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Association of Pre-Pregnancy Body Mass Index and Gestational Weight Gain with Preterm Births and Fetal Size: an Observational Study from Lebanon

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Abstract

Background: Pre-pregnancy body mass index (BMI) and gestational weight gain (GWG) are reported to impact the preterm birth (PTB) rate and newborn size. Most studies have been conducted in developed countries, although PTB and adverse pregnancy outcomes are more frequent in the developing world. The aim of this study is to elucidate the association of pre-pregnancy BMI and GWG on the occurrence of PTB and sub-optimal fetal size in Lebanon.

Methods: This is a retrospective cohort study using a hospital-based register covering 35% of births in Lebanon between 2001 and 2012. Data were collected on 170 428 pregnancies from 32 hospitals using medical records and interviews.

Results: After adjusting for confounders, underweight women had increased odds of having very preterm [odds ratio (OR) 1.58, 95% confidence interval (CI) 1.16, 2.14], preterm (OR 1.42, 95% CI 1.28, 1.58), and small for gestational age (SGA) (OR 1.50, 95% CI 1.37, 1.63) neonates. When BMI was analysed with GWG, only SGA remained significant in underweight women with low GWG. For all BMI groups, low GWG was protective against large for gestational age (LGA) and high GWG increased the odds of LGA. GWG, both low (OR 1.25, 95% CI 1.15, 1.35) and high (OR 1.43, 95% CI 1.32, 1.55) increased the risk of PTB in normal weight women. The same result was obtained for overweight women.

Conclusions: High GWG increased the risk of LGA for all groups and PTB in normal weight and overweight women, whereas low GWG increased the risk of SGA and PTB. Given that there are not many studies from middle income/developing countries on patterns of weight gain during pregnancy, findings from this study may help with pre-conception counselling with emphasis on the importance of an optimal pre-pregnancy BMI and appropriate weight gain during pregnancy.

Keywords: *body mass index, gestational weight gain, large for gestational age, preterm birth, small for gestational age.*

Preterm birth (PTB), defined as birth before 37 weeks of gestation, is now the second leading cause of neonatal mortality and a major contributor to neonatal morbidities and infections.[1,2] Similarly, suboptimal fetal growth, categorised as small for gestational age (SGA) and large for gestational age (LGA),[3,4] increases the risk of stillbirth and neonatal morbidities such as PTB.[5,6] PTB and suboptimal fetal growth are associated with long-term morbidities such as cardiac, pulmonary, and neurodevelopmental complications, leading to a significant health and economic burden.[2,7,8] More than 60% of PTB occur in Africa and South Asia, but rates are also high in developed countries ranging between 5% and 13% in Europe and USA.[2–4] The PTB rates in some African and South Asian countries are estimated to be up to 16% of total livebirths.[1]

The underlying pathways of PTB and/or suboptimal fetal size at birth are multifactorial and include genetic and non-genetic factors.[5,6] Both pre-pregnancy

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body mass index (BMI) and gestational weight gain (GWG) are reported to impact PTB rate and newborn size. GWG is also independently studied as a risk factor for PTB and aberrant gestational size, as well as in association to pre-pregnancy BMI.[9,10] The manageable nature of GWG after conception explains its importance for maternal and newborn health. The extent that GWG affects PTB and gestational size varies among studies due to variation in design, demographics, and ethnicity of the population, and cut-offs used for BMI and GWG values.[9,11–14] Most studies indicate an increased risk of PTB with higher GWG with the exception of underweight women where it decreases the odds of PTB and SGA.[11,15] In addition, low GWG according to the guidelines of the Institute of Medicine (IOM) is protective against LGA irrespective of pre-pregnancy BMI.[15]

Studies examining the association between birth outcomes and pre-pregnancy BMI and maternal GWG have been conducted in developed countries, although PTB and adverse pregnancy outcomes are more frequent in the developing world.[1,2,16] Pre-pregnancy BMI and GWG are mostly independently investigated with respect to gestational age. Thus, assessing pre-gestational BMI and GWG with respect to pregnancy outcomes in the developing world and assessing GWG as a modifier of the link between BMI and neonatal outcomes are warranted. To date, there are no studies from Lebanon or the Middle East that are large enough to assess the extent of contribution of BMI and GWG to PTB and sub-optimal fetal size. Subsequently, there is no consensus about adequate GWG and pre-pregnancy BMI for Lebanese women. The objective of this study was to examine the association between pre-pregnancy BMI and GWG, with gestational age and size in Lebanon.

