatal outcomes of pregnancies accompanied by DM.

A Brazilian study that analyzed data from 827 adult healthy pregnant women found that the predictors of BW were maternal age, total GWG, pregestational BMI, and the number of prenatal consultations [29]. In Silva et al. 283 Brazilian women with GDM were evaluated and the gestational age at delivery, the total GWG in the 1st and 3rd trimesters, fasting glucose in the 1st trimester, postprandial glucose in the 3rd trimester, and pregestational BMI were found to be predictive of BW [30].

As in these studies and our results, the GWG shows an important influence on BW, being a modifiable factor with intervention during prenatal care aiming at control during pregnancy. Similar results to the present study were found in the study by Mastela et al. [31], a Brazilian cohort of 474 pregnant women with GDM, which sought to evaluate the influence of GWG on BW and found that for each kilogram of weight gained in the 3rd trimester, the risk of LGA increased by 10%, regardless of the total GWG, remaining an independent factor for this outcome even with pharmacological treatment and glycated hemoglobin in the 3rd trimester, with the GWG having an insufficient or adequate protective effect on the risk of LGA when compared to the GWG above the recommendations.

In the study by Lemaitre et al. with French pregnant women with type 1 DM, they observed that the concentrations of glycated hemoglobin in the 1st. quarter > 6.5% were associated with a higher chance of the combined outcome, including an increased rate of LGA. In the study, the median (interquartile range) of body mass index (kg/m2) was 23.5 (21.3-26.7), suggesting that most French pregnant women had a prepregnancy body mass index adequate. In the present study, the rates of glycated hemoglobin during pregnancy did not influence the BW. We emphasize that in our study, 69% of the pregnant women were overweight or obese pre-pregnancy and 46.9% had excessive weight gain, which may have favored the relationship with BW [22].

In another Brazilian multicenter cohort comprising 2,244 pregnant women with GDM, it was found a higher risk of preterm birth (RR 1.70, 95% CI 1.08–2.70) and cesarean section (RR 1.21, 95% CI 1, 03-1,44) when excessive GWG occurred in the 3rd trimester [32], emphasizing the importance of nutritional monitoring throughout pregnancy and especially after the 28th week, where GWG may be more evident. Appropriate GWG programming combined with nutritional intervention and good patient adherence to nutritional therapy can promote adequate GWG and glycemic control, assisting in the positive evolution of BW in the newborn of women with pregestational DM, in addition to reducing the risk of morbidity. and perinatal mortality [19, 33].

The relationship between better adherence to nutritional guidelines and glycemic control combined with a minimum schedule of appointments with a nutritionist reinforces the importance of nutritional monitoring at this stage of life, especially in pregnancies with DM [34, 35]. The variables that most explain PN are those related to maternal nutritional status [36] and prenatal nutritional care can influence the effect on these variables. In the study by Oliveira et al. carried out with pregnant women with DM, it was found that nutritional monitoring with an average of 5 consultations contributed to the reduction of postprandial glycemia. And adherence to the guidelines improved with the increase in the number of individual consultations with the nutritionist [37].

The beginning of pregnancy with inadequate nutritional status can worsen the perinatal outcomes of women with DM, having more significant deleterious effects when the GWG is excessive, leading to a greater risk of LGA babies regardless of pregestational BMI, glycated hemoglobin, smoking, or ethnicity [38, 39].

In this study, it was observed that the majority of pregnant women had a GWG above the recommendation (46.9%), considering the pregestational BMI categories according to the recommendations of the Institute of Medicine [23]. Zhao et al. analyzed 1,617 Chinese women without comorbidities and observed that the higher the pre-pregnancy BMI, the greater the proportion of pregnant women with a GWG above the guidelines, corroborating this study and showing that a GWG above the recommended in women with overweight and obesity may be associated with fetal macrosomia ($p=0.005$) and with LGA newborn ($p=0.004$). On the other hand, the GWG below the recommendations can be associated with LBW ($p=0.027$) and with SGA newborns ($p=0.011$) and even in women with adequate pre-pregnancy BMI, the GWG above the recommendations can also be associated with macrosomia and with LGA newborns [40].

Brazilian studies, such as the one by Mastroeni et al. which analyzed 435 women without comorbidities, found that pregestational weight in BMI ranges greater than 25 kg/m² and excessive GWG independently influenced the occurrence of LGA newborns [41]. Parellada et al. analyzed 142 pregnant women and observed that BW was almost 0.5 kg higher in the children of women with type 2 DM and excessive GWG when compared to women with type 2 DM and non-excessive GWG, with more LGA babies being born in the group with excessive GWG ($p < 0.001$), in addition to higher rates of compound perinatal morbidity ($p= 0.047$) and neonatal hypoglycemia ($p= 0.03$) [39].

The results of the present study showed that most babies were born AGA (n=42; 55.3%), followed by LGA babies (n=27; 35.5%) according to INTERGROWTH-21st and 21.6% of babies were born macrosomic (n=19), considering BW ≥ 4,000 g.

It is known that the association of DM with several negative outcomes in pregnancy is well described in the literature, one of the most cited being fetal macrosomia [42]. In pregnant women with pregestational DM in Uruguay, a prevalence of 14.5% of macrosomia (n=304) was found, evidencing this diagnosis as an independent risk factor for this outcome, whereas women with pregestational DM had up to 1 .7 times greater risk of macrosomia [43].

In developed countries, higher rates of macrosomia than in this study were observed when analyzing pregnancies accompanied by pregestational DM and GDM. In a cohort study carried out in Sweden with 308 pregnant women, the prevalence of macrosomia was 39% among women with type 1 DM and 22% among women with type 2 DM, and the prevalence of LGA babies among the same groups of type 1 and type 2 DM was 50% and 23%, respectively [44]. Therefore, even though lower percentages were observed in studies, the rates found in this study are lower than in developed countries, showing that even though it is possible to improve these goals, the results found are satisfactory and may be related to the specialized assistance received by this group. in the prenatal care at the study site which, supported by a specialized multidisciplinary team, favors better adherence and adjustments of the treatment.

