Gestational diabetes mellitus treatment reduces obesity-induced adverse pregnancy and neonatal outcomes: the St. Carlos gestational study

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ABSTRACT

Background: Obesity and gestational diabetes mellitus (GDM) increase the morbidity of the mother and newborn, which could increase further should they coexist. We aimed to determine the risk of adverse pregnancy and neonatal outcomes associated with excess weight (EW), and within this group identify potential differences between those with and without GDM.

Methods: We carried out a post-hoc analysis of the St. Carlos Gestational Study which included 3312 pregnant women, arranged in 3 groups: normal-weight women (NWw) (2398/72.4%), overweight women (OWw) (649/19.6%) and obese women (OBw) (265/8%). NWw and OBw were grouped as EW women (EWw). We analyzed variables related to adverse pregnancy and neonatal outcomes.

Results: The relative risk (95% CI) for GDM was 1.82 (1.47 to 2.25; p<0.0001) for OWw, and 3.26 (2.45 to 4.35; p<0.0001) in OBw. Univariate analysis showed associations of EW to higher rates of prematurity, birth weight >90th centile, newborns admitted to neonatal intensive care unit (NICU), instrumental delivery and cesarean delivery (all p<0.005). Multivariate analysis, adjusted for parity and ethnicity, showed that EW increased the risk of prematurity, admission to NICU, cesarean and instrumental delivery, especially in EWw without GDM. NWw with GDM had a significantly lower risk of admission to NICU and cesarean delivery, compared with NWw without GDM.

Conclusions: EW is detrimental for pregnancy and neonatal outcomes, and treatment of GDM contributes to lowering the risk in EWw and NWw. Applying the same lifestyle changes to all pregnant women, independent of their weight or GDM condition, could improve these outcomes.

INTRODUCTION

Adverse maternal and neonatal outcomes are determined by two main risk factors: excess weight (EW) and hyperglycemia.1–3 Both are intimately related4–6 where having excess body mass index (BMI) increases the risk of having gestational diabetes mellitus (GDM). Previous studies have shown strong associations between pregestational obesity (OB) and increased maternal and neonatal morbidity,7–15 and similar results were found in those who gained excessive body weight during pregnancy.14–16 On the other hand, GDM significantly increases the risk for obstetric complications.2,3 Considering that both EW and GDM coexist frequently because of their shared physiopathological characteristics derived from insulin resistance, it becomes rather challenging to determine the specific effects on maternal and neonatal outcomes of each one independently.
Recently the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study revealed OB as being an independent risk factor for adverse maternal and neonatal outcomes, where GDM was found to provide an added risk. In this study those women diagnosed with GDM were not treated and only those who met the diagnostic criteria for diabetes were. Changes in lifestyle, including nutritional habits and physical activity, are a key measure adopted in the handling of hyperglycemia in pregnant women. These measures have shown improvements in obstetric and neonatal complications. While a few studies have suggested betterments in women treated before the pregnancy, others where treatment measures were adopted during the pregnancy showed mixed results. These results ranged from lacking improvements in pregnancy outcomes to having some in certain analyzed variables.

The St. Carlos Gestational Study has recently shown a 3.5-fold increase of GDM after the adoption of the International Association of Diabetes and Pregnancy Study Groups criteria (IADPSGc). However, parallel to this increase, a decrease in adverse maternal and neonatal outcomes was observed following the treatment of these women. Hence, this presents an opportunity to analyze EW as an independent risk factor for adverse maternal and neonatal outcomes through evaluation of the potential differences between women with pregestational EW and normal weight (NW). Additionally, we tried to determine whether women with EW and diagnosed with GDM (subjected to a specific intervention and follow-up) had lower risk for maternal and neonatal complications compared with those with EW who did not have GDM (who only received standard maternity care). We hypothesize that the negative impact of EW in pregnancy and neonatal complications can be significantly lowered when GDM is diagnosed and treated. Consequently, we carried out a post-hoc analysis of the St. Carlos Gestational Study.

SUBJECTS AND METHODS

Study design

The St. Carlos Hospital (HCSC) covers a population of 440,000 and it is the only specialized center in the heart of the Community of Madrid where centralized and universal screening of GDM is carried out. Our hospital is equipped with a specialized endocrinology unit (diabetes and pregnancy unit) where the management and follow-up of patients with GDM takes place. In April 2012 our endocrinology department adopted the application of the IADPSGc for the GDM diagnosis, switching from the former use of the Carpenter-Coustan criteria (CCc). This all lead to the emergence of the St. Carlos’ study which in turn motivated this post-hoc analysis.

