Article

Maternal body mass index and gestational weight gain and their association with pregnancy complications and perinatal conditions

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Abstract: This study aimed to evaluate the impact of selected pregnancy pathologies statistically depending on overweight/obesity and excessive maternal weight gain during pregnancy on women who gave birth in the years 2013–2015 at the Second Department of Gynecology and Obstetrics at the University Hospital in Bratislava, Slovakia. In a retrospective study, we analyzed data gathered from the sample, which consisted of 7,122 women. Our results indicate a positive statistical dependency of the groups of women with overweight and obesity and gestational hypertension (adjusted odds ratio [AOR]=15.3; 95% CI 9.0-25.8 for obesity), preeclampsia (AOR=3.4; 95% CI 1.9-6.0 for overweight and AOR=13.2; 95% CI 7.7-22.5 for obesity), and gestational diabetes mellitus (AOR=1.9; 95% CI 1.2-2.9 for overweight and AOR=2.4; 95% CI 1.4-4.0 for obesity). A higher incidence of pregnancies terminated by cesarean section was observed in the group of obese women. Gestational weight gain above the IOM (the Institute of Medicine) recommendations was associated with a higher risk of pregnancy terminated by C-section (AOR=1.2; 95% CI 1.0-1.3), gestational hypertension (AOR=1.7; 95% CI 1.0-2.7), and infant macrosomia (AOR=1.7; 95% CI 1.3-2.1). Overweight and obesity during pregnancy significantly contribute to the development of pregnancy pathologies and increased incidence of cesarean section. Systematic efforts to reduce weight before pregnancy through pre-pregnancy dietary counseling, regular physical activity, and healthy lifestyle should be the primary goal.

Keywords: retrospective hospital-based study, overweight, obesity, pregnancy pathologies, caesarean section, weight gain

1. Introduction

The obesity epidemic has become a worldwide phenomenon not only from a medical point of view but also from a social one. The alarming increase in obesity worldwide has led the World Health Organization (WHO) to classify obesity as one of the most pressing global health issues of the 21st century [1]. Today, obesity is considered to be the most common metabolic disorder, which has reached epidemic character. Obesity is defined as excess body fat that is highly likely to lead to health deterioration, increased morbidity, and mortality. The high increase in the prevalence of obesity has

also affected women of reproductive age. The most commonly used indicator of obesity is the body mass index (BMI). In 2009, based on the BMI, the Institute of Medicine (IOM) classified body weight into underweight (BMI<18.5 kg/m2), normal weight (BMI=18.5–24.9 kg/m2), overweight (BMI=25.0–29.9 kg/m2), and obese (BMI≥30kg/m2). Based on the BMI, obesity has three levels: BMI 30.0–34.9 (class I), BMI 35.0–39.9 (class II), and BMI≥40 (class III) or morbid obesity. Obesity in pregnancy is defined as BMI≥30 kg/m2 at the first prenatal counseling visit. The IOM recommendations estimate a range of weight gain for underweight (12.5–18.0 kg), normal weight (11.5–16.0 kg), overweight (7.0–11.5 kg), and obese (5.0–9.0 kg) [2]. Maternal obesity has become one of the most commonly occurring risk factors in obstetric practice [3–5].

Numerous experimental and epidemiological studies show that nutritional changes in prenatal and postnatal stages of life can have a significant impact on health and child development [6–7]. Professional scientific societies point to the fact that due to obesity in pregnancy, in the postnatal period and adulthood, there is a higher incidence of metabolic disorders, neurodevelopmental disorders, cancer, and adverse changes in the immunological functions of an individual [8–11]. In developed countries, most women of childbearing age are already overweight or obese before becoming pregnant. The number of obese pregnant women is rising, which poses a threat to the future health of children. The WHO reports that the prevalence of obesity during pregnancy ranges from 1.8% to 25.3% [1]. According to the European Perinatal Health Report [12], in most European countries, more than 30% of pregnant women are obese. The proportion of overweight or obese women ranges from 30% to 50%, with a prevalence of less than 30% in Croatia, Austria, and Slovenia and around 50% in the UK. Some EU countries, including Slovakia, do not systematically contribute to the database of the Euro-Peristat network on BMI data on maternal body weight. Therefore, in the literature, some European countries have no relevant data on maternal obesity.

