Gestational Weight Gain Influences Neonatal Outcomes in Women With Obesity and Gestational Diabetes

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Research Article

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Abstract

Background. Obesity and gestational diabetes mellitus (GDM) are associated to increased risk of perinatal complications and obesity in the offspring. However, the impact of gestational weight gain (GWG) on maternal and fetal outcomes has led to controversial results.

Research design and methods. Retrospective study of 220 women with GDM and pre-pregnancy body mass index (BMI) ≥ 30 kg/m2. Pregnant women were classified according to the Institute of Medicine (IOM) recommendations regarding prior BMI and GWG. We evaluated the impact of GWG on birth weight and perinatal outcomes.

Results. Mean maternal age was 34.7±5.3 years. Pre-pregnancy obesity was classified as grade I in 55.3% of cases, grade II in 32.0%, and grade III in 12.7%. GWG was adequate (5-9kg) in 24.2%, insufficient (< 5kg) in 41.8% and excessive (> 9kg) in 34.2%. Birthweight was within normal range in 81.9%, 3.6% were small for gestational age (SGA) and 14.4% were large for gestational age (LGA). Insufficient GWG was associated to a higher rate of SGA offspring, excessive GWG was associated to LGA and adequate GWG to normal birth weight.

Conclusion. GWG in women with pre-pregnancy obesity and GDM impacts neonatal birthweight. Insufficient GWG is associated to SGA and excessive GWG is associated to LGA. Women with adequate GWG according to IOM guidelines obtained better perinatal outcomes.

Introduction

Obesity in women of child-bearing age is worryingly increasing in prevalence worldwide [1, 2]. Data form the US National Health and Nutrition Examination Survey (NHANES) of women aged 20–39 years yielded an estimated prevalence of obesity of 31.8%, with half being classified as grade I obesity (body mass index, BMI 30-34.9 kg/m^2) [3]. The impact of this burden relies on several complications, including reduced fertility, increased time taken to conceive, increased rate of obesity-related comorbidities and a higher risk of adverse outcomes for the mother and her offspring in case of pregnancy. Specifically, women with obesity who become pregnant exhibit a higher likelihood of early pregnancy loss, increased risk of congenital fetal malformations, delivery of macrosomal infants, premature birth, difficulties during labour and delivery and stillbirth. In addition, pregnancy may be complicated by associated comorbidities such as gestational diabetes mellitus (GDM), pregnancy-induced hypertension, pre-eclampsia, thromboembolism and mental disturbances, all of which may compromise the future health of the new mother. Further on, maternal obesity has also been associated to long-term post-partum morbidities, including difficulties in breastfeeding, weight retention and metabolic alterations in both the mother and her children [2]. Effective and prompt interventions, especially regarding weight management, should be carried out to minimize maternal and fetal consequences related to maternal obesity.

GDM, defined diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation [4], is the most clearly related obesity-derived metabolic complication, with its risk increasing with maternal BMI. The prevalence of GDM may range depending on variations in criteria used to diagnose it, and there has been a large amount of controversy regarding which should be the most optimal approach to diagnosis [4, 5]. In any case, intervention to control maternal glucose levels reduces adverse obstetric outcomes, serious perinatal morbidity and may also improve the woman's health-related quality of life, although the long-term impact on the offspring has not been clearly determined [6–8]. First-line management of GDM relies on lifestyle modifications based on strict control of carbohydrates combined with light exercise [9, 10]. However, a recent systematic review advocates for an individualized modified nutritional manipulation from usual intake, including but not limited to carbohydrate restriction [11].

Gestational weight gain (GWG) directly affects overall pregnancy outcomes. Thus, the Institute of Medicine (IOM) described what would be desirable based on pre-gestational BMI exclusively [12]. Several previous studies have evaluated GWG in obese women and in GDM, independently, but the desirable weight management in the setting of both obesity and GDM and its consequences on maternal and fetal outcomes has not been clearly evaluated. The aim of this study is to analyze the relationship between GWG in women with obesity and GDM who follow a lifestyle treatment and its effects on maternal and fetal outcomes.