Study population

A total of 3312 pregnant women receiving prenatal medical care at the HCSC, who were screened for GDM at 24–28 weeks of gestation using an oral glucose tolerance test (OGTT) from April 2011 to March 2013, were included in this study. The population had a mean age of 31.6 years and the mean maternal BMI at the OGTT was 25.8 kg/m². Mean prepregnancy BMI (PPBMI), calculated based on patients’ self-reported prepregnancy body weight (PPBW), was 23 kg/m². Pregnant women were categorized into three groups according to PPBMI: normal-weight women (NWw)<25 kg/m², overweight women (OWw) 25–29.9 kg/m², (649/19.6%) and obese women (OBw)≥30 kg/m², (265/8%). For GDM diagnosis, CCc were applied from April 2011 to March 2012 and IADPSGc from April 2012 to March 2013.

Clinical variables

Demographic and clinical baseline variables regarding maternal characteristics were collected at the time of the OGTT, reflected in Table 1. These variables were based on aspects regarding age at pregnancy diagnosis (years), ethnicity (Caucasian, Hispanic, African, Asian, and others), self-reported maternal PPBW (kg), PPBMI (kg/m²), weight gain until the week of the OGTT, smoking habit, parity, family history of any component of metabolic syndrome (MetS) and history of prior miscarriage or GDM. Since women were followed up until delivery, we also collected data regarding adverse pregnancy and neonatal outcomes related to: gestation (gestational hypertension), delivery (cesarean and instrumental deliveries) and neonate status (prematurity <37 weeks, birth weight <10th centile and >90th centile, admission to neonatal intensive care unit (NICU), Apgar score <7 at 1 min).