Regarding the time of diagnosis of pregestational DM, although this is a non-modifiable predictive factor found in our study, type 1 and type 2 DM can be independently associated with a higher risk of preeclampsia, congenital anomalies, prematurity, macrosomia, perinatal mortality, among other unfavorable outcomes, increasingly demonstrating the need for preconception care to control the disease, since inadequate treatment of DM worsens the metabolic state and in the long term can reduce the possibilities of improving perinatal outcomes in case of pregnancy [42, 45].

Regarding the number of prenatal consultations, the average of 11 consultations observed in this study was higher than that recommended by the Ministry of Health, which guides a minimum of 6 consultations [26] and that found in the last National Survey of Demographics and Child Health and Women, where in the Southeast region, 88.2% of pregnant women had 6 or more consultations on average [46]. This data may be related to better outcomes, since the number of prenatal consultations was previously considered in other studies as a predictor of BW [29], improving this outcome and also preventing other negative complications in pregnant women with DM, such as premature birth, cesarean section and preeclampsia [47].

In addition, it is necessary to highlight that socio-demographic characteristic was not a predictor of BW in the present study, thus evidencing the importance of prenatal care at this stage of life, for the control of adequate GWG during pregnancy, to avoid negative outcomes associated with DM, since excessive GWG is detrimental to DM and GDM control [39, 48].

As a limitation of the study, we can point out the lack of information on some data and, in addition, the study was carried out in a single maternity hospital in the city of Rio de Janeiro, however, the maternity receives pregnant women on demand and also through the National Regulatory System, that is, pregnant women assisted in the Unified Health System have access to prenatal care at the unit.

Given the aspects observed, although the present study did not establish a correlation between the number of prenatal consultations and the PN, the rate of macrosomia found was lower than the rates found in studies of populations of pregnant women with DM in developed countries and this may be related to a longer and more effective follow-up in the assistance provided by the multidisciplinary team specialized in prenatal care. As for GPG control in the 3rd trimester, this proved to be an important modifiable factor for BW control, demanding attention to this specific phase accompanied by nutritional assistance to control this variable.

The best predictors of BW were weight gain in the 3rd trimester, gestational age at delivery, and time of diagnosis of DM. These results point to the need to review prenatal routines and formulate tools capable of integrating care for this group, with prenatal care and nutritional monitoring starting early in pregnancy, aiming to positively influence the PN of children of women with pregestational DM.

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TABLES

Table 1. Anthropometric, sociodemographic, and clinical characteristics of pregnant women with DM. A public maternity hospital in Rio de Janeiro, RJ, Brazil (2016-2020).

Maternal characteristics	***% (n)***
Pregestational nutritional status (BMI/kg²) (n=87)	
Low weight	0.0 (0)
Eutrophy	31.0 (27)
Overweight	35.6 (31)
Obesity	33.3 (29)
Adequacy of weight gain (n=81)	
Below	13.6 (11)
Adequate	39.5 (32)
Above	46.9 (38)
Occupation (n=85)	
Performs paid activity	64.7 (55)
Housewife/ does not work	35.3 (30)
Marital status (n=85)	
Lives with partner	83.5 (71)
Single, divorced or widowed	16.5 (14)
Number of people in the family (n=81)	
≤ 3 people	71.6 (58)
> 3 people	28.4 (23)
Instruction level (n=86)	
Incomplete high school	32.5 (28)
Completed high school or higher	67.5 (58)
Housing sanitation conditions (n=83)[a]	
Inadequate	3.6 (3)
Adequate	96.4 (80)
Skin color (n=83)	
White	31.3 (26)
Mixed black and white	41.0 (34)
Black	27.7 (23)

DM type (n=86)	
Type 1 diabetes	50.0 (43)
Type 2 diabetes	46.5 (40)
Unclassified DM	3.5 (3)
Presence of comorbidities (n=78)	
With comorbidities	30.8 (24)
No comorbidities	69.2 (54)
Type of delivery (n=81)	
Normal	12.3 (10)
Cesarean	87.7 (71)

Subtitle: DM - Diabetes Mellitus, [a] Housing sanitation conditions -adequate conditions when there was running water, regular garbage collection and sewage network and inadequate conditions when one of the services was absent

TABLE 2

Table 2. Means and standard deviation of maternal and newborn characteristics of pregnant women with pregestational DM. A public maternity hospital in Rio de Janeiro, RJ, Brazil (2016-2020).

Maternal and newborn characteristics	***n***	***Mean***	***Standard Deviation (SD)***
Maternal and newborn variables			
Maternal age (years)	87	30.41	6.59
DM diagnosis time (years)	86	8.35	7.00
Gestational age at delivery by ultrasound (weeks)	81	37.13	1.47
Birth weight (g)	81	3313.93	696.08
Length at birth (cm)	77	47.47	3.36
Head circumference at birth (cm)	74	34.19	2.25
Obstetric and clinical variables			
Number of pregnancies	86	2.36	1.50
Number of deliveries	86	0.87	1.02
Number of abortions	86	0.52	0.87
Number of prenatal care consultations	86	11.01	3.97
Number of prenatal consultations with a nutritionist	87	5.17	1.74
1st-trimester fasting blood glucose (mg/dL)	53	137.61	60.39
2nd-trimester fasting blood glucose (mg/dL)	71	119.02	42.08
3rd-trimester fasting blood glucose (mg/dL)	63	114.45	115.57
1st-trimester glycated hemoglobin (%)	73	7.16	1.44
2st-trimester glycated hemoglobin (%)	73	6.60	1.28
3st-trimester glycated hemoglobin (%)	56	6.45	0.76
Maternal anthropometric variables			
1nd-trimester gestational weight gain (kg)	64	2.54	3.15
2nd-trimester gestational weight gain (kg)	64	5.52	2.50
3rd-trimester gestational weight gain (kg)	77	4.76	2.72
Total gestational weight gain (kg)	81	12.37	5.43
Pre-pregnancy BMI (kg/m²)	87	28.20	5.10
Subtitle: DM - Diabetes Mellitus; BMI - Body Mass Index.			