Research Design And Methods

Study population

From January 2016 to October 2019 there were 9114 women who delivered in our Hospital. Of these, 747 were followed-up at some point in our Department of Endocrinology, mainly because of GDM diagnosis. We collected data on the 249 pregnant women who were diagnosed with GDM and had a pre-gestational BMI $\geq$ 30 kg/m^2. We then excluded 29 patients due to follow-up loss and/or lack of important data for our objectives, leaving a total sample of 220 pregnant women. The Ethics and Clinical Research Committee of our Hospital approved the study protocol, and was in compliance with the Helsinki Declaration. Patient anonymity was preserved. All data were treated in a pseudonymized way, ensuring technical and functional separation between the research team and the person in charge of the pseudonymization.

Study design

According to our Hospital’s protocol, GDM screening was performed in obese pregnant women during the first trimester, with the two-step approach [4]. If diagnosis of GDM was initially ruled out, the same approach was repeated during the second trimester, around weeks 24–28 of pregnancy. Additional work-up with oral glucose tolerance tests (OGTT) was performed in case of excessive amniotic fluid or large for gestational age fetuses, regardless of prior negative GDM results. All patients with GDM were referred to the endocrinologist. In case women were not able to tolerate the OGTT, they were also referred to the endocrinologist and frequent glucose monitoring was performed until a clinical decision was made regarding the presence or absence of GDM.

Patients were individually counseled by the endocrinologist and a registered dietician on strategies to maintain a healthy lifestyle, diet, exercise and glucose monitoring, according to each patient's energy requirements. Treatment with insulin was started in cases of insufficient glucose control with diet alone.

We evaluated diet adherence, glucose auto-monitoring, maternal weight and gestational outcomes (estimation of amniotic fluid and estimated fetus weight in each programmed sonographic evaluation), at the first visit, at weeks 20, 24, 32, and immediately before delivery. Pre-pregnancy weight was also recalled. Delivery data were collected, with special attention to the type of delivery, birth weight, perinatal complications and hospital stay.

Categorization of gestational weight gain and classification of birth weight

According to the IOM recommendations [12], adequate GWG was defined according to pre-pregnancy BMI. For the particular case of women with obesity (BMI $\geq$ 30 kg/m^2), adequate GWG was considered to be between 5 and 9 kg. Thus, insufficient GWG was considered as < 5 kg and excessive GWG was considered as > 9kg.

For birth weight, normality was considered between 2.5 and 4 kg, LGA as considered for birth weights > 4 kg and SGA if birth weight was < 2.5 kg.

Statistical analysis

Statistical analysis was performed using SPSS version 25.0 (IBM SPSS Statistics Inc., Chicago, IL, USA). For descriptive data, results were expressed as mean ± standard deviation for continuous variables, and as frequency and percentages for categorical variables. Possible existing associations between gestational outcomes and GWG were evaluated using two-sided analysis of variance. Comparison between categorical groups was assessed with chi-square test. Univariate and multivariate analyses were performed to evaluate further associations. Significance was considered at $p < 0.05$.

Results

Baseline characteristics

Mean age of the women included in our study was 34.7 ± 5.3 years old and mean weight was 89.0 ± 13.0 kg (BMI 35.2 ± 4.3 kg/m^2). Before pregnancy, 122 (55.5%) women were classified as grade I obesity, 70 (31.8%) as grade 2, 26 (11.8%) as grade 3 and 2 (0.9%) as grade 4. For most women (120, 54.5%) this was the first pregnancy, for 76 (34.5%) the second one, for 20 (9.1%) the third one and for 4 women (1.8%) this was the fourth pregnancy. Only 7 (3.2%) pregnancies were multiple, and 17 (7.7%) were pregnancies after assisted reproductive techniques. Twenty five patients (11.4%) had undergone a previous C-section.

Diagnosis and management of gestational diabetes mellitus

Diagnosis of GDM was performed during the first trimester in 105 cases (47.7%), during the second trimester, as part of the universal screening at weeks 24–28 of gestation, in 74 (33.6%), and after the universal screening in 41 cases (18.6%). Upon evaluation during the second trimester, 33 patients (15.0%) required insulin, but the number increased to 46 (20.9%) during the third trimester.