GDM—lifestyle treatment procedure

Women diagnosed with GDM were referred to the Diabetes and Pregnancy Unit of the HCSC where they were given lifestyle and dietary recommendations aimed at an optimal glucose control. These recommendations were built on Mediterranean diet principles, based on a daily consumption of at least two servings of vegetables, at least two pieces of fruit, increasing intake of extra virgin olive oil, oily fish, nuts, whole grain cereals and skimmed milk while avoiding processed foods, cakes, pastries, soft drinks and juices. They were simultaneously encouraged to increase their aerobic physical activity, daily when possible. The glycemic targets were defined by fasting and preprandial glucose <90 mg/dL (5.0 mmol/L) and 1-hour postmeal <120 mg/dL (6.6 mmol/L). These measures were not aimed at a weight loss, which however could have happened indirectly. Patients without GDM received a standard pregnancy follow-up at the obstetric clinic. For all pregnant women weight gain during pregnancy depended on their PPBMI, where NWw, OWw and OBw were recommended to gain a total of 11.5–16 kg (0.42 kg/per week), 7–11.5 kg (0.28 kg/per week) and 5–9 kg (0.22 kg/per week), respectively.
| Table 1 | Characteristics of maternal population, gestation and delivery outcomes by prepregnancy BMI (kg/m²) |
|---------|-----------------------------------------------------------------------------------------------|
|         | All <25 kg/m² | 25–29.9 kg/m² | p Value 25–29.9 vs <25 kg/m² | ≥30 kg/m² | p Value ≥30 vs <25 kg/m² | p Value ≥25 vs <25 kg/m² |
| N       | 3312 | 2398 (72.4) | 649 (19.6) | 265 (8.0) | 0.093 | 0.865 | 0.372 |
| Age (year) | 31.6±5.7 | 31.5±5.8 | 32.2±5.6 | 0.0001 | 0.001 | 0.01 |
| BW (kg)  | 69.4±12.5 | 63.3±6.4 | 75.2±7.3 | 0.0001 | 0.001 | 0.002 |
| BMI (kg/m²) | 25.8±3.1 | 23.9±2.4 | 29.0±1.9 | 0.0001 | 0.001 | 0.001 |
| Prepregnancy BW (kg) | 61.9±11.7 | 56.9±6.6 | 69.9±6.9 | 0.0001 | 0.001 | 0.001 |
| Prepregnancy BMI (kg/m²) | 23.0±4.3 | 21.5±2.1 | 27.0±1.4 | 0.0001 | 0.001 | 0.001 |
| ≥5 kg | 1468 (34.0) | 667 (27.8) | 303 (46.7) | 0.001 | 0.001 | 0.001 |
| >5 kg | 2187 (66.0) | 1731 (72.2) | 346 (53.3) | 0.001 | 0.001 | 0.001 |
| Ethnicity (in rows) | | | | | | |
| Caucasian | 2056 (62.1) | 1568 (76.3) | 335 (16.3) | 153 (7.4) | 0.001 | 0.001 |
| Hispanic | 1140 (34.4) | 750 (65.8) | 286 (25.1) | 104 (9.1) | 0.001 | 0.001 |
| African | 39 (1.2) | 35 (89.7) | 2 (5.1) | 2 (5.1) | 0.001 | 0.001 |
| Asian | 59 (1.8) | 31 (52.5) | 23 (39) | 5 (8.5) | 0.001 | 0.001 |
| Others | 18 (0.5) | 13 (72.2) | 3 (16.7) | 2 (11.1) | 0.001 | 0.001 |
| Prenatal smoker | 438 (13.5) | 336 (14.0) | 74 (11.4) | 88 (13) | 0.001 | 0.001 |
| Current smoker | 356 (10.8) | 254 (10.6) | 74 (11.4) | 75 (11.9) | 0.001 | 0.001 |
| Family history of MetS | 1510 (45.6) | 937(39.1) | 385 (59.3) | 188 (70.9) | 0.001 | 0.001 |
| Prior miscarriage | 790 (23.9) | 543 (22.6) | 180 (27.7) | 67 (25.2) | 0.001 | 0.001 |
| Prior GDM | 62 (1.9) | 39 (1.6) | 10 (1.5) | 78 (13.9) | 0.001 | 0.001 |
| CCc GDM-screens (n) | 1750 | 1185 | 421 | 144 | | |
| GDM/NGT (n) | 185/1565 | 68/1117 | 82/339 | 35/109 | 0.0001 | 0.0001 |
| GDM rate (%) | 10.6 | 5.7 | 19.5 | 24.3 | 0.001 | 0.001 |
| Weight gain at screening (kg, GDM/NGT) | 5.9±6.8/ | 7.3±8.0/ | 5.0±4.2/ | 3.1±4.2/ | 0.001 | 0.001 |
| IADPSGc GDM-screens (n) | 1562 | 1213 | 228 | 121 | | |
| GDM/NGT (n) | 542/1020 | 319/894 | 142/86 | 81/40 | 0.0001 | 0.0001 |
| GDM rate (%) | 34.7 | 26.3 | 62.2 | 66.9 | 0.0001 | 0.0001 |
| Weight gain at screening (kg, GDM/NGT) | 5.8±3.8/ | 6.5±3.1/ | 5.2±3.8/ | 3.7±5.3/ | 0.001 | 0.001 |
| GDM pooled RR (95% CI) | 1 | 1.82 (1.47–2.25) | 3.26 (2.45–4.35) | 0.001 | 0.001 |
| Maternal | | | | | | |
| Gestational hypertension | 125 (3.8) | 86 (3.6) | 28 (4.3) | 50.2 | 0.001 | 0.001 |
| Cesarean section | 755 (22.8) | 476 (19.8) | 189 (29.1) | 0.01 | 0.003 | 0.001 |
| Instrumental delivery | 402 (12.1) | 250 (10.4) | 95 (14.7) | 0.013 | 0.01 | 0.014 |

Results expressed as means±SDM or n (%).

BMI, body mass index; BW, body weight; CCc, Carpenter-Coustan criteria; GDM, gestational diabetes mellitus; IADPSGc, International Association of Diabetes and Pregnancy Study Groups criteria; MetS, metabolic syndrome; NGT, normal glucose tolerance; RR, relative risk; WG, weeks of gestation.
Clinical care/education/nutrition/psychosocial research