Table 3. Result of multiple linear regression of predictive factors of birth weight of newborns of pregnant women with pregestational diabetes mellitus. A public maternity hospital in Rio de Janeiro, RJ, Brazil (2016-2020).

Variables	**ß gross**	**p**	**CI (95%)**	**ß adjusted**	**p**	**CI (95%)**
The model I - 1st-trimester						
Time of diagnosis of Diabetes Mellitus (years)	24.10	0.031	2.25 – 45.96	19.39	0.07	-1.95 - 40.733
Total weight gain in the 3rd trimester (kg)	79.10	0.05	24.26 – 133.94	60.42	**0.04**	3.72- 117.11
Gestational age at delivery by ultrasound (weeks)	237.41	<0.001	146.29 – 328.53	194.03	**<0.001**	91.74 – 296.32
1st-trimester glycated hemoglobin	-110.39	0.064	-227.60-6.80	-21.36	0.70	-134.13 – 91.40
The Model II - 2st-trimester						
Time of diagnosis of Diabetes Mellitus (years)	24.10	0.031	2.25 – 45.96	21.60	0,05	-0.53 – 43.74
Total weight gain in the 3rd trimester (kg)	79.10	0.05	24.26 – 133.94	58.73	**0.04**	119,138-333,97
Gestational age at delivery by ultrasound (weeks)	237.41	<0.001	146.29 – 328.53	226,555	**<0.001**	2,378 – 115.09
2 nd-trimester glycated hemoglobin	-95.72	0.28	-270.01-78.57	55,835	0,53	-119,044 – 230.71
The Model III -3rd trimester						
Time of diagnosis of Diabetes Mellitus (years)	24.10	0.031	2.25 – 45.96	28.52	**0.01**	6.36-50.68

Total weight gain in the 3rd trimester (kg)	79.10	0.05	24.26 – 133.94	68.86	**0.02**	10.45-127.28
Gestational age at delivery by ultrasound (weeks)	237.41	<0.001	146.29 – 328.53	232.99	**<0.001**	134.83-331.16
3 rd-trimester glycated hemoglobin	-95.29	0.37	-306.43-115.86	0.50	0.38	-0.63-1.63

Adjusted for: gestational age at delivery, time of diagnosis of Diabetes Mellitus, total weight gain in the 3rd trimester, and glycated hemoglobin. CI- confidence interval

Diabetes Research and Clinical Practice

PREDICTIVE FACTORS OF WEIGHT AT BIRTH OF NEWBORNS OF ADULT WOMEN WITH PREGESTATIONAL DIABETES MELLITUS - A RETROSPECTIVE OBSERVATIONAL STUDY

--Manuscript Draft--

Manuscript Number:	
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Corresponding Author:	Mayara Silva dos Santos Federal University of Rio de Janeiro Maternity School Rio de Janeiro, Rio de Janeiro BRAZIL
First Author:	Mayara Silva dos Santos
Order of Authors:	Mayara Silva dos Santos
Abstract:	Aims: To identify predictive factors of birth weight (BW) of newborns of women with pregestational diabetes mellitus (DM).Methods: Retrospective observational study with data from pregnant women who started prenatal care up to 28 weeks, singleton pregnancy and BW information. Quantitative variables, mean and standard deviation (SD) were analyzed. Predictive factors were identified using multivariate linear regression.Results: Eighty-six pregnant women were analyzed, 50% with type 1 DM, 46.5% with type 2 DM, and 3.5% with unclassified DM; 68.9% were overweight or obese pregestational. The mean BW was 3313.9g (SD=696.08). The predictive factors identified in the models were: I - gestational weight gain (GWG) in the 3rd trimester (ß=60.42; p=0.04) and gestational age (GA) at delivery (ß=194.03; p<0.001); II - GWG in the 3rd trimester (ß=58.73; p=0.04) and GA at delivery (ß=226.55; p<0.001); III - time since DM diagnosis (ß=28.52; p=0.01, GWG in the 3rd trimester (ß=68.86; p=0.02) and GA at delivery (ß =232.99; p<0.001); adjusted for time since DM diagnosis and 1st, 2nd and 3rd trimester.Conclusion: The results indicate that GWG in the 3rd trimester and GA at delivery explain the BW. The results contribute to the review of the prenatal routines of this group, as they are modifiable variables
Suggested Reviewers:	Eliane Rosado Federal University of Rio de Janeiro elianerosado@nutricao.ufrj.br
	Melanie Rodacki Federal University of Rio de Janeiro melanierodacki@gmail.com
	Lívia Itajahy liviaitajahy@gmail.com
	Carlos Antônio Negrato carlosnegrato@uol.com.br
	Karina Bilda karinabilda@gmail.com
Opposed Reviewers:	

Rio de Janeiro, December, 29th, 2022.

Dear Editors,

Please find enclosed the manuscript entitled "**Predictive factors of weight at birth of newborns of adult women with pregestational Diabetes Mellitus - a Retrospective Observational Study"** which we are submitting for your appreciation in order to be published in the **Diabetes Research and Clinical Practice.**

The authors – Mayara Silva dos Santos, Luciana da Cunha Bernardes Argenta, Letícia Barbosa Gabriel da Silva, Karina dos Santos, Lenita Zajdenverg, Erlaine de Souza Gomes, Mariana Campos de Moraes and Cláudia Saunders from the Research Group in Maternal's and Child's Health (Grupo de Pesquisa em Saúde Materna e Infantil – GPSMI, http://dgp.cnpq.br/dgp/espelhogrupo/3232947737128189) from Federal University of Rio de Janeiro, Brazil - declare that the article is original and that its content has not been published in whole or in part and will not be submitted for publication elsewhere without the consent of the Diabetes Research and Clinical Practice. I declare that the manuscript has been read and approved by all authors.

Santos MS and Saunders C designed and planned the study; Santos MS, Argenta LCB, Silva LBG, Santos K, Zajdenverg L, Gomes ESG, Moraes MC and Saunders C collected the data; Santos MS, Argenta LCB, Silva LBG and Saunders C analysed the data; and Santos MS, Argenta LCB, Silva LBG, Santos K, Zajdenverg L, Gomes ESG, Moraes MC and Saunders C participated in the writing and revision of the final version of the manuscript. We also certify that the research project was approved by the Research Ethics Committee with Human Beings, ceded at the Maternity School of the State University of Rio de Janeiro. The authors declare none conflict of interest.

