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Title:

Excessive gestational weight gain is an independent risk factor for gestational diabetes mellitus in singleton pregnancies: results from a French cohort study.

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Highlights:

- This study evaluates the impact of maternal obesity and excessive GWG on pregnancy.
- Maternal obesity and excessive GWG are associated with gestational diabetes, C-section and macrosomia.
- This study confirms that excessive GWG is an independent risk factor for gestational diabetes.

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Abstract: 274 words

References: 38

Tables/figures: 5 tables and 1 figure

Supplementary appendix: 3 tables

Abstract:

Objective: Increase in prevalence of maternal obesity worldwide raises concern among health professionals. Our purpose was to evaluate the impact of maternal obesity and of excessive gestational weight gain (GWG) on the course of singleton pregnancies in a French maternity ward.

Study design: 3599 consecutive women who delivered from April 2013 to May 2015 at Brest University Hospital were included in HPP-IPF cohort study, a study designed to evaluate clinical and biological determinants of postpartum hemorrhage (PPH). Maternal obesity was defined by a pre-pregnancy Body Mass Index (BMI) ≥ 30 kg/m² and excessive GWG was defined according to the Institute of Medicine 2009 guidelines. Obstetric complications (including gestational diabetes mellitus (GDM), gestational hypertension, pre-eclampsia, venous thromboembolism, PPH, cesarean section (C-section) and macrosomia) were collected prospectively in a standardized case report form. For each complication, Odd Ratios (OR) according to pre-pregnancy BMI and GWG were calculated in univariable and multivariable analyses.

Results: Out of the 3162 women analyzed for this report, 583 (18.4%) were overweight, 400 (12.7%) were obese and 36.6% had excessive GWG. In multivariable analysis, after adjustment for confounding factors, obese women were at increased risk of GDM (OR 5.83, 95%CI 4.37-7.79), PPH (OR 1.69, 95%CI 1.19-2.41), C-section (OR 2.50, 95%CI 1.92-3.26) and macrosomia (OR 1.90, 95%CI 1.31-2.76). Similarly, women with excessive GWG were at increased risk of GDM (OR 1.55, 95%CI 1.17-2.06), C-section (OR 1.46, 95%CI 1.16-1.83) and macrosomia (OR 2.09, 95%CI 1.50-2.91).

Conclusions: Maternal obesity and excessive GWG are independent risk factors for GDM, C-section and macrosomia in singleton pregnancies. Further studies are needed to evaluate if a lifestyle intervention aiming at avoiding excessive GWG could improve clinical outcomes in pregnant women.

Trial registration: NCT02884804.

Key words: Obesity; Gestational Weight Gain; Pregnancy; Diabetes, Gestational; Cesarean Section; Fetal Macrosomia.

Abbreviations:

BMI = body mass index

C-section = cesarean section

CI = confidence interval

GDM = gestational diabetes mellitus

GWG = gestational weight gain

OR = odd ratio

PPH = postpartum hemorrhage

VTE = venous thromboembolism

WG = weeks of gestation

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Main text:

1. Introduction:

The prevalence of maternal obesity has increased during the last thirty years, along with obesity outbreak worldwide [1]. In a French national survey conducted by EPOPE (équipe de recherche en EPidémiologie Obstétricale PERinatale et PEdiatrique), the proportion of obese women (Body Mass Index (BMI) ≥ 30 kg/m²) rose steadily from 7.5% in 2003 to 11.8% in 2016 [2]. During the same period, the authors noticed an increase in gestational diabetes mellitus (GDM) from 7.2% to 10.8% [2].