Statistical analysis
SPSS V.15.0 (SPSS, Chicago, Illinois, USA) was used for statistical analysis. Continuous variables are expressed as mean±standard deviation of mean (SDM), and categorical variables as percentages or numbers. The statistical differences between the averages of continuous variables were determined with the Student’s t-test or non-parametric Mann-Whitney test and categorical variables by the one-way variance tests and χ² test. PPBMI categories for univariate analysis were NWw, OWw and OBw. Multivariate analysis adjusted for ethnicity and parity was performed to assess the risk of overweight (OW) and OB with adverse pregnancy and neonatal outcomes, but due to sample size problems both were included in the same group defined as EW women (EWw). Results for each adverse outcome are presented as ORs with 95% CI. Also, this study’s cohort was stratified as follows into five groups considering BMI and the absence or presence of GDM: (a) NWw, no GDM as reference group (b) NWw, GDM, (c) raw EW, (c1) EWw, no GDM, (c2) EWw, GDM. We proceeded to make comparisons of ORs of each group to the group of reference, and determined associations of different maternal PPBMI categories with different adverse pregnancy and neonatal outcomes. Values of p<0.05 were considered significant.

The study protocol was reviewed and approved by the Ethics Committee of the HCSC and conducted according to the Declaration of Helsinki.

RESULTS
Table 1 shows the characteristics of the studied cohort. NWw, OWw and OBw rates in Caucasians were 76.3%, 16.3% and 7.4%, respectively, whereas the prevalence of EWw seemed to be more frequent in Hispanics (65.8%, 25.1 and 9.1%, respectively) as well as in Asians (52.5%, 39% and 8%, respectively). OWw and OBw compared with NWw had a higher rate of prior miscarriages (27.7% and 25.5% vs 22.6%; p<0.001, respectively), had more frequently a family history of MetS (59.3% and 70.9% vs 39.1%; p<0.001, respectively) and were less frequently primiparous (33.6% and 35.2% vs 48.3%; p<0.001, respectively). No differences related to age, smoking and gestational age at diagnosis were observed. Women with EW (OW and OB) happened to have gained less weight at GDM screening than those with NW (5.2±3.9 kg and 3.6±5.4 kg vs 6.5±4.3 kg; p<0.001, respectively). Table 1 displays weight gain of women with GDM or normal glucose tolerance (NGT) in both CCc and IADPSGc groups. GDM prevalence in the CCc group was of 10.6% (185/1750) and in the IADPSGc group was of 34.7% (185/514). In addition, OWw and OBw had higher GDM rates than NWw, in both the CCc (82/421 (19.5%) and 35/144 (24.3%) vs 68/1185 (5.7%); p<0.0001, respectively) and IADPSGc group (142/228 (62.2%) and 81/121 (66.9%) vs 319/1213 (26.3%); p<0.0001, respectively). The pooled relative risk (95% CI) for GDM was 1.82 (1.47 to 2.25; p<0.0001) for OWw, and 3.26 (2.45 to 4.35; p<0.0001) in OBw. Compared with NWw, those with EW had higher rates of Cesarean section (C-section) (p<0.001) and instrumental delivery (p<0.014).

Table 2 provides information regarding characteristics of fetal development and newborn. EWw compared with NWw had babies with a higher abdominal circumference (AC, cm) in the third trimester (28.5±2.0 vs 27.9±2.5; p<0.025), higher weight estimation (g) (2019±295 vs 1956±263; p<0.0001) and a lower normal intrauterine growth (NIG) for gestational age in the second trimester which prevailed in the third trimester (85.3% vs 87%; p<0.019). Compared with NWw, those with EW had higher rates of prematurity (p<0.0001), newborns with a birth weight >90th centile (p<0.042) and newborns admitted to NICU (p<0.001).

Table 3 shows a multivariate analysis adjusted for ethnicity and parity clustering both OWw and OBw in the same group (EWw), using NWw with no GDM as the reference group. OR for EWw were significantly higher for prematurity (OR 2.42 (95% CI 1.73 to 3.39); p<0.0001), admission to NICU (OR 2.93; 95% CI 2.15 to 3.99; p<0.0001), cesarean delivery (OR 1.53; 95% CI 1.19 to 1.97; p<0.001) and instrumental delivery (OR 1.35; 95% CI 1.04 to 1.76; p<0.026). This tendency was mainly observed in EWw with no GDM, while ORs for EWw with GDM are similar to those found in the reference group. Moreover, NWw with GDM had a significantly lower risk of admission to NICU (OR 0.61; 95% CI 0.39 to 0.95; p<0.03) and C-section (OR 0.42; 95% CI 0.31 to 0.57; p<0.001), in comparison to NWw without GDM. No significant differences were found in other analyzed variables.