Gestational weight gain and obstetric outcomes

Mean maternal weight increased progressively to 93.2 ± 12.4 kg, 95.5 ± 13.0 kg, 97.8 ± 13.4 kg at 20, 32 and last visit before delivery, respectively. The average gestational week of the last visit in the Endocrinology Department before delivery was 32.1 ± 7.0. Mean total GWG was 6.3 ± 6.7 (interquartile range 2.6–11.0) kg. According to the IOM guidelines, 41.8% had an insufficient GWG, 24.2% an adequate GWG and 34.0% an excessive GWG. We did not find a significant correlation between GWG and age ($R = 0.012$, $p = 0.866$).

Birthweight and obstetric outcomes

Mean neonatal birthweight was 3421.0 ± 575.9 g, with 82.0% being considered as normal, 14.4% as LGA and 3.6% as SGA. GWG was significantly correlated with neonatal birthweight ($R = 0.228$, $p = 0.001$) (Fig. 1). Women with insufficient GWG (< 5kg) had a higher rate of SGA infants (7.4%) in comparison to those who had an adequate GWG (0.0%) or an excessive GWG (1.5%). Women with excessive GWG (> 9kg), on their part, had a higher rate of LGA infants (24.2%), in comparison to women with adequate GWG (8.5%) or insufficient GWG (9.9%). An adequate GWG was associated to a higher rate of adequate infant birthweight (91.5%), in comparison to cases with insufficient or excessive GWG (82.7% and 74.2%, respectively). Comparisons yielded statistical significance ($p = 0.009$) (Fig. 2). GWG was not different between women with or without insulin treatment ($p = 0.784$).

Thirty women (13.4%) developed pre-eclampsia. There were 7 cases of miscarriage before week 20, and 1 case of intra-uterus death at 38 weeks of gestation. Delivery occurred at median week 40 (interquartile range 38–40), therefore the majority of them were considered full-term deliveries (78.4%), but there were 29 cases (13.2%) of pre-term deliveries (before week 37). Delivery was induced in 60 cases (27.3%), required instrumental devices in 32 cases (14.6%) and 71 women (32.3%) underwent a C-section. We did not find any statistically significant associations between GWG and any other maternal or perinatal adverse outcomes.

Discussion

In this study, we found that GWG in pregnant women with obesity and GDM determines neonatal birthweight, with a higher percentage of women with excessive GWG delivering LGA infants, and those with insufficient GWG delivering more SGA infants. We observed that women with GDM and adequate

GWG according to the IOM recommendations regarding their prior BMI, had a higher percentage of infants with normal birthweight.

To our knowledge, this is the first time that IOM GWG recommendations are assessed in women with both obesity and GDM, and not only based on pre-pregnancy BMI. The impact of obesity and GDM on birth weight and pregnancy outcomes are well known, but the potential influence of GWG has not been as deeply studied, especially in the setting of the coexistence of both comorbidities. Obese women are more prone to excessive GWG and its derived complications [13, 14], but a strict dietary approach, to which patients may adhere more frequently in cases of GDM, may lead to insufficient GWG and SGA. In fact, our patients with insufficient GWG had a higher rate of SGA infants, despite their previous obesity and GDM, which are well-known risk factors for LGA. Thus, optimal management is crucial for optimal outcomes, but it is not always easy to achieve. In our cohort, many patients met IOM criteria for insufficient or excessive GWG, and patients with an IOM adequate GWG were the fewest. This is in accordance with a recent publication [15] and a recent metanalysis, which found that women have difficulties in adhering to IOM GWG recommendations, even in clinical trials, despite the fact that these recommendations truly seem to help achieve better pregnancy outcomes [16]. Our results suggest that GWG does, in fact, determine neonatal birthweight, as it has been previously described [17] and should therefore be carefully addressed; healthcare providers should try to find efficient strategies to achieve a healthier GWG as defined by the IOM recommendations.

Attention to GWG becomes increasingly important as the prevalence of obesity and GDM increases worldwide in women of child-bearing age [18]. Indeed, GDM occurred in around 8% of pregnant women in our hospital, and obesity was identified in 30.7% of them. Obesity entails a higher risk of associated comorbidities, which may, on their part, increase the rate of adverse obstetric outcomes [2, 19]. For instance, a recent Scottish study [20] identified a prevalence of obesity of almost 20% from the total cohort of pregnant women, and an odds ratio of 8.25 of developing GDM. In addition, maternal age has been identified as another adverse factor, since its increase over the past years in high-income countries has been associated to a higher risk of GDM. In this regard, mean age in our cohort was almost 35 years, which is slightly higher than what has been reported in some previous studies [21–23], and this may have influenced the total prevalence of obesity and GDM in our cohort.