This spreading trend has raised a lot of concern among health professionals in charge of pregnant women. Several studies focusing on the impact of pre-pregnancy maternal BMI and excessive gestational weight gain (GWG) have shown deleterious effects of these two parameters on the progress of pregnancy and delivery [3-7]. A retrospective Japanese study based on a register of 97 157 women with singleton pregnancies concluded that a high pre-pregnancy maternal BMI was associated with an increased incidence of GDM, gestational hypertension, macrosomia, cesarean section (C-section), postpartum hemorrhage (PPH), and post-term birth [8]. In all pre-pregnancy BMI category groups, excessive GWG was associated with a higher frequency of macrosomia. Besides, a recent meta-analysis on 4429 women with singleton pregnancies found that excessive GWG was associated with an increased risk of C-section and macrosomia [9]. The impact of GWG on the risk of GDM is more controversial [5,6,8].

In 2009, the Institute of Medicine (IOM) published guidelines for weight gain during pregnancy according to maternal pre-pregnancy BMI in order to limit obstetric complications associated with inappropriate GWG [10]. For obese women, advised GWG is between five and nine kg, whereas for women with a normal pre-pregnancy BMI, advised weight gain is between 11.5 and 16 kg.

The aim of this report was to evaluate the impact of maternal obesity and excessive GWG, defined according to the IOM 2009 guidelines, on the course of pregnancy and delivery, in women with singleton pregnancies who delivered consecutively in a French maternity ward.

2. Material and Methods:

2.1. Design and setting:

All consecutive unselected women admitted for delivery in the maternity ward of Brest University Hospital between April 1, 2013 and May 29, 2015 were asked to participate in an observational study called « HPP-IPF » (clinicaltrials.gov identifier: NCT02884804) initially designed to evaluate clinical and biological determinants of PPH [11].

Women who had expressed their opposition to participate to the study were excluded.

2.2. Population:

For this report, we restricted the population to singleton pregnancies with a delivery after 24 weeks of gestation (WG). Women for which the values of pre-pregnancy BMI or GWG were not recorded in the medical files were not included in this study.

2.3. Variables:

Clinical data were collected by midwives and obstetricians during antenatal care visits, labour and delivery, and recorded by trained research assistants in a standardized electronic case report form.

This form included maternal data (socio-demographic characteristics, personal medical, surgical and obstetric history), as well as all data on the course of pregnancy and delivery.

Maternal obesity was defined by a pre-pregnancy BMI ≥ 30 kg/m² and excessive GWG was defined according to the Institute of Medicine 2009 guidelines.

Pre-pregnancy BMI were recorded for all women at the first visit (before 15 WG). Pre-pregnancy BMI of all participants were classified into four categories according to the IOM 2009 guidelines for gain weight during pregnancy [10]: underweight for a BMI < 18.5 kg/m², normal for a BMI between 18.5 and 24.9 kg/m², overweight for a BMI between 25 and 29.9 kg/m² and obese for a BMI ≥ 30 kg/m².

GWG was defined as the difference between the weight at the last pregnancy visit (maximum one month before birth) and the weight at the first visit. GWG were classified into three categories according to the same guidelines [10]: inadequate GWG (below recommended GWG), adequate GWG or excessive GWG (above recommended GWG).

2.4. Outcomes:

In HPP-IPF study, the main outcome was immediate PPH, defined according to the French 2014 guidelines as an estimated blood loss > 500 ml, whatever the mode of delivery [11]. In

this report, the following other obstetric complications were also reported: GDM, gestational hypertension, pre-eclampsia, venous thromboembolism (VTE) during pregnancy, C-section and macrosomia.

GDM was diagnosed using a fasting blood glucose test between 24 and 28 WG.

Gestational hypertension and pre-eclampsia were defined according to the American College of Obstetricians and Gynecologists' definition published in 2013 [12].

VTE was defined as a diagnosis of distal or proximal deep vein thrombosis or pulmonary embolism assessed using objective, standardized and validated criteria. All VTE were validated by experienced physicians not involved in patient's care.

Macrosomia was defined *a posteriori* as a newborn weight ≥ 4000 grams.

Finally, we distinguished scheduled C-section from C-section performed in emergency.