Obesity in pregnancy is associated with an increase in pregnancy complications, such as the risk of miscarriage, fetal and congenital anomalies, thromboembolism, preeclampsia and gestational hypertension, fetal macrosomia, gestational diabetes mellitus, IUGR, and stillbirth, as well as intrapartum and postpartum complications and neonatal mortality [13–26]. In connection with obesity, a higher number of cesarean sections [27–28] and a lower number of lactating women [29] are recorded, compared with women with a normal BMI. Obesity may be a risk factor for maternal mortality: the "Confidential Enquiry into Maternal and Child Health" report on children's health and maternal mortality within the three-year period from 2003 to 2005 states that 28% of mothers who died in connection with obesity were obese [30], 30% of women who died in 2011–2013 in the UK were obese and 22% were overweight [31].

Gestational weight gain is also an important predictor of adverse maternal and neonatal health outcomes. Insufficient weight gain is associated with increased risks of preterm birth and delivery of a low-birth-weight infant, whereas excessive weight gain is associated with increased risks of gestational hypertension, preterm birth, delivery of a high-birth-weight infant, and cesarean delivery [32–33].

This study aimed to evaluate the impact of selected pregnancy pathologies statistically depending on overweight/obesity and excessive maternal weight gain during pregnancy on women who gave birth in 2013–2015 at the Second Department of Gynecology and Obstetrics at the University Hospital in Bratislava, Slovakia.

2. Materials and Methods

In our retrospective study, we analyzed a group of 7,122 pregnant women during the period of January 1, 2013, to December 31, 2015. The study data were obtained from a computerized obstetrics database (Hospital Information System) and included demographic characteristics, medical and obstetric histories, and information on maternal and perinatal outcomes. We analyzed all singleton deliveries after 37 weeks of gestation, excluding pregnancies with chronic hypertension, fetal anomalies, and diabetes mellitus types 1 and 2. Women were categorized into four groups based on their prepregnancy BMI and three groups of gestational weight gain (GWG) relative to the IOM guidelines [2].

Prepregnancy weight was measured at the first antenatal visit during the first trimester of pregnancy; final pregnancy weight was measured at the last antenatal visit or the time of delivery. Body weight was assessed using a standard method during each antenatal visit. BMIs were categorized according to the WHO's classifications: underweight (<18.5), normal weight (18.5–24.9), overweight (≥25.0), and obese (≥30).

Gestational weight gain was defined as the difference between the final weight and the prepregnancy weight and was classified into three groups based on prepregnancy BMI and GWG relative to the IOM guidelines: (i) weight gain below the guidelines, (ii) weight in the range, and (iii) weight gain above the guidelines.

We examined the following maternal outcomes: preeclampsia, gestational hypertension, gestational diabetes mellitus (GDM), gestational hepatopathy, intrauterine growth restriction (IUGR), and cesarean delivery in relation to maternal advanced age (over 35). The neonatal outcomes examined were low birth weight (<2,500 g) and macrosomia (>4,000 g), which were defined according to the WHO's birth weight classification [34]. The American College of Obstetricians and Gynecologists (ACOG) have adopted the definition of IUGR as an estimated fetal weight of less than 10th percentile [34].

Gestational hypertension was defined on the basis of a systolic pressure greater than or equal to 140mm Hg or a diastolic pressure greater than or equal to 90 mm Hg on two separate occasions 2–240 hours apart after 20 weeks of gestation in the absence of proteinuria. Preeclampsia was defined as gestational hypertension with either proteinuria, which was defined as greater than or equal to 300 mg in a 24-hour sample [35].

Gestational diabetes mellitus is defined as any glucose intolerance with the onset or first recognition during pregnancy. We used a 50 g oral glucose challenge test (OGCT) as a screening method for GDM at 24–28 weeks of gestation [36].

The outcomes for the second part of our analysis of gestational weight gain were gestational hypertension, preeclampsia, GDM, cesarean section delivery, and IUGR in relation to maternal advanced age (over 35), gestational age, and smoking.

Data obtained were statistically compared among particular groups of women. In each group, we analyzed and statistically evaluated the incidence of pathological conditions complicating the course of pregnancy. Indications for deliveries terminated by cesarean section were statistically evaluated and compared in particular statistical groups.

Regarding statistical analysis, the continuous variables were expressed as mean ± standard deviation as determined by ANOVA. For the categorical variables, the categorical Mantel-Haenszel analysis was used. Associations of selected parameters with the BMI and GWG outside the IOM guidelines and adverse perinatal outcomes were analyzed by using a multivariable logistic regression with the adjusted odds ratios (AOR) and at 95% confidence intervals (CI). Statistical significance was evaluated at the significance level of p<0.05. Statistical analysis was performed using the SPSS software, Version 24.