We would be delighted if this manuscript could be considered for publication in Diabetes Research and Clinical Practice, and we hope that we have met all formatting recommendations. We are available for any clarification.

Yours sincerely,

The authors.

PREDICTIVE FACTORS OF WEIGHT AT BIRTH OF NEWBORNS OF ADULT WOMEN WITH PREGESTATIONAL DIABETES MELLITUS - A RETROSPECTIVE OBSERVATIONAL STUDY

Mayara Silva dos Santos [a], Luciana da Cunha Bernardes Argenta [b], Letícia Barbosa Gabriel da Silva [b,c], Karina dos Santos [b,c], Lenita Zajdenverg [b], Erlaine de Souza Gomes [c], Mariana Campos de Moraes [c], Cláudia Saunders [a,b,c]

[a] Multiprofessional Residency Program in Perinatal Health, Maternidade Escola, Universidade Federal do Rio de Janeiro (UFRJ), Rua das Laranjeiras, 180, Laranjeiras, CEP 22240-003 Rio de Janeiro, RJ, Brazil.
[b] Maternidade Escola, Universidade Federal do Rio de Janeiro (UFRJ), Rua das Laranjeiras, 180, Laranjeiras, CEP 22240-003 Rio de Janeiro, RJ, Brazil.
[c] Instituto de Nutrição Josué de Castro, Centro de Ciências da Saúde, Universidade Federal do Rio de Janeiro (UFRJ), Av. Carlos Chagas Filho, 373, bl. J 2°, andar, Cidade Universitária, CEP 21941.590 Rio de Janeiro, RJ, Brazil.

Corresponding author:
Mayara Silva dos Santos
Maternidade Escola
Universidade Federal do Rio de Janeiro
Rua das Laranjeiras, 180, Laranjeiras, Rio de Janeiro, RJ, 22240-003, Brazil.
Phone: 55 (21) 99114-6578
E-mail: mayarasantos0794@gmail.com; mayarassants1@gmail.com.

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PREDICTIVE FACTORS OF WEIGHT AT BIRTH OF NEWBORNS OF ADULT WOMEN WITH PREGESTATIONAL DIABETES MELLITUS - A RETROSPECTIVE OBSERVATIONAL STUDY

ABSTRACT

Aims: To identify predictive factors of birth weight (BW) of newborns of women with pregestational diabetes mellitus (DM).

Methods: Retrospective observational study with data from pregnant women who started prenatal care up to 28 weeks, singleton pregnancy and BW information. Quantitative variables, mean and standard deviation (SD) were analyzed. Predictive factors were identified using multivariate linear regression.

Results: Eighty-six pregnant women were analyzed, 50% with type 1 DM, 46.5% with type 2 DM, and 3.5% with unclassified DM; 68.9% were overweight or obese pregestational. The mean BW was 3313.9g (SD=696.08). The predictive factors identified in the models were: I - gestational weight gain (GWG) in the 3rd trimester (ß=60.42; p=0.04) and gestational age (GA) at delivery (ß=194.03; p<0.001); II - GWG in the 3rd trimester (ß=58.73; p=0.04) and GA at delivery (ß=226.55; p<0.001); III - time since DM diagnosis (ß=28.52; p=0.01, GWG in the 3rd trimester (ß=68.86; p=0.02) and GA at delivery (ß =232.99; p<0.001); adjusted for time since DM diagnosis and 1st, 2nd and 3rd trimester.

Conclusion: The results indicate that GWG in the 3rd trimester and GA at delivery explain the BW. The results contribute to the review of the prenatal routines of this group, as they are modifiable variables.

Keywords: Pregestational Diabetes Mellitus; Birth Weight; Gestational Weight Gain.

1. INTRODUCTION

According to the International Diabetes Federation (IDF, 2021), the worldwide prevalence of individuals aged between 20 and 79 years with Diabetes Mellitus (DM) was 10.5% in 2021, with a projection for the year 2045 of 12.2% [1]. In addition, 16.7% of newborns worldwide were born from mothers affected by hyperglycemia during pregnancy, considering pregnant women aged between 20 and 49 years, and the prevalence of pregestational DM in pregnant women aged 10.6% of DM cases during pregnancy [2]. In 2019, the National Health Survey of Brazil described that 15.9% of adults over 18 years of age reported a diagnosis of DM [3]. In another national study also from 2019, it was shown that women have a higher prevalence of DM when compared to men (7.8% vs. 7.1%, respectively) and there was an inverse association with the level of education [4].

The association between type 2 DM and excess weight is well established in the literature, increasing the risk as the body mass index (BMI) increases [5, 6]. The rates of individuals with type 2 DM increased concomitantly with the rates of overweight and obesity in the population. In Brazil, the prevalence of obesity in adults jumped 72% between 2006 and 2019, from 11.8% to 20.3%, respectively, and among women, 74.6% are overweight or obese (53.9% and 20.7%, respectively) [4].

The increase in the prevalence of DM in recent decades and the impact of this increase in the frequency of pregestational DM in women of childbearing age [7] highlights the importance of avoiding short-term consequences for women with pregestational DM, such as cesarean section. and preeclampsia, and short-term and long-term harm to their children, such as the increased risk of large-for-gestational-age (LGA) newborns, prematurity [8], increased risk of type 1 DM in early childhood [9], lower IQ, higher risk of autism spectrum disorders [10] and higher risk of overweight and obesity in preschool-age [11].

It is known that birth weight (BW) is a predictor of comorbidities that influences the health of the newborn from the perinatal period to adulthood [12], such as for overweight or obesity in childhood [13], risk types 1 and 2 DM in childhood and adolescence [14; 15] and increased risk of cardiovascular disease in adults [16].