2.5. Statistical analysis:

Continuous variables (in particular BMI, GWG and newborn weight) were categorized using standard clinical definitions. Categorical variables (e.g. parity) were redefined according to relevant class for analysis. Descriptive statistics were used to summarize women's characteristics. Continuous variables were presented as median with interquartile range (IQR), and categorical variables as counts and percentage.

Univariable logistic regression analysis was used to assess the association between obesity, excessive GWG and each obstetric complication. Unadjusted odds ratios (OR) were calculated and reported with their 95% confidence intervals (CI).

To determine independent predictors for each obstetric complication, age, parity, geographical origin, tobacco use, gestational age, preexisting diabetes and preexisting chronic hypertension, as well as other informative variables with a p value $\leq 15\%$ in univariable analyses, were included in a multivariable logistic regression model. Adjusted ORs and their 95% CIs were calculated.

Missing data were not replaced for univariable and multivariable analyses.

Statistical significance was considered with p values less than 0.05. All statistical tests were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

3. Results:

3.1. General results:

Between April 2013 and Mai 2015, 4036 women delivered from April 2013 to Mai 2015 at Brest University Hospital and 3599 were included in HPP-IPF cohort study after oral informed consent. 437 women were excluded of this study because of missing data on pre-pregnancy BMI and/or GWG or because of gemellar pregnancy or a delivery before 24 WG. Finally, 3162 women were analyzed in this report (**Figure 1**).

Out of these 3162 women, 583 (18.4%) were overweight and 400 (12.7%) were obese before pregnancy (**Table 1**). 1156 (36.6%) women had excessive GWG and 968 (30.6%) had inadequate GWG. In other words, 67.2% of the study population did not follow the IOM 2009 guidelines for weight gain during pregnancy (**Supplement S1**). Obese and overweight women had more frequently excessive GWG than women with normal BMI (52.3%) or underweight women (54%).

3.2. Obstetric complications according to pre-pregnancy BMI:

Compared to women with a normal pre-pregnancy BMI, in univariable analysis, both overweight and obese women were at increased risk of GDM (OR 2.62, 95%CI, 2.00-3.44 and OR 5.89, 95%CI, 4.50-7.71 respectively) and C-section (OR 1.52, 95%CI 1.21-1.90 and OR 2.41, 95%CI, 1.89-3.06 respectively) (**Table 2**).

Overweight women were also at increased risk of gestational hypertension (OR 2.50, 95%CI 1.05-5.96) and VTE during pregnancy (OR 8.35, 95%CI 1.62-43.14), whereas obese women were at increased risk of PPH (OR 1.75, 95%CI 1.26-2.43) and macrosomia (OR 2.02, 95%CI 1.43-2.85) (**Table 3**).

In multivariable analysis, after adjustment for confounding factors, both overweight and obese women remained associated with GDM (OR 2.56, 95%CI, 1.92-3.42 and OR 5.83, 95%CI, 4.37-7.79 respectively) and C-section (OR 1.49, 95%CI, 1.16-1.91 and OR 2.50, 95%CI, 1.92-3.26 respectively) (**Table 4**).

Overweight women were also at increased risk of VTE during pregnancy (OR 6.46, 95%CI 1.16-36.03), whereas obese women were at increased risk of PPH (OR 1.69, 95%CI, 1.19-2.41) and macrosomia (OR 1.90, 95%CI, 1.31-2.76).

3.3. Obstetric complications according to GWG:

Compared to women with an adequate GWG, in univariable analysis, women with excessive GWG presented increased risks of GDM (OR 1.44, 95%CI 1.10-1.87), C-section (OR 1.43, 95%CI, 1.16-1.77) and macrosomia (OR 2.05, 95%CI, 1.50-2.79) (**Supplement S2**).

Women with inadequate GWG were only at increased risk of GDM (OR 1.52, 95%CI 1.16-2.00).