Methods

Study population

This is a retrospective cohort study using data from the National Collaborative Perinatal Neonatal Network (NCPNN) between 2001 and 2012. The NCPNN is a hospital-based network across Lebanon covering around 35% of national births. Hospitals were located in all geographical areas of the country in varying socio-economic settings. The network includes daily perinatal and neonatal data on all deliveries in participating hospitals. Data are collected by trained personnel based on direct interviews and from maternal and neonatal medical records. Singleton livebirths with gestational age between 28 and 42 weeks were included in the analysis.

Exposures

Maternal height and weight values (before conception and upon delivery) were either recorded as self-reported during the interviews with the delivering mothers or extracted from the medical record when available. BMI was then computed and categorised following the World Health Organization's recommendations as: underweight (BMI <18.5 kg/m^2), normal (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2), and obese (≥30 kg/m^2). GWG was defined as maternal weight at delivery minus the reported weight at conception divided by gestational age in weeks. Throughout data cleaning, women with weight loss of more than 15 kg or gain of more than 40 kg were removed from the analysis. GWG was then categorised for each BMI category according to Carnero *et al*.,[11] which used the 2009 IOM Recommendations on weight gain during pregnancy and the approach of Schieve *et al*.[9] to calculate the GWG rate categories.

Outcomes

SGA and LGA were calculated according to previously validated growth charts from our population. SGA was defined by birthweight below the 10th percentile compared with the expected weight for the same sex and gestational age, and LGA as those above 90th percentile for gender and gestational age-matched value.[6] Appropriate for gestational age was used as a comparison category for both outcomes. Gestational age was calculated in completed weeks by the use of ultrasonic examinations of the fetus, performed most often during the first or early second trimesters. In few cases where ultrasonic examination was not available, gestational age was calculated by the use of the last menstrual period. Very PTB and PTB were defined as <33 weeks and <37 weeks of gestation respectively.

Confounders

Variables considered in the study as potential confounders relate to characteristics of the newborn and his/her parents. These included maternal and paternal age, maternal education, parity, parental consanguinity (those considered consanguineous include first and second cousins or more distantly related),[17] smoking during pregnancy, and newborn gender.

Statistical analysis

Analysis was performed using SPSS version 20 (IBM, New York, New York, USA). Cross-tabulations between study outcomes (PTB, very PTB, SGA, and LGA) and maternal and neonatal covariates were performed to assess associations using the chi-square test. Crude odds ratios and 95% confidence intervals were calculated using logistic regression analysis with the baseline category being normal pre-pregnancy BMI and moderate GWG. All significant variables associated with the various outcomes at the bivariate level were used in the multiple logistic regression analysis to assess the independent effect of pre-pregnancy BMI and GWG on the risk of early PTB, all PTB, SGA, and LGA. Crude and adjusted odds ratios were then calculated to assess the risk of weight gain on the various outcomes stratified by pre-pregnancy BMI using adequate gain as reference for each BMI. BMI as a continuous variable was included in this analysis (Table 4) to address the possibility of residual confounding.

Results

A total of 170 428 singleton pregnancies were included in this study. Table 1 shows the general characteristics of the population under study. Most mothers (78.4%) were between 20 and 34 years of age. With respect to pre-gestational BMI, 63.9%, 23.3%, 8.2% and 4.7% were normal, overweight, obese, and underweight, respectively. Underweight and normal weight women had mostly adequate weight gain (40.3% and 43%, respectively), whereas overweight and obese women had more excessive GWG (54.1% and 59%, respectively). With respect to pregnancy outcomes, 0.8% and 6.7% were very preterm and preterm, respectively, whereas 8.5% and 9.6% were SGA and LGA respectively.