A study that analyzed the effects of maternal blood glucose on the BW of the children of 472 women without DM found that the duration of pregnancy, gender of the newborn, pregestational BMI, and gestational weight gain (GWG) influenced this outcome, being impaired glucose tolerance (defined as altered fasting or post-oral glucose tolerance test result) is also an independent factor on BW [17]. Hu et al. when investigating the association of BW and DM in adults, found that both low weight (BW < 2,500 g) and macrosomia (BW > 4,000 g) are associated with the risk of type 2 DM in adulthood in women [18], demonstrating the contribution to the intergenerational perpetuation of the disease if birth weight is not controlled.

Some variables, such as GPG or maternal blood glucose, can be modified with early prenatal care, supported by a multidisciplinary team, including nutritional monitoring. Thus, obstetric and perinatal outcomes can be favored [19], reducing low birth weight [20]. In pregnant women with gestational diabetes mellitus (GDM), obesity, or hypertension, the adoption of a healthy diet can influence modifiable factors such as glycemic control, the incidence of preeclampsia, and birth weight-related factors such as fetal macrosomia and LGA [21].

Lemaitre et al. in a retrospective study of French pregnant women with type 1 DM, showed that levels of glycated hemoglobin in the 1st. trimester >6.5% were associated with a greater chance of the combined outcome - prematurity large for gestational age (LGA), small for gestational age (SGA), or cesarean delivery (OR 2.81; 95% CI 1.01-7, 86) and an increased rate of LGA (OR 2.20; 95% CI 1.01-4.78). Reinforcing the importance of glycemic control in early pregnancy to optimize perinatal outcomes and reduce the risk of LGA [22].

The modifiable factors associated with BW are described in the literature, but there is a lack of studies on pregnant women with pregestational DM. From this perspective, the study aimed to identify the predictive factors of BW in newborns of adult women with pregestational DM treated at a public maternity hospital in Rio de Janeiro.

2. MATERIAL AND METHODS

2.1. Study design

This is an observational, prospective study, nested within a randomized clinical trial (Rebec - RBR-4tbgv6), carried out with data from pregnant women and their children attended at a public maternity hospital in Rio de Janeiro, Rio de Janeiro - Brazil, in the period of November/2016 to March/2020.

2.2. Ethical Issues

The present study used data from the research "Effect of the DASH Diet on the Perinatal Outcome of Pregnant Women with Diabetes Mellitus" (Rebec-RBR-4tbgv6), a controlled clinical trial to test the adapted DASH Diet on the perinatal outcome of Brazilian adult pregnant women with DM. The larger study was approved by the Research Ethics Committee (CEP) of Maternity School/UFRJ on 07/31/15 (CAAE 47335515.0.0000.5275).

Likewise, the present study was approved by the Ethics and Research Committee of Maternity School/UFRJ on 11/17/2021 (CAAE 52970921.6.0000.5275).

2.3. Eligibility Criteria

Inclusion criteria were: adult pregnant women (age >18 years at conception), diagnosis of pregestational DM (Types 1 and 2 or unclassified), singleton pregnancy, prenatal care at the maternity unit studied beginning at gestational age (GA) < 28 weeks (diagnosed by ultrasound), non-smokers, non-users of alcoholic beverages and with the availability of information on birth weight in medical records. Exclusion criteria were: diagnosis of other chronic diseases (except obesity) and women with DM complications, such as diabetic retinopathy and nephropathy.

2.4. Data collection and definition of variables

Data were obtained from medical records. In the original study, all pregnant women were followed up during prenatal care by a multidisciplinary team (physicians, psychologists, nurses, and nutritionists). During the consultations, a complete nutritional assessment was carried out and an individualized food plan was developed, based on nutritional needs and the recommended GWG schedule at each stage of pregnancy, according to pregestational BMI (IOM, 2009) [23].

In the nutritional assessment, pregestational weight (kg) was considered as referring to the maximum period of two months before conception or obtained up to the 14th gestational week. Height (m) was measured at the first prenatal consultation and gestational weight (kg) was measured at all prenatal consultations, using a Filizola® scale and a stadiometer attached to the scale. The measurements were taken by trained professionals [24]. For the classification of pregestational BMI, the following cutoff points were used: low weight (<18.5 kg/m²), adequate (18.5-24.99 kg/m²), overweight (25-29.99 kg/m²), m²) and obesity (≥30.0 kg/m²) [25]. To assess the adequacy of the total GWG, the total gain ranges of 12.5–18 kg for underweight

BMI, 11.5–16 kg for adequate BMI, 7–11.5 kg for overweight BMI, and 5-9 were considered. kg for obesity BMI [23].

Fasting glucose < 95 mg/dL, 1h postprandial < 140 mg/dL, and 2h postprandial < 120 mg/dL were considered as parameters for assessing glycemic control and average values per quarter were considered.

For the analysis of newborn data, weights <2500 g were classified as having low birth weight (LBW) and fetal macrosomia when the weight was ≥4000 g [26]. The GA at birth was evaluated according to ultrasonography in the first trimester, and the newborns were classified as preterm (<37 weeks), the term (37-42 weeks), and post-term (>42 weeks) [27]. The classification of weight for GA at birth (by gender) was performed considering as small for gestational age (SGA) BW < Z-score -2 for gestational age; suitable for gestational age (AGA) between Z-score -2 and +2; and large for gestational age (LGA) >Z-score +2 according to the INTERGROWTH-21st curves [28].

2.5. Variables analyzed

The dependent variable was BW in grams (considering the first weight measured shortly after birth, measured by a pediatrician using a pediatric Welmy infant scale®).

The independent variables and variables analyzed for sample characterization were: maternal age (years), pregestational BMI (kg/m²) - considering pregestational weight (kg) and height (m),- number of pregnancies, abortions, and deliveries, number of prenatal care consultations and prenatal nutritional assistance, gestational age at the first prenatal consultation (weeks of gestation), time of DM diagnosis (years), type of delivery, maternal and fetal complications, skin color, marital status, occupation, education level, sanitation conditions in the housing (garbage collection, piped water, sewage network), and number of people in the family. As for the newborns, the characterization variables collected at delivery were: sex, conditions at birth, complications, gestational age at delivery, head circumference, length, and Apgar score. As for the type of pregestational DM, the variables were DM Type 1, DM Type 2, and unclassified DM.