This study was approved by the University Hospital Ethics Committee No. EK/101/2018.

3. Results

Of the 7,122 women, 741 (10.4%) accounted for the category of women with maternal underweight, 5,400 (76.0%) women with normal weight, 602 (8.5%) women with overweight, and 358 (5.0%) women with obesity. Because of missing data, 21 women were excluded from the total group and 7,101 women remained for the analysis.

Table 1 summarizes the results of the statistical analysis of the selected data of the women and the selected pathological conditions in pregnancy in the BMI categories, which indicated a statistical significance in the comparison of the groups with obesity and overweight with the group of women with normal BMI and underweight. Obese women had a significantly higher prevalence of gestational hypertension (10.6%), preeclampsia (10.9%), and GDM (8.7%) than normal-weight and underweight women (p<0.001). Pregnancy terminated by cesarean section was more often seen in the group of obese and overweight women (57%) than in the group of

normal-weight women (34.7%; p<0.001). The prevalence of IUGR was higher in the group of obese women (3.9%) than in the group of women with normal weight (1.2%; p<0.001). In the group of underweight women, the prevalence of IUGR was 1.8%. In the group of obese mothers, the number of smokers was significantly higher (7.3%) than in the group with normal-weight mothers (1.6%; p<0.001). The prevalence of infants with macrosomia was higher in overweight (9.3%) and obese women (9.6%) than in normal and underweight women (7.0%; p<0.05).

Table 1. Maternal/fetal outcomes among BMI categories in the sample of pregnant women (N=7,101)

	Underweight N = 741 (10.5%)	Normal weight N = 5400 (76.0%)	Overweight N = 602 (8.5%)	Obese N = 358 (5.0%)	p-value
Pre-pregnancy BMI	17.7 ± 0.7	21.2 ± 1.6	26.8 ± 1.3	34.9 ± 3.7	< 0.001
Maternal BMI before delivery	22.7 ± 1.8	26.3 ± 2.4	30.6 ± 2.5	37.2 ± 5.3	< 0.001
Gestational weight gain	14.3 ± 4.9	14.0 ± 5.0	10.3 ± 6.8	6.5 ± 11.8	< 0.001
C-section	211 (28.5)	1875 (34.7)	229 (38.0)	204 (57.0)	< 0.001
Gestational hypertension	6 (0.8)	50 (0.9)	9 (1.5)	38 (10.6)	< 0.001
Preeclampsia	8 (1.1)	56 (1.0)	17 (2.8)	39 (10.9)	< 0.001
Gestational DM	18 (2.4)	100 (1.9)	25 (4.2)	31 (8.7)	< 0.001
IUGR	13 (1.8)	65 (1.2)	7 (1.2)	14 (3.9)	< 0.001
Smoking	15 (2.0)	84 (1.6)	14 (2.3)	26 (7.3)	< 0.001
Low birth weight	43 (5.8)	262 (4.8)	36 (6.1)	8 (2.4)	n.s.
Macrosomia	35 (4.7)	378 (7.0)	55 (9.3)	32 (9.6)	< 0.05

N-Number of cases; n.s.-non significant

Table 2 shows the results of the multivariable logistic regression analysis assessing the independent effect of overweight/obesity on selected maternal pathologies controlling for age, gestational age, gestational weight gain, and smoking. There was a positive statistical dependency in the groups of women with overweight/obesity and pregnancy pathologies, such as gestational hypertension for obesity (AOR 15.3; 95% CI 9.0–25.8), preeclampsia for overweight (AOR 3.4; 95% CI 1.9–6.0) and obesity (AOR 13.2; 95% CI 7.7–22.5), gestational diabetes mellitus for overweight (AOR 1.9; 95% CI 1.2–2.9) and obesity (AOR 2.4; 95% CI 1.4–4.0), IUGR for obesity (AOR 3.7; 95% CI 1.8–7.8) and infant macrosomia for overweight (AOR 1.7; 95% CI 1.2–2.3) and obesity (AOR 1.8; 95% CI 1.2–2.7). In obese women, there was also a significantly higher risk of terminated pregnancy by C-section (AOR 2.1; 95% CI 1.7–2.8) and lower risk of a low-birthweight infant (AOR 0.2; 95% CI 0.1–0.5). In contrast, underweight women had a significantly lower risk of caesarian delivery (AOR 0.8; 95% CI 0.6–0.9) and infant macrosomia (AOR 0.7; 95% CI 0.5–0.9).