In multivariable analysis, women with excessive GWG had increased risks of GDM (OR 1.55, 95%CI, 1.17-2.06), C-section (OR 1.46, 95%CI, 1.16-1.83) and macrosomia (OR 2.09, 95%CI, 1.50-2.91) (**Table 5**).

When compared to women with an adequate GWG, women with an inadequate GWG had also an increased risk of GDM (OR 1.59, 95%CI 1.19-2.13).

Furthermore, among women with excessive GWG, women with a normal pre-pregnancy BMI presented only an increased risk of macrosomia (OR 1.87, 95%CI, 1.22-2.87) (**Supplement S3**).

4. Comment:

In this cohort study of 3162 consecutive French women with singleton pregnancies, maternal obesity and excessive GWG appear as independent risk factors for GDM, C-section and macrosomia. Our findings also support that maternal obesity is associated with PPH but not with VTE during pregnancy, gestational hypertension or pre-eclampsia.

Our study has some limitations. It is a monocentric study conducted in a level 3 maternity ward and our population could be unrepresentative of all pregnant women delivering in France, limiting the generalizability of our results. Obstetric complications such as VTE, gestational hypertension and pre-eclampsia were infrequent, thus the associations between these complications and maternal obesity or excessive GWG could have been missed. Then, the exact chronology of GWG according to the trimester of pregnancy was not recorded. Similarly, the influence of maternal obesity according to class of obesity was not tested. Last, the impact of maternal socioeconomic level on the occurrence of excessive GWG was not evaluated, what could have been relevant to target at best pregnant women at risk needing a closer supervision.

Our study has also some strengths. First, pregnant women were recruited consecutively. Then, data on pregnancies and deliveries were collected systematically and prospectively, so few data were missing.

Our findings are consistent with data from the medical literature on pregnant women.

The impact of maternal obesity on obstetric complications is well documented, in mothers, as well as in newborns. Thus, studies conclude unanimously that macrosomia and C-

section are strongly associated with maternal obesity, what we confirmed in this study [5,7,14,15].

In several large studies, obese pregnant women appeared to be at increased risk of gestational hypertension, pre-eclampsia and GDM [5-7,16-18]. We only confirmed that maternal obesity was associated with GDM. The association between maternal obesity and GDM is supported by the fact that maternal obesity epidemic progresses concomitantly with GDM epidemic, as illustrated by the results of the French survey EPOPE [2]. Moreover, maternal hyperglycemia in the context of obesity with GDM, is believed to promote placental glucose transfer, resulting in increased fetal growth and macrosomia [19], what is consistent with our results.

In our study, PPH was also associated with maternal obesity but not with excessive GWG. Stones RW *et al* also reported in 1993 an increased risk of PPH in obese pregnant women [20]. Fyfe *et al* noted a twofold increased risk of major PPH in obese women compared to women with a normal BMI [21]. According to Wetta LA *et al*, this susceptibility could be explained by uterine atony, which accounts for up to 80% of PPH cases [22]. A recent population-based cohort study identified that in women with a normal pre-pregnancy BMI and in overweight women, the risk of PPH increased also with GWG [23]. However, in this study, definitions of GWG and of PPH were different from those used in our study.

The impact of excessive GWG on other obstetric complications has also been evaluated in numerous studies.

Liu *et al* assessed in a retrospective Chinese study of 2973 singleton pregnancies that, in nulliparous women, excessive GWG increased the incidence of C-section and macrosomia, what we confirmed in this study [24].

However, they also found an association between excessive GWG and pre-eclampsia, what we did not bring out. Similarly, a Canadian population-based cohort of women with singleton gestations delivered between 2001 and 2007 found increased rates of macrosomia in case of excessive GWG, independently of maternal pre-pregnancy BMI [25]. This study also noted an association between excessive GWG and gestational hypertension, what we were not able to demonstrate. A meta-analysis confirmed the association between excessive GWG and macrosomia, as well as C-section [26].