Independent variables tested in linear regression models were selected for biological plausibility or p<0.20 in bivariate analysis.

2.6. Statistical treatment of data

In the exploratory data analysis of the quantitative variables, the means and standard deviation (SD) were calculated as measures of central tendency and dispersion, respectively.

Bivariate and multivariate linear regression were performed. As an inclusion criterion in the multivariate model, variables with $p<0.20$ were selected in the bivariate analysis, and for biological plausibility, $p<0.05$ was adopted as the criterion for permanence in the final model to identify the variables that predict birth weight. All analyzes were performed using SPSS statistical software for Windows version 21.0.

3. RESULTS

The initial study sample consisted of 86 pregnant women with pregestational DM, with a mean age of 30 years (SD=6.59), 43 with Type 1 DM (50%), 40 with Type 2 DM (46, 5%), and 3 with unclassified DM (3.5%).

According to the pregestational maternal nutritional status, 35.6% were overweight and 33.3% had obesity. Most women had inadequate GWG, with 46.9% above the recommendations and 13.6% below (Table 1).

Regarding sociodemographic conditions, most women had a paid job during pregnancy (64.7%; n=55), lived with a partner (83.5%; n=71), and most had 3 or fewer people in the family composition. (71.6%; n=58), completed high school (67.5%; n=58), lived in housing with adequate sanitation conditions (96.4%; n=80), had had black or mixed black and white (68.7%; n=57), had no associated comorbidities (69.2%; n=54) and had a cesarean delivery (87.7%; n=71) (Table 1).

All pregnant women used insulin during pregnancy. As for maternal complications, the most frequent were Hypertensive Syndromes of Pregnancy (22.8%; n=18), preeclampsia (15.2%; n=12), and gestational hypertension (7.6%; n=8). Regarding prenatal consultations, the pregnant women had an approximate average of 11 consultations (SD=3.97). The average number of consultations with the nutritionist was approximately 5 (SD=1.74).

The mean time of DM diagnosis in these women was 8.35 years (SD=7.00). Regarding glycemic control, 87.2%, 79%, and 66.1% of pregnant women had inadequate control in the three trimesters of pregnancy, respectively. The mean pre-pregnancy BMI was 28.20 kg/m² (SD=5.10) and the mean total GWG was 12.37 kg (SD=5.43, Table 2).

Regarding newborns, the mean BW was 3313.93g (SD=696.08), the mean gestational age at birth was 37.13 weeks (SD=1.47), the mean length was 47.47 cm (SD=3.36) and the mean head circumference was 34.19 cm (SD=2.25, Table 2). Most were born AGA (n=42, 55.3%), followed by LGA (n=27, 35.5%) and SGA (n=7, 9.2%), 21.6% (n=19) were classified as macrosomic, 10.2% (n=9) were LBW and 25.9% were preterm (Table 2).

The predictive factors identified were: in the model I -gestational weight gain (GWG) at the 3rd trimester (ß=60.42; p=0.04), and gestational age at delivery (ß=194.03; p<0.001); in model II - GWG at the 3rd trimester (ß=58.73; p=0.04), and gestational age at delivery (ß=226.55; p<0.001); in model III -time of diagnosis of DM (ß=28.52; p=0.01), GWG at the 3rd trimester (ß=68.86; p=0.02), and gestational age at delivery (ß=232.99; p<0.001). All models were fitted for the glycated hemoglobin of the 1st, 2nd, and 3rd trimesters (Table 3).

4. DISCUSSION

This study shows that the predictive variables of BW of newborns born to women with pre-gestational DM were the total GWG in the 3rd trimester and the time of diagnosis of DM, adjusted for the gestational age at delivery. These results corroborate what the scientific literature currently discusses about the perinatal outcomes of pregnancies accompanied by DM.

A Brazilian study that analyzed data from 827 adult healthy pregnant women found that the predictors of BW were maternal age, total GWG, pregestational BMI, and the number of prenatal consultations [29]. In Silva et al. 283 Brazilian women with GDM were evaluated and the gestational age at delivery, the total GWG in the 1st and 3rd trimesters, fasting glucose in the 1st trimester, postprandial glucose in the 3rd trimester, and pregestational BMI were found to be predictive of BW [30].

As in these studies and our results, the GWG shows an important influence on BW, being a modifiable factor with intervention during prenatal care aiming at control during pregnancy. Similar results to the present study were found in the study by Mastela et al. [31], a Brazilian cohort of 474 pregnant women with GDM, which sought to evaluate the influence of GWG on BW and found that for each kilogram of weight gained in the 3rd trimester, the risk of LGA increased by 10%, regardless of the total GWG, remaining an independent factor for this outcome even with pharmacological treatment and glycated hemoglobin in the 3rd trimester, with the GWG having an insufficient or adequate protective effect on the risk of LGA when compared to the GWG above the recommendations.

In the study by Lemaitre et al. with French pregnant women with type 1 DM, they observed that the concentrations of glycated hemoglobin in the 1st. quarter > 6.5% were associated with a higher chance of the combined outcome, including an increased rate of LGA. In the study, the median (interquartile range) of body mass index (kg/m2) was 23.5 (21.3-26.7), suggesting that most French pregnant women had a prepregnancy body mass index adequate. In the present study, the rates of glycated hemoglobin during pregnancy did not influence the BW. We emphasize that in our study, 69% of the pregnant women were overweight or obese pre-pregnancy and 46.9% had excessive weight gain, which may have favored the relationship with BW [22].

In another Brazilian multicenter cohort comprising 2,244 pregnant women with GDM, it was found a higher risk of preterm birth (RR 1.70, 95% CI 1.08–2.70) and cesarean section (RR 1.21, 95% CI 1, 03-1,44) when excessive GWG occurred in the 3rd trimester [32], emphasizing the importance of nutritional monitoring throughout pregnancy and especially after the 28th week, where GWG may be more evident. Appropriate GWG programming combined with nutritional intervention and good patient adherence to nutritional therapy can promote adequate GWG and glycemic control, assisting in the positive evolution of BW in the newborn of women with pregestational DM, in addition to reducing the risk of morbidity. and perinatal mortality [19, 33].