The difference between true GDM and preexisting not previously identified intolerance to carbohydrates is not always straightforward in pregnant women with obesity. In fact, because routine screening is not widely performed in non-pregnant women of reproductive age, screening during pregnancy may reveal preexisting hyperglycemia, and not a mere increase in insulin resistance inherent to the second and third terms of pregnancy [4, 24]. Universal screening before pregnancy or during the first trimester is still controversial [25], and early screening protocols in our cohort could overestimate the resulting GDM prevalence [4, 26, 27]. But, in any case, intervention to maintain glucose levels under control deems necessary for better pregnancy outcomes, and this is frequently associated to a strict control of GWG. For instance, a previous study that evaluated weight changes in women with GDM observed that an excessive GWG was associated to adverse obstetric outcomes, including higher rate of LGA infants; and insufficient GWG, or even weight loss, could be associated to a lower frequency of needing hypoglycemic medications, C-sections and macrosomia, without increasing the prevalence of SGA infants [28].

Our study has some limitations regarding bias on nutritional interventions for obese women with GDM, since these patients usually have more frequent follow-up check-ups than patients with no metabolic background. However, the aim of our study was precisely to evaluate the outcomes of women with these two issues regarding GWG and their outcome. We do not have long-term data on maternal weight and carbohydrate status after delivery, nor on their infants' long-term metabolic outcome. However, this was beyond the objectives of our retrospective observational study. More long-term and interventional studies are required to evaluate postpartum consequences for both mother and offspring, and evaluate if GWG recommendations should be universal only based on prior BMI, regardless of coexisting GDM or any other form of previous glucose intolerance.

In conclusion, we remark the importance of controlling GWG during pregnancy with intensive intervention and follow-up, especially in obese women with GDM, in whom background metabolic and behavioral issues may entail opposing weight trends. IOM guidelines on GWG seem to be useful also in the setting of concomitant GDM. GWG may truly affect birthweight and pregnancy outcome and should therefore be appropriately managed.

Declarations

Funding.

This study was not subject to any funding from public or private entities.

Conflicts of interest.

The authors declare that there is no conflict of interest that could be perceived as directly or indirectly prejudicing the impartiality of the research reported.

Availability of data and material.

We acknowledge that all data and materials, as well as software application, support our reported findings and comply with field standards. Data and study material are not publicly available, but are available from the corresponding author upon reasonable request, ensuring data transparency.

Ethics approval.

The Ethics and Clinical Research Committee of our Hospital approved the study protocol, and was in compliance with the Helsinki Declaration. Patient anonymity was preserved. All data were treated in a pseudonymized way, ensuring technical and functional separation between the research team and the person in charge of the pseudonymization.

Consent to participate.

Not applicable.

Consent for publication.

Not applicable.

Code availability.

Not applicable.

Authors' contributions.

GRC, CGF, EGV, ACB, PBM and RVT contributed to study conception and design, followed-up patients, researched, analyzed and interpreted data, and reviewed and edited the manuscript. ARL analyzed and interpreted data and wrote the manuscript. All authors critically revised the final version of the manuscript and approved it for submission and subsequent potential publication.

References

1. Stothard KJ, Tennant PWG, Bell R, Rankin J. Maternal overweight and obesity and the risk of congenital anomalies: a systematic review and meta-analysis. JAMA 2009; 301: 636–650.
2. Poston L, Caleyachetty R, Cnattingius S, Corvalán C, Uauy R, Herring S, Gillman MW. Preconceptional and maternal obesity: epidemiology and health consequences. Lancet Diabetes Endocrinol. 2016;4(12):1025-1036.
3. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of childhood and adult obesity in the United States, 2011–2012. JAMA 2014; 311: 806–14.
4. American Diabetes Association. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes—2021. Diabetes Care 2021 Jan; 44(Supplement 1): S15-S33.
5. Hillier TA, Pedula KL, Ogasawara KK, Vesco KK, Oshiro CES, Lubarsky SL, Van Marter J. A Pragmatic, Randomized Clinical Trial of Gestational Diabetes Screening. N Engl J Med 2021;384(10):895-904.
6. Crowther CA, Hiller JE, Moss JR, McPhee AJ, Jeffries WS, Robinson JS. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. N Engl J Med 2005;352(24):2477-86.