Table 2. The relation among weight categories and selected maternal outcomes (multivariable logistic regression analysis)

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	Underweight	Normal weight	Overweight	Obese	
	Adjusted OR	Adjusted OR	Adjusted OR	Adjusted OR	
	[95% CI]	[95% CI]	[95% CI]	[95% CI]	
C-section	0.8 [0.6-0.9]**	1	1.0 [0.9-1.2]	2.1 [1.7-2.8]***	
Gestational	0.0.10.4.2.21	1	1 5 [0 7 2 2]	1E 2 [0 0 2 E 9]***	
hypertension	0.9 [0.4-2.2]	1	1.5 [0.7-3.2]	15.3 [9.0-25.8]***	
Preeclampsia	1.1 [0.5-2.3]	1	3.4 [1.9-6.0]***	13.2 [7.7-22.5]***	
Gestational DM	1.4 [0.9-2.4]	1	1.9 [1.2-2.9]**	2.4 [1.4-4.0]**	
IUGR	1.3 [0.7-2.5]	1	0.6 [0.3-1.6]	3.7 [1.8-7.8]**	
Low birth weight	1.1 [0.7-2.5]	1	0.9 [0.6-1.4]	0.2 [0.1-0.5]***	
Macrosomia	0.7 [0.5-0.9]*	1	1.7 [1.2-2.3]**	1.8 [1.2-2.7]**	

OR-Odds Ratio; CI-Confidence Interval; *p<0.05; **p<0.01; ***p<0.001

Adjusted for maternal age, gestational age, gestational weight gain, smoking

Distribution of GWG according to BMI categories is illustrated in Figure 1. Adequate amount of weight gain was observed in 47.2% of the underweight women, 37% of whom were below the IOM range and only 15.7% had excessive weight gain during pregnancy. Inadequate weight gain was mostly seen in the underweight and normal BMI groups, whereas excessive GWG was observed in overweight and obese mothers. GWG above the recommended range was observed in 48.2% of the overweight mothers and 49.7% of the obese mothers.

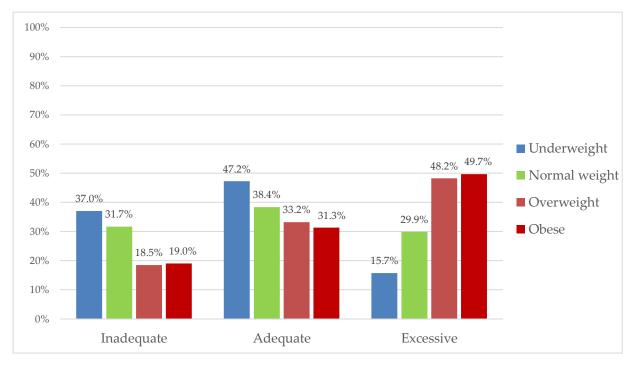


Figure 1. Proportion of maternal BMI categories in gestational weight gain groups (IOM recommendations)

A statistical analysis of selected pregnancy pathologies in women according to the GWG IOM recommendations is shown in Table 3. Women with excessive GWG had significantly higher pre-pregnancy BMI (22.74±4.39 vs. 21.67±3.64; p<0.001), higher BMI before delivery (29.65±4.01 vs. 26.53±3.19; p<0.001), longer gestation (39.31±1.25 vs. 39.20±1.33; p<0.001), higher

occurrence of cesarean delivery (38.5% vs. 34.0%; p<0.05), higher occurrence of gestational hypertension (2.2% vs. 1.1%; p<0.05), and higher incidence of infant macrosomia (10.3% vs. 6.1%; p<0.001) compared with women with GWG in the normal range. Mothers with lower-than-recommended GWG had higher incidence of IUGR (2.2% vs. 1.3%; p<0.001) and a low-birth-weight infant (9.1% vs. 3.5%; p<0.001) compared with those who gained the recommended amount of weight.