DISCUSSION
Data obtained in this study associates EWw with having an increased risk of adverse maternal and neonatal outcomes, in particular in terms of rates of GDM, prematurity, birth weight >90th centile, admission to NICU, cesarean and instrumental delivery. After adjusting for confounding factors, EW continued to be associated with higher rates of prematurity, admission to NICU, C-section and instrumental delivery. Surprisingly, the results of this study suggest that these adverse outcomes seem to be somewhat reduced in EWw with GDM, when this condition was treated. In fact, this group displayed similar risks to NWw with no GDM, leading us to believe that through treatment of GDM adverse pregnancy and neonatal outcomes could be reduced. In addition, NWw with treated GDM had significantly lower rates of admission to NICU and cesarean delivery in comparison to those who did not have GDM. To the best of our knowledge, in all the literature available this is the first study to associate GDM diagnosis with a reduction of adverse pregnancy and neonatal outcomes. However, recently it has been reported how treatment of GDM with nutritional therapy could be associated with having a lower...
|                  | All         | <25 kg/m² | 25–29.9 kg/m² | ≥30 kg/m² | p Value 25–29.9 vs <25 kg/m² | p Value ≥30 vs <25 kg/m² | p Value ≥25 vs <25 kg/m² |
|------------------|-------------|-----------|---------------|-----------|----------------------------|--------------------------|--------------------------|
| **N**            | 3312        | 2398 (72.4) | 649 (19.6)    | 265 (8.0) |                           |                          |                          |
| **Fetal growth** |             |           |               |           |                           |                          |                          |
| GA at 2nd trimester | 20.3±3.8    | 20.2±1.5  | 20.5±8.1      | 0.179     | 20.4±1.2                   | 0.151                    | 0.165                    |
|                  | 4.9±1.0     | 4.9±1.2   | 4.8±0.9       | 0.185     | 4.9±0.6                    | 0.866                    | 0.234                    |
|                  | 15.6±1.5    | 15.5±1.8  | 15.7±1.8      | 0.678     | 15.6±1.5                   | 0.222                    | 0.362                    |
|                  | 3.3±0.7     | 3.3±0.4   | 3.3±0.4       | 0.377     | 3.5±1.9                    | 0.001                    | 0.029                    |
| NIG for GA n (%) | 2882 (87)   | 2096(87.4) | 554 (85.5)    | 0.016     | 230(86.8)                  | 0.067                    | 0.048                    |
| GA at 3rd trimester | 32.1±5.7    | 32.2±6.7  | 32.0±1.0      | 0.549     | 32.0±1.2                   | 0.197                    | 0.468                    |
|                  | 8.2±2.1     | 8.3±2.4   | 8.2±1.0       | 0.800     | 8.2±0.4                    | 0.788                    | 0.723                    |
|                  | 28.1±2.6    | 27.9±2.5  | 28.6±2.5      | 0.034     | 28.5±2.0                   | 0.001                    | 0.025                    |
|                  | 6.2±1.5     | 6.2±1.8   | 6.1±0.3       | 0.809     | 6.1±0.4                    | 0.980                    | 0.791                    |
| Weight estimation (g) | 1968±269    | 1956±263  | 1991±277      | 0.011     | 2019±295                   | 0.002                    | 0.0001                   |
| NIG for GA n (%) | 2931 (86.5) | 2086 (87) | 558 (86)      | 0.049     | 226(85.3)                  | 0.035                    | 0.019                    |
| **Newborn**      |             |           |               |           |                           |                          |                          |
| GA (weeks)       | 39.2±1.8    | 39.1±1.9  | 38.2±1.9      | 0.501     | 38.5±1.1                   | 0.964                    | 0.339                    |
| Prematurity (<37 weeks) | 199 (6.0)  | 94 (3.9)  | 64 (9.8)      | 0.001     | 41 (15.5)                  | 0.0001                   | 0.0001                   |
| Birth weight (g) | 3201±501    | 3170±486  | 3242±513      | 0.288     | 3307±521                   | 0.090                    | 0.083                    |
| Birth weight >90 centile | 148 (4.2)  | 93 (3.8)  | 31 (4.8)      | 0.064     | 24 (9.1)                   | 0.001                    | 0.042                    |
| Birth weight<10 centile | 228 (6.9)  | 170 (7.1) | 38 (5.9)      | 0.091     | 20 (7.5)                   | 0.337                    | 0.411                    |
| Apgar score<7 at 1 min | 120 (3.6)  | 75 (3.1)  | 17 (2.7)      | 0.387     | 28 (10.6)                  | 0.190                    | 0.202                    |
| Admission to NICU | 238 (7.2)  | 110 (4.6) | 80 (12.3)     | 0.001     | 48 (18.1)                  | 0.001                    | 0.001                    |