An association was also described between excessive GWG and GDM [27-30] but data from the literature are contradictory. Thus, some studies found no association between excessive GWG and GDM and on the contrary an association between inadequate GWG and

GDM [5,6,7,31]. Our study reveals that both women with inadequate GWG and women with excessive GWG are at increased risk of GDM, compared to women with normal GWG. It is more intuitive to admit that excessive GWG could be associated with an increased risk of GDM. Indeed, women who gain excessive weight during pregnancy are more susceptible to achieve a BMI ≥ 25 kg/m² and to become overweight or obese, which is, in itself, a risk factor for GDM. The association of an inadequate GWG with GDM is less obvious. Some authors have speculated that women diagnosed with GDM at second trimester of pregnancy may have received more advice about weight control and paid more attention to diet and exercise during the third trimester, what would have strongly limited gain weight [31].

It is also interesting to note that, in our study, women with a normal pre-pregnancy BMI who had an excessive GWG suffered more macrosomia but not more GDM. Indeed, 80% of macrosomia occur in the absence of maternal diabetes [32].

There are some unresolved issues related to our topic's study. GWG analysis is of known interest but we did not record the exact chronology of GWG, what could have been useful to identify the trimester of pregnancy the most at risk of future obstetric complications. This information would be of great interest to monitor and advise more precisely pregnant women throughout pregnancy in order to avoid obstetric complications associated with excessive GWG. Indeed, two Chinese studies showed that an excessive GWG in early pregnancy (before 17 WG in the first study and before 20 WG in the second study) was a risk factor for GDM [33,34].

Finally, our study revealed that up to 67.2% of the pregnant women did not follow the IOM 2009 guidelines for weight gain during pregnancy [10]. Obese and overweight women had more frequently excessive GWG than women with a normal BMI or than underweight women, what means that pregnancy supervising and counseling must be strengthened in this particular population who is the most at risk of obstetric complications [35]. Excessive GWG is a potentially modifiable risk factor for obstetric complications in pregnant women. Some studies reported a positive impact of diet and physical activity interventions to reduce excessive GWG and incidence of GDM [36]. Nevertheless, two multicenter randomized controlled trials evaluating the effect of behavioral intervention in obese pregnant women found no benefit of such an intervention on prevention of GDM or macrosomia, in spite of a better control of GWG [37,38]. However, health professionals must keep on monitoring closely diet regimen, weight gain and physical activity in obese pregnant women to prevent short and long-term complications for them and for their offspring.

5. Conclusion:

The results of this observational study conducted in a French maternity ward confirm that maternal obesity and excessive GWG are independent risk factors for GDM, C-section and macrosomia in singleton pregnancies. Further studies are needed to evaluate if a lifestyle intervention aiming at avoiding excessive GWG could improve clinical outcomes in pregnant women.

Declarations:

Ethics approval and consent to participate:

In France, observational studies must be approved by the local ethics committee and participants must give their oral consent (non-opposition procedure), but they do not have to sign a written consent.

An information letter explaining the purpose of the study was given to every woman admitted to Brest maternity ward for delivery. In the meantime, the investigator explained the study orally to the woman. If the woman gave her oral consent to participate in the study, the investigator had to sign the information letter, give her a copy of it and store it in her medical file.

Thus, informed oral consents were obtained from all participants.

All methods were carried out in accordance with relevant guidelines and regulations under Ethics approval.

This research has been approved by the West 6 Ethical Research Committees, the Advisory Committee for Data Processing in Health Research (CCTIRS) and the National Commission for Data Protection and Liberties (CNIL-France).

The West 6 ethics committee approved the procedure for verbal consent on August the 23th 2011, according to the 2004 French Public Health law on non-interventional research.

Availability of data and materials:

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interest:

The authors state that they have no conflict of interest.