7. Johns EC, Denison FC, Norman JE, Reynolds RM. Gestational Diabetes Mellitus: Mechanisms, Treatment, and Complications. Trends Endocrinol Metab. 2018;29(11):743-754.
8. Szmuilowicz ED, Josefson JL, Metzger BE. Gestational Diabetes Mellitus. Endocrinol Metab Clin North Am. 2019 Sep;48(3):479-493.
9. Hernandez TL, Mande A, Barbour LA, Nutrition therapy within and beyond gestational diabetes. Diabetes Res Clin Pract. 2018; 145: 39–50.
10. Duarte-Gardea MO, Gonzales-Pacheco DM, Reader DM, Thomas AM, Wang SR, Gregory RP, Moloney L. Academy of Nutrition and Dietetics Gestational Diabetes Evidence-Based Nutrition Practice Guideline. J Acad Nutr Diet 2018; 118: 1719–1742.
11. Farabi SS, Hernandez TL. Low-Carbohydrate Diets for Gestational Diabetes. Nutrients 2019;11(8):1737.
12. IOM (Institute of Medicine), NRC (National Research Council). Weight gain during pregnancy: reexamining the guidelines In: Rasmmussen KM, Yaktine AL, ed. Weight gain during pregnancy: reexamining the guidelines. 2009: 210–212. Available from: http://iom.nationalacademies.org/_/media/Files/Report Files/2009/Weight-Gain-During-Pregnancy-Reexamining-the-Guidelines/Report Brief - Weight Gain During Pregnancy.pdf.
13. Deputy NP, Sharma AJ, Kim SY, Hinkle SN. Prevalence and characteristics associated with gestational weight gain adequacy. Obstet Gynecol. 2015; 125(4):773–781
14. Kominiarek MA, Peaceman AM. Gestational weight gain. Am J Obstet Gynecol 2017;217(6):642-651.
15. Liang CC, Chao M, Chang SD, Chiu SY. Pregnancy weight gain may affect perinatal outcomes, quality of life during pregnancy, and child-bearing expenses: an observational cohort study. Arch Gynecol Obstet. 2021 Mar 4. doi: 10.1007/s00404-021-05983-2.
16. Rogozińska E, Zamora J, Marlin N, Betrán AP, Astrup A, Bogaerts A, et al, International Weight Management in Pregnancy (i-WIP) Collaborative Group. Gestational weight gain outside the Institute of Medicine recommendations and adverse pregnancy outcomes: analysis using individual participant data from randomised trials. BMC Pregnancy Childbirth 2019;19(1):322.
17. Goldstein RF, Abell SK, Ranasinha S, Misso M, Boyle JA, Black MH, et al. Association of Gestational Weight Gain With Maternal and Infant Outcomes: A Systematic Review and Meta-analysis JAMA 2017; 317(21): 2207-2225.
18. Collier A, Abraham EC, Armstrong J, Godwin J, Monteath K, Lindsay R. Reported prevalence of gestational diabetes in Scotland: The relationship with obesity, age, socioeconomic status, smoking and macrosomia, and how many are we missing? J Diabetes Investig. 2017;8(2):161-167
19. Gaillard R, Durmuş B, Hofman A, Mackenbach JP, Steegers EA, Jaddoe VW. Risk factors and outcomes of maternal obesity and excessive weight gain during pregnancy. Obesity (Silver Spring). 2013;21(5):1046-55
20. Doi L, Williams AJ, Marryat L, Frank J. Cohort study of high maternal body mass index and the risk of adverse pregnancy and delivery outcomes in Scotland. BMJ Open. 2020;10(2):e026168