Table 3. Maternal outcomes associated with GWG (IOM recommendations)

	GWG (IOM recommendations)			
Maternal outcomes	Below	Range	Above	p-value
	N = 2172 (31.9)	N = 2738 (38.6)	N = 2191 (30.9)	
Weight gain	8.37 ± 2.69	13.50 ± 2.29	19.16 ± 4.20	<0.001
Pre-pregnancy BMI	21.54 ± 3.38	21.67 ± 3.64	22.74 ±4.39	< 0.001
Maternal BMI before delivery	24.57 ± 2.96	26.53 ± 3.19	29.65 ± 4.01	< 0.001
C-section	744 (34.3)	932 (34.0)	843 (38.5)	< 0.05
Gestational hypertension	26 (1.2)	29 (1.1)	48 (2.2)	< 0.05
Preeclampsia	28 (1.3)	46 (1.7)	46 (2.1)	n.s.
Gestational DM	63 (2.9)	67 (2.4)	44 (2.0)	n.s.
IUGR	47 (2.2)	35 (1.3)	17 (0.8)	< 0.001
Low birth weight	197 (9.1)	95 (3.5)	57 (2.6)	< 0.001
Macrosomia	106 (4.9)	168 (6.1)	226 (10.3)	< 0.001

GWG-gestational weight gain; N-Number of cases; n.s.-non significant

The relationship among GWG and selected maternal outcomes explored using multiple logistic regression is presented in Table 4. Excessive weight gain was significantly associated with increased risk of caesarean section (AOR 1.2 [95% CI 1.0–1.3]), gestational hypertension (AOR 1.7 [95% CI 1.0–2.7]), and infant macrosomia (AOR 1.7 [95% CI 1.3–2.0]) and lower risk of GDM (AOR 0.6 [95% CI 0.4–0.9]) compared with adequate weight gain during pregnancy. Women with weight gain lower than the IOM recommendations were more likely to be in advanced age (AOR 1.3 [95% CI 1.1–1.6]), had lower risk of preeclampsia (AOR 0.5 [95% CI 0.3–0.9]), and were in a higher risk of delivering a low-birth-weight infant (AOR 2.0 (95% CI 1.5–2.7) compared with mothers with adequate GWG.

Table 4. The relation among GWG (IOM recommendations) and selected maternal outcomes (multiple logistic regression analysis)

	Inadequate GWG	Excessive GWG
	Adjusted OR	Adjusted OR
	[95% CI]	[95% CI]
C-section	0.9 [0.9-1.1]	1.2 [1.0-1.3]**
Gestational hypertension	1.1 [0.6-1.8]	1.7 [1.0-2.7]*
Preeclampsia	0.5 [0.3-0.9]*	0.9 [0.6-1.5]
Gestational DM	1.2 [0.9-1.8]	0.6 [0.4-0.9]*
IUGR	0.9 [0.6-1.5]	0.5 [0.3-1.0]
Low birth weight	2.0 [1.5-2.7]***	0.9 [0.6-1.4]
Macrosomia	0.8 [0.6-1.1]	1.7 [1.3-2.1]***

GWG-gestational weight gain; OR-Odds Ratio; CI-Confidence Interval; *p<0.05; **p<0.01; ***p<0.001

Adjusted for maternal age, gestational age, maternal BMI, smoking

4. Discussion

The prevalence of obesity in pregnant women worldwide ranges from 1.8% to 25.3% [1]. In developed countries as well as in Slovakia, obesity is on the rise. In our retrospective study, we had 602 (8.5%) overweight women and 358 (5.0%) obese women. Comparing the percentages of obese women in individual years, we observe a slight annual increase of obesity in pregnancy: 3.96% in 2013, 4.23% in 2014, and 4.39% in 2015. A total of 7,122 women who gave birth in those years in our hospital came from different regions in Slovakia and are working and living in the Bratislava agglomeration. In the observed period, although the women with overweight and obesity in our sample belonged to a lower limit of the obesity prevalence in pregnancy in the EU, based on our results, we can conclude that not only obesity with BMI ≥ 30.0 but also overweight with BMI between 25.0 and 29.9 is a high-risk factor for the occurrence of pathological conditions in pregnancy, such as preeclampsia, GDM, gestational hypertension, and IUGR [37-38]. Liu et al. [39] showed that compared with antenatal weight gain within the IOM recommendations, excessive weight gain increased the incidence of cesarean section, preeclampsia, and infant macrosomia and reduced the incidence of GDM, while inadequate antenatal weight gain increased the incidence of GDM and low birth weight. The results of our study are consistent with several publications that confirm that obesity is a significant risk factor contributing to a higher incidence of pregnancies terminated by cesarean section [40]. Within the given period, in our obese group, up to 57% of pregnancies were terminated by cesarean section; this figure significantly exceeds the national average of pregnancies terminated by cesarean section in Slovakia (31% in 2016) [41].