Authors' contribution:

M. Lautrédou designed the study, collected, analyzed and interpreted the data; G. Drugmanne participated in the elaboration of the data form, collected data and ensured the good progress of the study; E. Nowak contributed to the statistical analyses; PF. Dupré, F. Anouilh, C. Trémouilhac, D. Briend, C. Salomon, and P. Merviel contributed to the study execution and inclusion of women; L. Gourhant, E. Le Moigne, K. Lacut and S. Robin contributed to the data interpretation; B. Pan Petesch designed the study, contributed to the study execution and the data interpretation; C. de Moreuil contributed to the data interpretation and wrote the manuscript. All authors revised the manuscript and approved the final version to be published.

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Legends of figures and tables:

Figure 1: Flow chart of the study

WG = weeks of gestation; BMI: body mass index; GWG: gestational weight gain.

Table 1: Maternal characteristics and obstetric complications according to pre-pregnancy body mass index and gestational weight gain of the 3599 pregnant women.

BMI = body mass index; C-section = cesarean section; GDM = gestational diabetes mellitus; GWG = gestational weight gain; PPH = postpartum hemorrhage; VTE = venous thromboembolism; WG = weeks of gestation.

Table 2: Obstetric complications according to pre-pregnancy BMI in univariable analysis.

*OR (95% CI): odds ratio and 95% confident interval.

C-section = cesarean section; GDM = gestational diabetes mellitus; VTE = venous thromboembolism.

Table 3: Obstetric complications according to pre-pregnancy BMI in multivariable analysis.

OR (95% CI): odds ratio and 95% confident interval.

Confounding factors included in the multivariable analysis were: age, parity, geographical origin, tobacco use, gestational age, preexisting diabetes and preexisting chronic hypertension.

C-section = cesarean section; GDM = gestational diabetes mellitus; VTE = venous thromboembolism.

Table 4: Obstetric complications according to gestational weight gain in univariable analysis.

OR (95% CI): odds ratio and 95% confident interval.

C-section = cesarean section; GDM = gestational diabetes mellitus; VTE = venous thromboembolism.

Table 1: Maternal characteristics and obstetric complications according to pre-pregnancy body mass index and gestational weight gain of the 3599 pregnant women.

Variable		BMI (kg/m ²)				GWG (kg)		
		Underweight	Normal	Overweight	Obese	Inadequate	Adequate	Excessive
n		247	1932	583	400	968	1038	1156
Age	<20	22 (8.9)	49 (2.5)	13 (2.2)	5 (1.3)	31 (3.2)	21 (2.0)	37 (3.2)
	≥35	40 (16.2)	346 (17.9)	122 (20.9)	92 (23.0)	191 (19.7)	193 (18.6)	216 (18.7)
	[20-35[185 (74.9)	1537 (79.6)	448 (76.9)	303 (75.7)	746 (77.1)	824 (79.4)	903 (78.1)
Geographical origin	African	8 (3.2)	104 (5.4)	54 (9.3)	35 (8.8)	56 (5.8)	49 (4.7)	96 (8.3)
	Asian	4 (1.6)	24 (1.2)	6 (1.0)	4 (1.0)	13 (1.3)	12 (1.2)	13 (1.1)
	European	217 (87.9)	1638 (84.8)	467 (80.1)	329 (82.3)	816 (84.3)	877 (84.5)	958 (82.9)
Tobacco use		92 (37.2)	557 (28.8)	158 (27.1)	113 (28.3)	258 (26.7)	292 (28.1)	370 (32.0)
Preexisting hypertension		3 (1.2)	22 (1.1)	11 (1.9)	12 (3.0)	15 (1.5)	13 (1.3)	20 (1.7)
Preexisting diabetes		1 (0.4)	13 (0.7)	5 (0.9)	10 (2.5)	9 (0.9)	9 (0.9)	11 (1.0)
Parity	0	114 (46.2)	875 (45.3)	228 (39.1)	124 (31.0)	399 (41.2)	413 (39.8)	529 (45.8)
	1-2	121 (49.0)	954 (49.4)	310 (53.2)	222 (55.5)	492 (50.8)	561 (54.0)	554 (47.9)
	≥3	12 (4.8)	103 (5.3)	45 (7.7)	54 (13.5)	77 (8.0)	64 (6.2)	73 (6.3)
Assisted pregnancy		11 (4.5)	89 (4.6)	26 (4.5)	17 (4.3)	46 (4.8)	53 (5.1)	44 (3.8)
GDM		21 (8.5)	146 (7.6)	103 (17.7)	130 (32.5)	139 (14.4)	103 (9.9)	158 (13.7)
Gestational hypertension		2 (0.8)	12 (0.6)	9 (1.5)	4 (1.0)	6 (0.6)	6 (0.6)	15 (1.3)
Pre-eclampsia		1 (0.4)	30 (1.6)	15 (2.6)	11 (2.8)	13 (1.3)	17 (1.6)	27 (2.3)
VTE during pregnancy		1 (0.4)	2 (0.1)	5 (0.9)	1 (0.3)	5 (0.5)	2 (0.2)	2 (0.2)
C-section		38 (15.4)	325 (16.8)	137 (23.5)	131 (32.8)	177 (18.3)	183 (17.6)	271 (23.4)
Scheduled C-section		10 (4.0)	127 (6.6)	39 (6.7)	52 (13.0)	74 (7.6)	60 (5.8)	94 (8.1)