The relationship between better adherence to nutritional guidelines and glycemic control combined with a minimum schedule of appointments with a nutritionist reinforces the importance of nutritional monitoring at this stage of life, especially in pregnancies with DM [34, 35]. The variables that most explain PN are those related to maternal nutritional status [36] and prenatal nutritional care can influence the effect on these variables. In the study by Oliveira et al. carried out with pregnant women with DM, it was found that nutritional monitoring with an average of 5 consultations contributed to the reduction of postprandial glycemia. And adherence to the guidelines improved with the increase in the number of individual consultations with the nutritionist [37].

The beginning of pregnancy with inadequate nutritional status can worsen the perinatal outcomes of women with DM, having more significant deleterious effects when the GWG is excessive, leading to a greater risk of LGA babies regardless of pregestational BMI, glycated hemoglobin, smoking, or ethnicity [38, 39].

In this study, it was observed that the majority of pregnant women had a GWG above the recommendation (46.9%), considering the pregestational BMI categories according to the recommendations of the Institute of Medicine [23]. Zhao et al. analyzed 1,617 Chinese women without comorbidities and observed that the higher the pre-pregnancy BMI, the greater the proportion of pregnant women with a GWG above the guidelines, corroborating this study and showing that a GWG above the recommended in women with overweight and obesity may be associated with fetal macrosomia (p=0.005) and with LGA newborn (p=0.004). On the other hand, the GWG below the recommendations can be associated with LBW (p=0.027) and with SGA newborns (p=0.011) and even in women with adequate pre-pregnancy BMI, the GWG above the recommendations can also be associated with macrosomia and with LGA newborns [40].

Brazilian studies, such as the one by Mastroeni et al. which analyzed 435 women without comorbidities, found that pregestational weight in BMI ranges greater than 25 kg/m² and excessive GWG independently influenced the occurrence of LGA newborns [41]. Parellada et al. analyzed 142 pregnant women and observed that BW was almost 0.5 kg higher in the children of women with type 2 DM and excessive GWG when compared to women with type 2 DM and non-excessive GWG, with more LGA babies being born in the group with excessive GWG ($p < 0.001$), in addition to higher rates of compound perinatal morbidity (p= 0.047) and neonatal hypoglycemia (p= 0.03) [39].

The results of the present study showed that most babies were born AGA (n=42; 55.3%), followed by LGA babies (n=27; 35.5%) according to INTERGROWTH-21st and 21.6% of babies were born macrosomic (n=19), considering BW ≥ 4,000 g.

It is known that the association of DM with several negative outcomes in pregnancy is well described in the literature, one of the most cited being fetal macrosomia [42]. In pregnant women with pregestational DM in Uruguay, a prevalence of 14.5% of macrosomia (n=304) was found, evidencing this diagnosis as an independent risk factor for this outcome, whereas women with pregestational DM had up to 1 .7 times greater risk of macrosomia [43].

In developed countries, higher rates of macrosomia than in this study were observed when analyzing pregnancies accompanied by pregestational DM and GDM. In a cohort study carried out in Sweden with 308 pregnant women, the prevalence of macrosomia was 39% among women with type 1 DM and 22% among women with type 2 DM, and the prevalence of LGA babies among the same groups of type 1 and type 2 DM was 50% and 23%, respectively [44]. Therefore, even though lower percentages were observed in studies, the rates found in this study are lower than in developed countries, showing that even though it is possible to improve these goals, the results found are satisfactory and may be related to the specialized assistance received by this group. in the prenatal care at the study site which, supported by a specialized multidisciplinary team, favors better adherence and adjustments of the treatment.

Regarding the time of diagnosis of pregestational DM, although this is a non-modifiable predictive factor found in our study, type 1 and type 2 DM can be independently associated with a higher risk of preeclampsia, congenital anomalies, prematurity, macrosomia, perinatal mortality, among other unfavorable outcomes, increasingly demonstrating the need for preconception care to control the disease, since inadequate treatment of DM worsens the metabolic state and in the long term can reduce the possibilities of improving perinatal outcomes in case of pregnancy [42, 45].

Regarding the number of prenatal consultations, the average of 11 consultations observed in this study was higher than that recommended by the Ministry of Health, which guides a minimum of 6 consultations [26] and that found in the last National Survey of Demographics and Child Health and Women, where in the Southeast region, 88.2% of pregnant women had 6 or more consultations on average [46]. This data may be related to better outcomes, since the number of prenatal consultations was previously considered in other studies as a predictor of BW [29], improving this outcome and also preventing other negative complications in pregnant women with DM, such as premature birth, cesarean section and preeclampsia [47].

In addition, it is necessary to highlight that socio-demographic characteristic was not a predictor of BW in the present study, thus evidencing the importance of prenatal care at this stage of life, for the control of adequate GWG during pregnancy, to avoid negative outcomes associated with DM, since excessive GWG is detrimental to DM and GDM control [39, 48].

As a limitation of the study, we can point out the lack of information on some data and, in addition, the study was carried out in a single maternity hospital in the city of Rio de Janeiro, however, the maternity receives pregnant women on demand and also through the National Regulatory System, that is, pregnant women assisted in the Unified Health System have access to prenatal care at the unit.

Given the aspects observed, although the present study did not establish a correlation between the number of prenatal consultations and the PN, the rate of macrosomia found was lower than the rates found in studies of populations of pregnant women with DM in developed countries and this may be related to a longer and more effective follow-up in the assistance provided by the multidisciplinary team specialized in prenatal care. As for GPG control in the 3rd trimester, this proved to be an important modifiable factor for BW control, demanding attention to this specific phase accompanied by nutritional assistance to control this variable.

The best predictors of BW were weight gain in the 3rd trimester, gestational age at delivery, and time of diagnosis of DM. These results point to the need to review prenatal routines and formulate tools capable of integrating care for this group, with prenatal care and nutritional monitoring starting early in pregnancy, aiming to positively influence the PN of children of women with pregestational DM.

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TABLES

Table 1. Anthropometric, sociodemographic, and clinical characteristics of pregnant women with DM. A public maternity hospital in Rio de Janeiro, RJ, Brazil (2016-2020).