In our study, inadequate, adequate, and excessive gestational weight gain were observed: in the inadequate GWG group, 37.0% underweight, 31.7% normal weight, 18.5% overweight, and 19.0% obese; in the adequate GWG group, 47.2% underweight, 38.4% normal weight, 33.2% overweight, and 33.3% obese; in the excessive GWG group, 15.7% underweight, 29.9% normal weight, 48.2% overweight, and 49.7% obese. Gestational weight gain greatly differed per maternal prepregnancy BMI group and was gradually higher across higher BMI groups. It was concluded that obese women are more likely to exceed the GWG recommendations.

Both extremes, excessive or inadequate GWG, can lead to adverse pregnancy outcomes. According to several studies [42–44], women whose weight gain is outside the IOM-recommended ranges are also associated with a higher incidence of pregnancy complications compared with women with normal weight gain. In our analysis, we found that excessive weight gain is associated with hypertensive disorders in pregnancy, GDM, delivery of a macrosomic infant, and higher incidence of C-section, which corresponds to a number of published results [42, 45–46]. In a study conducted in Ireland, maternal obesity and increased GWG were associated with an increased risk of caesarean section and preeclampsia [47]. Some studies have reported that weight gain above the recommendations is associated with an increased risk of delivering a macrosomic infant, whereas

less-than-recommended weight gain is associated with an increased risk of delivering an infant with low birth weight, consistent with our results [48–49].

The rate of overweight and obesity is also increasing in the Australian obstetric population. Women who are overweight and obese have an increased risk of adverse pregnancy outcomes. In particular, obese women are at increased risk of developing gestational diabetes (relative risk [RR] 2.10 [95% CI 1.17, 3.79]), gestational hypertension, and preeclampsia (relative risk [RR] 2.99 [95% confidence intervals [CI] 1.88, 4.73]) [50].

In Nova Scotia, Canada, moderately obese women have an increased risk of developing gestational hypertension (AOR 2.38 [95% CI 2.24, 2.52]) and cesarean delivery (AOR 1.60 [95% CI 1.53, 1.67]). Severely obese women have an increased risk of developing gestational hypertension (AOR 3.00 [95% CI 2.49, 3.62]) and cesarean delivery (AOR 2.46 [95% CI 2.15, 2.81]) [51].

In our study, the increased adjusted risk of gestational hypertension, preeclampsia, GDM, cesarean delivery, IUGR, and macrosomia was higher in overweight and obese women, when adjusted for age, gestational age, GWG, and smoking.

The strength of our study is its large sample of pregnant women obtained retrospectively from an electronic obstetric database of the Hospital Information System (HIS) of the University Hospital Bratislava, which includes the demographic, obstetric, and neonatal characteristics of hospitalized women. Its limitation is its restriction to the Bratislava agglomeration only, even though families from all regions of Slovakia come to the area for work. The other limitation is its short-time retrospective design (2013–2015) instead of a longitudinal study design. In the multivariate logistic regression analysis, we could adjust only for age, gestational age, and smoking; data on socioeconomic and marital status were not available.

The next issue is that we recorded maternal weight at the beginning of the first trimester of pregnancy. Prepregnancy weight was recorded only through self-report, and it could not correspond to the true prepregnancy weight.

We fully understand that studies on the impact of obesity and GWG require the use of more precise data collection methods and calculations of body weight and GWG. Researchers and clinicians should use uniform definitions and diagnostic criteria for maternal and neonatal outcomes to allow for a better comparison of maternal weight and GWG data and their influence on maternal and infant outcomes.

In spite of these limitations, our data provide information on maternal weight and GWG and their impact on pregnancy outcomes, and these findings could have important implications for the clinical practice.

5. Conclusion

In our study, we comprehensively analyzed the influence of prepregnancy BMI and GWG on perinatal outcomes. We confirmed that both prepregnancy BMI and GWG cause adverse perinatal outcomes

Prepregnancy dietary counseling, regular physical activity, and a healthy lifestyle could help reduce the incidence of gestational obesity. Systematic efforts to reduce weight before pregnancy and excessive GWG should be the primary goal. Achieving optimal weight for every pregnant woman is the basis for the development of a healthy population and an essential factor for the physiological course of pregnancy and childbirth and thus contributes to a significant decline in the number of cesarean sections and perinatal complications and a reduction of fetal and neonatal morbidity and mortality.

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the manuscript and did the language, style and spell check. Language, style and spell check was also provided by a native speaker. All authors have approved the submitted version.

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