Results expressed as mean±SDM or n (%).
AC, abdominal circumference; BMI, body mass index; GA, gestational age; NICU, neonatal intensive care unit; NIG, normal intrauterine growth.
risk of having certain adverse pregnancy and neonatal outcomes.\textsuperscript{22}

The rates of OWw (19%) and OBw (8%) are markedly lower to that obtained in the HAPO study\textsuperscript{7} however similar to those provided by other studies performed in the same geographical area as ours\textsuperscript{6,3} which reports the prevalence of EW in women at childbearing age.\textsuperscript{24} In contrast with the HAPO study, where women meeting GDM criteria were not treated, those in our study were the main focus of treatment is on achieving an optimal glycemic control mainly managed by changing these women’s lifestyle, which indirectly positively affected

### Table 3

| Outcome                          | OR   | 95% CI           | p Value |
|----------------------------------|------|------------------|---------|
| Prematurity &lt;37 weeks         |      |                  |         |
| No excess weight no GDM          | 1    |                  |         |
| GDM                              | 0.742| 0.437 to 1.258   | 0.267   |
| Excess weight                    | 2.423| 1.734 to 3.385   | 0.0001  |
| No GDM                           | 3.144| 2.148 to 4.593   | 0.0001  |
| GDM                              | 1.161| 0.539 to 2.369   | 0.639   |
| Birth weight &lt;10 centile      |      |                  |         |
| No excess weight no GDM          | 1    |                  |         |
| GDM                              | 0.893| 0.592 to 1.346   | 0.588   |
| Excess weight                    | 1.116| 0.816 to 1.536   | 0.453   |
| No GDM                           | 1.145| 0.785 to 1.677   | 0.450   |
| GDM                              | 1.023| 0.562 to 1.835   | 0.967   |
| Birth weight &gt;90 centile      |      |                  |         |
| No excess weight no GDM          | 1    |                  |         |
| GDM                              | 0.979| 0.569 to 1.682   | 0.937   |
| Excess weight                    | 1.082| 0.722 to 1.622   | 0.701   |
| No GDM                           | 1.116| 0.711 to 1.689   | 0.952   |
| GDM                              | 1.362| 0.663 to 2.798   | 0.401   |
| Apgar score &lt;7 at 1 min       |      |                  |         |
| No excess weight no GDM          | 1    |                  |         |
| GDM                              | 0.827| 0.452-1.514      | 0.539   |
| Excess weight                    | 1.270| 0.755 to 2.136   | 0.220   |
| No GDM                           | 1.273| 0.672 to 2.413   | 0.284   |
| GDM                              | 1.363| 0.544 to 3.423   | 0.511   |
| Admission to NICU                |      |                  |         |
| No excess weight no GDM          | 1    |                  |         |
| GDM                              | 0.610| 0.390 to 0.953   | 0.030   |
| Excess weight                    | 2.929| 2.154 to 3.983   | 0.0001  |
| No GDM                           | 4.051| 2.735 to 6.106   | 0.0001  |
| GDM                              | 1.650| 1.013 to 2.716   | 0.049   |
| Gestational hypertension         |      |                  |         |
| No excess weight no GDM          | 1    |                  |         |
| GDM                              | 0.658| 0.394 to 1.100   | 0.110   |
| Excess weight                    | 1.059| 0.686 to 1.637   | 0.795   |
| No GDM                           | 0.738| 0.347 to 1.531   | 0.403   |
| GDM                              | 1.229| 0.717 to 2.107   | 0.454   |
| Cesarean section                 |      |                  |         |
| No excess weight no GDM          | 1    |                  |         |
| GDM                              | 0.419| 0.310 to 0.566   | 0.001   |
| Excess weight                    | 1.528| 1.187 to 1.967   | 0.001   |
| No GDM                           | 1.932| 1.393 to 2.679   | 0.0001  |
| GDM                              | 1.050| 0.701 to 1.575   | 0.724   |
| Instrumental delivery            |      |                  |         |
| No excess weight no GDM          | 1    |                  |         |
| GDM                              | 1.218| 0.906 to 1.636   | 0.191   |
| Excess weight                    | 1.349| 1.036 to 1.755   | 0.026   |
| No GDM                           | 1.540| 1.077 to 2.201   | 0.010   |
| GDM                              | 1.071| 0.714 to 1.626   | 0.404   |