Emergency C-section		28 (11.3)	198 (10.2)	98 (16.8)	79 (19.8)	103 (10.6)	123 (11.8)	177 (15.3)
PPH		21 (8.5)	160 (8.3)	62 (10.6)	55 (13.8)	77 (8.0)	91 (8.8)	130 (11.2)
Macrosomia		5 (2.0)	127 (6.6)	51 (8.7)	50 (12.5)	32 (3.3)	64 (6.2)	137 (11.9)
Induction of labour		69 (27.9)	464 (24.0)	193 (33.1)	154 (38.5)	228 (23.6)	274 (26.4)	378 (32.7)
Term at delivery (WG)	<37	30 (12.1)	153 (7.9)	54 (9.3)	38 (9.5)	128 (13.2)	77 (7.4)	70 (6.1)
	>41	19 (7.7)	220 (11.4)	69 (11.8)	46 (11.5)	66 (6.8)	108 (10.4)	180 (15.6)
	[37-41]	198 (80.2)	1559 (80.7)	460 (78.9)	316 (79.0)	774 (80.0)	853 (82.2)	906 (78.4)

BMI = body mass index; C-section = cesarean section; GDM = gestational diabetes mellitus; GWG = gestational weight gain; PPH = postpartum hemorrhage; VTE = venous thromboembolism; WG = weeks of gestation.

Table 2: Obstetric complications according to pre-pregnancy BMI in univariable analysis.

Obstetric complications	Underweight vs normal	Overweight vs normal	Obese vs normal	p*
Unadjusted OR (CI 95%)				
GDM	1.14 (0.70-1.83)	2.62 (2.00-3.44)	5.89 (4.50-7.71)	< 0.001
Gestational hypertension	1.31 (0.29-5.87)	2.50 (1.05-5.96)	1.61 (0.52-5.02)	0.228
Pre-eclampsia	0.26 (0.04-1.90)	1.67 (0.89-3.12)	1.79 (0.89-3.59)	0.088
VTE during pregnancy	3.92 (0.35-43.42)	8.35 (1.62-43.14)	2.42 (0.22-26.74)	0.08
Postpartum hemorrhage	1.02 (0.63-1.64)	1.31 (0.96-1.79)	1.75 (1.26-2.43)	0.006
C-section	0.90 (0.62-1.30)	1.52 (1.21-1.90)	2.41 (1.89-3.06)	< 0.001
Scheduled C-section	0.60 (0.31-1.16)	1.02 (0.70-1.48)	2.12 (1.51-2.99)	< 0.001
Macrosomia	0.29 (0.12-0.72)	1.36 (0.97-1.91)	2.02 (1.43-2.85)	< 0.001

*OR (95% CI): odds ratio and 95% confident interval.