21. Abouzeid M, Versace VL, Janus ED, Davey MA, Philpot B, Oats J, Dunbar JA. A population-based observational study of diabetes during pregnancy in Victoria, Australia, 1999-2008. BMJ Open. 2014;4(11):e005394.
22. Eades CE, Cameron DM, Evans JMM. Prevalence of gestational diabetes mellitus in Europe: A meta-analysis. Diabetes Res Clin Pract. 2017;129:173-181.
23. Hildén K, Magnuson A, Hanson U, Simmons D, Fadl H. Trends in pregnancy outcomes for women with gestational diabetes mellitus in Sweden 1998-2012: a nationwide cohort study. Diabet Med 202037(12):2050-2057.
24. Huvinen E, Koivusalo SB, Meinilä J, et al. Effects of a lifestyle intervention during pregnancy and first postpartum year: findings from the RADIEL study. J Clin Endocrinol Metab 2018;103:1669–1677
25. Yefet E, Jeda E, Tzur A, Nachum Z. Markers for undiagnosed type 2 diabetes mellitus during pregnancy-A population-based retrospective cohort study. J Diabetes 2020;12:205–214
26. McIntyre HD, Sacks DA, Barbour LA, Feig DS, Catalano PM, Damm P, McElduff A. Issues With the Diagnosis and Classification of Hyperglycemia in Early Pregnancy. Diabetes Care. 2016;39(1):53-4.
27. Mission JF, Catov J, Deihl TE, Feghali M, Scifres C. Early pregnancy diabetes screening and diagnosis: prevalence, rates of abnormal test results, and associated factors. Obstet Gynecol 2017;130:1136–1142
28. Viecceli C, Remonti LR, Hirakata VN, Mastella LS, Gnielka V, Oppermann ML, Silveiro SP, Reichelt AJ. Weight gain adequacy and pregnancy outcomes in gestational diabetes: a meta-analysis. Obes Rev. 2017;18(5):567-580.