BMI, body mass index; GDM, gestational diabetes mellitus; NICU, neonatal intensive care unit.
weight gain. The main cornerstones of this intervention was both consuming low caloric density and glycemic index foods, achieved through incorporation of a daily intake of nuts and whole cereals as well as avoidance of foods with a high glycemic index. Women who followed these recommendations had better outcomes than EWw with no GDM. Whether these benefits come from the controlled weight gain that consequently this intervention entails remains unclear because, unfortunately, we were unable include and therefore analyze weight gain after GDM screening in the no GDM group.

As would be expected we found that pregestational EW was associated with higher rates of Hispanic ethnicity, family history of MetS (including OB), obstetric history of prior miscarriages, GDM, and multiparity. After adjustment, pregestational EW remains associated with higher risks of prematurity, admission to NICU, C-section and instrumental delivery. These findings are in the line with what has been published previously, where OB increases the risk of prematurity, cesarean delivery and admission to NICU. Pregestational EW had a significantly higher 2.4-fold risk of prematurity, in particular regarding EWw with no GDM (3.1-fold risk). OB is linked to a proinflammatory status caused by both production of adipokines and cytokines. These make spontaneous labor more probable as they promote cervical ripening and contractions, following stimulation of prostaglandins. EW also had a higher risk of instrumental and cesarean deliveries possibly caused by excess adipose tissue in the pelvis which hinders the birth canals.

It could also be to slow cervical dilation in EWw, leading to a longer labor and ultimately resulting in further complications for the mother and the newborn. In fact, babies of EWw have an increased risk of admission to NICU, which could be due to prematurity and loss of fetal well-being. Meanwhile, prematurity, C-section, instrumental delivery and admission to NICU rates were lower in EWw with GDM than those without GDM. These results suggest a possible association between diagnosed GDM and better maternal and neonatal outcomes. All these benefits could be because women diagnosed with GDM received specific management (aimed at a control of weight gain and glycemia levels) designed for them. Meanwhile those who did not have GDM received standard follow-up alone.

This study is not without limitations. First, the fact that it is a cross-sectional study and lacks of interventional nature prevents us from being able to establish causality in our results. Moreover, our study population included women diagnosed with GDM based on two different diagnostic criteria, where during the first period the IADPSGc were used and in the second it was the IADPSGc. Another important limitation to consider is the differences in OB rates between this study and others like the HAPO study where rates of OB were much higher than ours. Our sample size was not big enough, forcing us to unify OWw and OBw in one same group of EWw and possibly entailing differences between the results.

This could have led to differences between our results and those of other studies. Furthermore, pregestational weight is self-reported by patients leading to a possible loss of accuracy of this collected data. Finally, registering weight gain of pregnant women only until GDM screening is an important limitation. Despite this, our study shows associations between EW and higher rates of adverse outcomes. More importantly, it shows how proper treatment of GDM provides a protective effect against these outcomes.

The findings of this study indicate associations between EW and adverse maternal and neonatal outcomes, where GDM treatment seems to be protective. The loss of weight prior to the pregnancy in EWw should be as important a recommendation as supplementation with folic acid and iodine. While designing the appropriate lifestyle for EWw, the attention should focus on the content itself (a healthy diet, performance of regular physical activity…) but it is also detrimental to facilitate the adherence to this change. A main goal should be to consider counseling as a key aspect, where these women should be educated about GDM risks, as well as discussing individual impediments they might encounter to fulfill the lifestyle changes. In addition, providing all pregnant women with the same interventional tools used for GDM treatment, regardless of their GDM condition or PPBMI, should be envisioned as a possible universal clinical practice.

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