Maternal characteristics	*% (n)*
Pregestational nutritional status (BMI/kg²) (n=87)	
Low weight	0.0 (0)
Eutrophy	31.0 (27)
Overweight	35.6 (31)
Obesity	33.3 (29)
Adequacy of weight gain (n=81)	
Below	13.6 (11)
Adequate	39.5 (32)
Above	46.9 (38)
Occupation (n=85)	
Performs paid activity	64.7 (55)
Housewife/ does not work	35.3 (30)
Marital status (n=85)	
Lives with partner	83.5 (71)
Single, divorced or widowed	16.5 (14)
Number of people in the family (n=81)	
≤ 3 people	71.6 (58)
> 3 people	28.4 (23)
Instruction level (n=86)	
Incomplete high school	32.5 (28)
Completed high school or higher	67.5 (58)
Housing sanitation conditions (n=83)[a]	
Inadequate	3.6 (3)
Adequate	96.4 (80)
Skin color (n=83)	
White	31.3 (26)
Mixed black and white	41.0 (34)
Black	27.7 (23)

DM type (n=86)	
Type 1 diabetes	50.0 (43)
Type 2 diabetes	46.5 (40)
Unclassified DM	3.5 (3)
Presence of comorbidities (n=78)	
With comorbidities	30.8 (24)
No comorbidities	69.2 (54)
Type of delivery (n=81)	
Normal	12.3 (10)
Cesarean	87.7 (71)

Subtitle: DM - Diabetes Mellitus, [a] Housing sanitation conditions -adequate conditions when there was running water, regular garbage collection and sewage network and inadequate conditions when one of the services was absent

TABLE 2

Table 2. Means and standard deviation of maternal and newborn characteristics of pregnant women with pregestational DM. A public maternity hospital in Rio de Janeiro, RJ, Brazil (2016-2020).

Maternal and newborn characteristics	***n***	***Mean***	***Standard Deviation (SD)***
Maternal and newborn variables			
Maternal age (years)	87	30.41	6.59
DM diagnosis time (years)	86	8.35	7.00
Gestational age at delivery by ultrasound (weeks)	81	37.13	1.47
Birth weight (g)	81	3313.93	696.08
Length at birth (cm)	77	47.47	3.36
Head circumference at birth (cm)	74	34.19	2.25
Obstetric and clinical variables			
Number of pregnancies	86	2.36	1.50
Number of deliveries	86	0.87	1.02
Number of abortions	86	0.52	0.87
Number of prenatal care consultations	86	11.01	3.97
Number of prenatal consultations with a nutritionist	87	5.17	1.74
1st-trimester fasting blood glucose (mg/dL)	53	137.61	60.39
2nd-trimester fasting blood glucose (mg/dL)	71	119.02	42.08
3rd-trimester fasting blood glucose (mg/dL)	63	114.45	115.57
1st-trimester glycated hemoglobin (%)	73	7.16	1.44
2st-trimester glycated hemoglobin (%)	73	6.60	1.28
3st-trimester glycated hemoglobin (%)	56	6.45	0.76
Maternal anthropometric variables			
1nd-trimester gestational weight gain (kg)	64	2.54	3.15
2nd-trimester gestational weight gain (kg)	64	5.52	2.50
3rd-trimester gestational weight gain (kg)	77	4.76	2.72
Total gestational weight gain (kg)	81	12.37	5.43
Pre-pregnancy BMI (kg/m²)	87	28.20	5.10

Subtitle: DM - Diabetes Mellitus; BMI - Body Mass Index.

Table 3. Result of multiple linear regression of predictive factors of birth weight of newborns of pregnant women with pregestational diabetes mellitus. A public maternity hospital in Rio de Janeiro, RJ, Brazil (2016-2020).

Variables	ß gross	p	CI (95%)	ß adjusted	p	CI (95%)
The model I - 1st-trimester						
Time of diagnosis of Diabetes Mellitus (years)	24.10	0.031	2.25 – 45.96	19.39	0.07	-1.95 - 40.733
Total weight gain in the 3rd trimester (kg)	79.10	0.05	24.26 – 133.94	60.42	**0.04**	3.72- 117.11
Gestational age at delivery by ultrasound (weeks)	237.41	<0.001	146.29 – 328.53	194.03	**<0.001**	91.74 – 296.32
1st-trimester glycated hemoglobin	-110.39	0.064	-227.60-6.80	-21.36	0.70	-134.13 – 91.40
The Model II - 2st-trimester						
Time of diagnosis of Diabetes Mellitus (years)	24.10	0.031	2.25 – 45.96	21.60	0,05	-0.53 – 43.74
Total weight gain in the 3rd trimester (kg)	79.10	0.05	24.26 – 133.94	58.73	**0.04**	119,138-333,97
Gestational age at delivery by ultrasound (weeks)	237.41	<0.001	146.29 – 328.53	226,555	**<0.001**	2,378 – 115.09
2 nd-trimester glycated hemoglobin	-95.72	0.28	-270.01-78.57	55,835	0,53	-119,044 – 230.71
The Model III -3rd trimester						
Time of diagnosis of Diabetes Mellitus (years)	24.10	0.031	2.25 – 45.96	28.52	**0.01**	6.36-50.68

Total weight gain in the 3rd trimester (kg)	79.10	0.05	24.26 – 133.94	68.86	**0.02**	10.45-127.28
Gestational age at delivery by ultrasound (weeks)	237.41	<0.001	146.29 – 328.53	232.99	**<0.001**	134.83-331.16
3 rd-trimester glycated hemoglobin	-95.29	0.37	-306.43-115.86	0.50	0.38	-0.63-1.63

Adjusted for: gestational age at delivery, time of diagnosis of Diabetes Mellitus, total weight gain in the 3rd trimester, and glycated hemoglobin. CI- confidence interval

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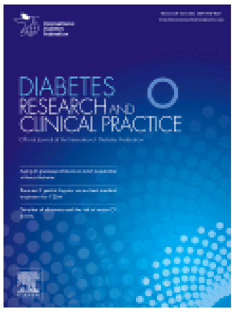

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