C-section = cesarean section; GDM = gestational diabetes mellitus; VTE = venous thromboembolism.

Table 3: Obstetric complications according to pre-pregnancy BMI in multivariable analysis.

Obstetric complications	Underweight vs normal	Overweight vs normal	Obese vs normal	p**
Adjusted OR (CI 95%)				
GDM	1.18 (0.72-1.93)	2.56 (1.92-3.42)	5.83 (4.37-7.79)	< 0.001
Pre-eclampsia	0.20 (0.03-1.55)	1.91 (0.96-3.81)	1.55 (0.63-3.80)	0.077
VTE during pregnancy	4.36 (0.39-48.63)	6.46 (1.16-36.03)	2.70 (0.24-30.47)	0.199
Postpartum hemorrhage	1.03 (0.63-1.69)	1.29 (0.93-1.78)	1.69 (1.19-2.41)	0.024
C-section	0.85 (0.57-1.25)	1.49 (1.16-1.91)	2.50 (1.92-3.26)	< 0.001
Macrosomia	0.20 (0.06-0.64)	1.32 (0.92-1.89)	1.90 (1.31-2.76)	< 0.001

OR (95% CI): odds ratio and 95% confident interval.

Confounding factors included in the multivariable analysis were: age, parity, geographical origin, tobacco use, gestational age, preexisting diabetes and preexisting chronic hypertension.

C-section = cesarean section; GDM = gestational diabetes mellitus; VTE = venous thromboembolism.

Table 4: Obstetric complications according to gestational weight gain in univariable analysis.

Obstetric complications	Gestational Weight Gain		p*
	Inadequate vs adequate	Excessive vs adequate	
Unadjusted OR (CI 95%)			
GDM	1.52 (1.16-2.00)	1.44 (1.10-1.87)	0.005
Gestational hypertension	1.07 (0.35-3.34)	2.26 (0.87-5.85)	0.132
Pre-eclampsia	0.82 (0.40-1.69)	1.44 (0.78-2.65)	0.211
VTE during pregnancy	2.69 (0.52-13.90)	0.90 (0.13-6.38)	0.298
Postpartum hemorrhage	0.91 (0.66-1.24)	1.32 (0.99-1.74)	0.029
C-section	1.05 (0.83-1.31)	1.43 (1.16-1.77)	< 0.001
Scheduled C-section	1.35 (0.95-1.92)	1.44 (1.03-2.02)	0.088
Macrosomia	0.52 (0.34-0.80)	2.05 (1.50-2.79)	< 0.001

OR (95% CI): odds ratio and 95% confident interval.

C-section = cesarean section; GDM = gestational diabetes mellitus; VTE = venous thromboembolism.

Table 5: Obstetric complications according to gestational weight gain in multivariable analysis.

Obstetric complications	Gestational Weight Gain		p**
	Inadequate vs adequate	Excessive vs adequate	
	Adjusted OR (CI 95%)		
GDM	1.59 (1.19-2.13)	1.55 (1.17-2.06)	0.002
Gestational hypertension	0.85 (0.27-2.75)	1.99 (0.73-5.41)	0.186
Postpartum hemorrhage	0.91 (0.65-1.27)	1.26 (0.93-1.69)	0.099
C-section	0.94 (0.73-1.21)	1.46 (1.16-1.83)	< 0.001
Macrosomia	0.53 (0.33-0.84)	2.09 (1.50-2.91)	< 0.001

OR (95% CI): odds ratio and 95% confident interval.

Confounding factors included in the multivariable analysis were: age, parity, geographical origin, tobacco use, gestational age, preexisting diabetes and preexisting chronic hypertension.

C-section = cesarean section; GDM = gestational diabetes mellitus.