Figures

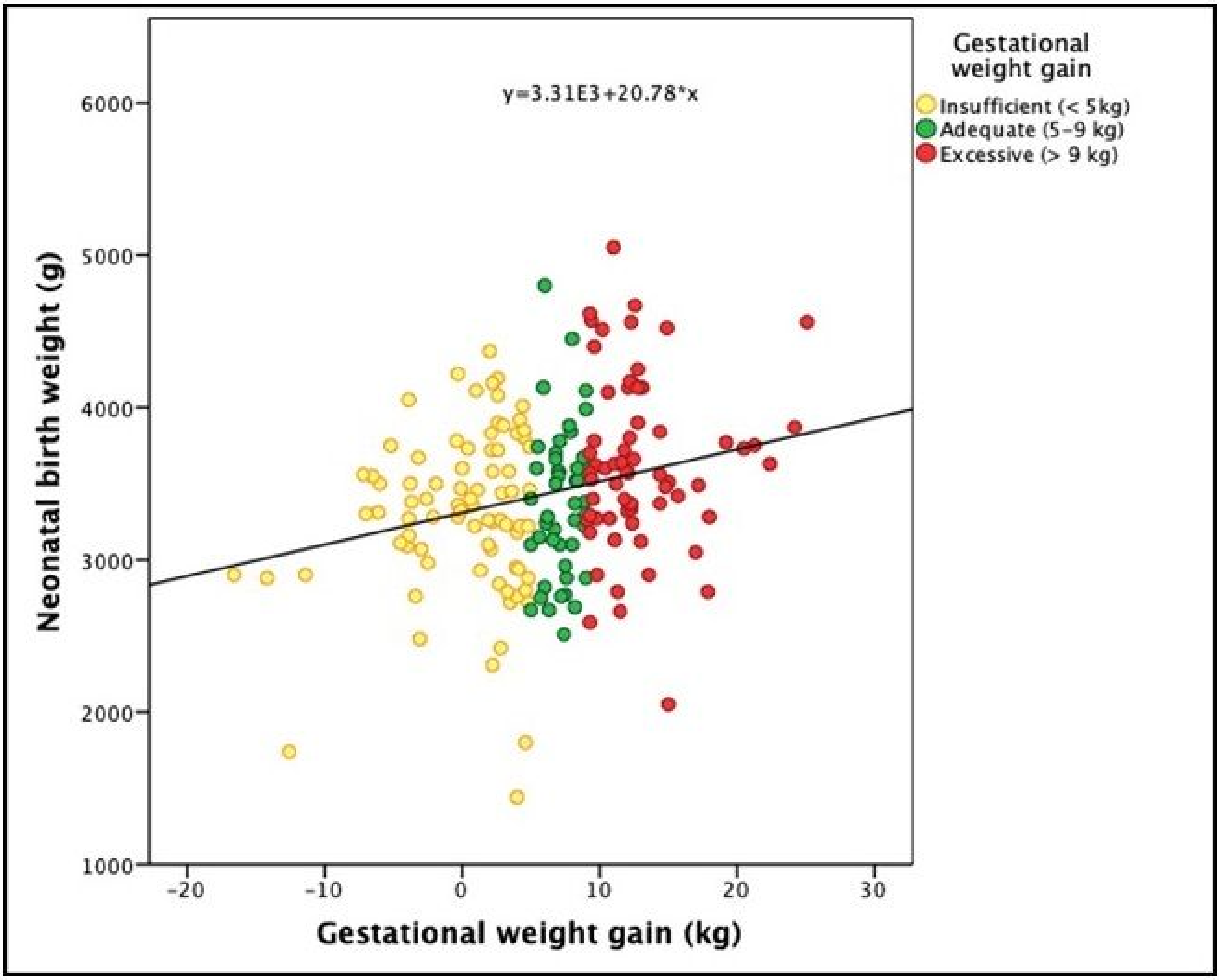

Figure 1

Point dispersion graph representing the correlation between maternal gestational weight gain (GWG) and neonatal birth weight, according to the categorization of GWG adequacy of the IOM guidelines.

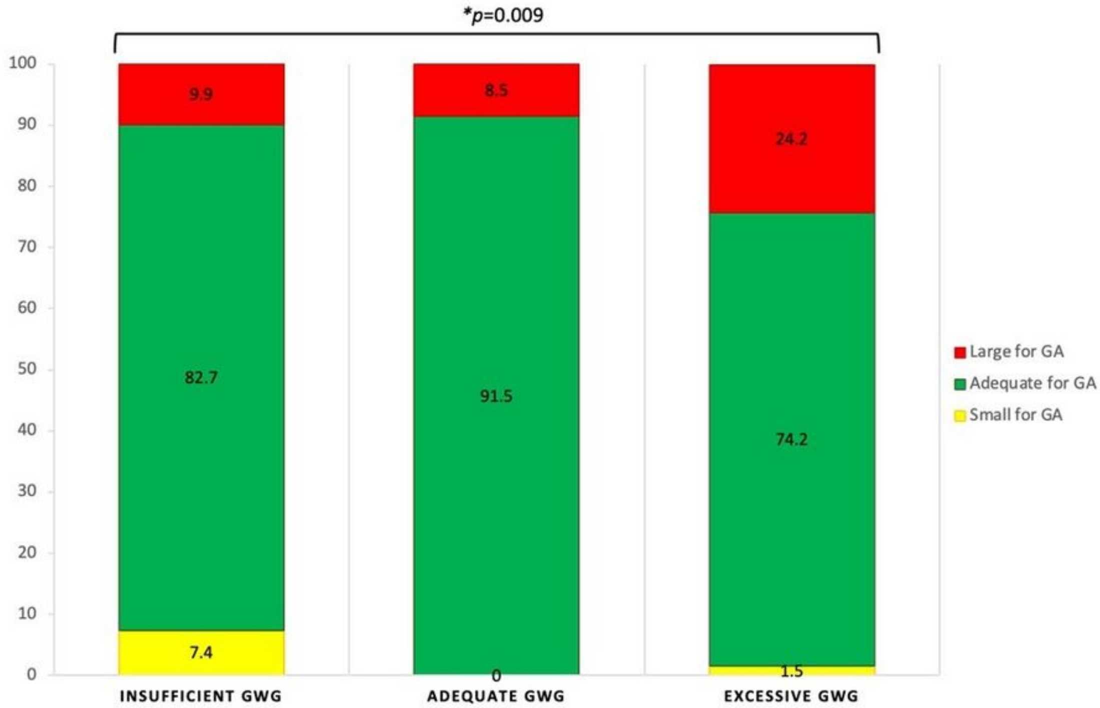

Figure 2

Bar chart representing the percentage of infants who were born small, adequate or large for gestational age (GA), according to the adequacy of maternal gestational weight gain (GWG) according to the IOM guidelines. Comparison yielded statistical significance (p=0.009).