After adjusting for maternal and neonatal confounders, we examined the odds of PTB and very PTB with respect to normal weight women (Table 2). Underweight and obese women were more likely to have both very PTB (adjusted odds ratio (OR) 1.58,

Table 1. General characteristics of the population under study (NCPNN 2001–2012)

	Total number	%
Maternal age (years)		
<20	6777	4.2
20–34	126 453	78.4
≥35	28 018	17.4
Paternal age (years)		
<25	4957	3.8
25–44	117 396	90.1
≥45	8006	6.1
Maternal education (range of years studied)		
Illiterate to elementary (<6 years)	21 990	14.5
Intermediate (<10 years)	39 745	26.3
Secondary/technical (<13 years)	43 279	28.6
University	46 234	30.6
Parity		
Primiparae (0)	58 915	35.4
Multiparae (≥1)	107 291	64.6
Parental consanguinity		
Not related	133 361	85.5
Related	22 632	14.5
Smoking during pregnancy (cigarette and/or shisha)		
Yes	22 463	14.9
No	127 980	85.1
Newborn gender		
Male	86 354	51.6
Female	81 109	48.4
Body mass index (*N* = 138 193)		
Underweight (<18.5)	6471	4.7
Normal (18.5–24.9)	88 288	63.9
Overweight (25.0–29.9)	32 160	23.3
Obese (≥30.0)	11 274	8.2
Gestational age (GA)		
Very preterm (<33 weeks)	1386	0.8
Preterm (<37 weeks)	11 354	6.7
Normal GA	157 688	92.5
Gestational weight gain (range)		
Underweight women		
Insufficient (<0.32)	2391	37.4
Adequate (0.32–0.46)	2576	40.3
Excessive (>0.46)	1427	22.3
Women with normal BMI		
Insufficient (<0.28)	27 987	31.9
Adequate (0.28–0.40)	37 658	43.0
Excessive (>0.40)	21 959	25.1
Overweight women		
Insufficient (<0.17)	3712	11.7
Adequate (0.17–0.28)	10 868	34.2
Excessive (>0.28)	17 155	54.1
Obese women		
Insufficient (<0.13)	1812	18.0
Adequate (0.13–0.23)	2310	23.0
Excessive (>0.23)	5940	59.0
Gestational outcome (size)		
Large for gestational age	16 292	9.6
Small for gestational size	14 545	8.5
Normal size	139 591	81.9

Table 2. Unadjusted and adjusted odds ratios and 95% confidence intervals for the association of pre-pregnancy body mass index with very preterm and preterm delivery (NCPNN 2001, 2012)

	Very preterm delivery			Preterm delivery		
Pre-pregnancy body mass index	*N* (%)	Unadjusted OR (95% CI)	Adjusted OR[a] (95% CI)	*N* (%)	Unadjusted OR (95% CI)	Adjusted OR[b] (95% CI)
Normal	549 (0.6)	1.00 (Reference)	1.00 (Reference)	5288 (6.0)	1.00 (Reference)	1.00 (Reference)
Underweight	61 (0.9)	1.52 (1.16, 1.98)	1.58 (1.16, 2.14)	523 (8.1)	1.38 (1.25, 1.51)	1.42 (1.28, 1.58)
Overweight	200 (0.6)	1.00 (0.85, 1.17)	0.94 (0.77, 1.14)	1945 (6.0)	1.01 (0.95, 1.06)	0.98 (0.92, 1.04)
Obese	95 (0.8)	1.35 (1.09, 1.69)	1.33 (1.02, 1.74)	780 (6.9)	1.16 (1.07, 1.26)	1.10 (1.01, 1.21)

[a]OR adjusted for maternal education, maternal age, paternal age, smoking during pregnancy, newborn sex, consanguinity, and parity.
[b]OR adjusted for maternal education, maternal age, paternal age, smoking during pregnancy, newborn sex, and consanguinity.

95% confidence interval (CI) 1.16, 2.14 and OR 1.33, 95% CI 1.02, 1.74, respectively) and PTB (OR 1.42, 95% CI 1.28,1.58 and OR 1.10, 95% CI 1.01, 1.21, respectively), although to a lesser extent in obese women (Table 2).

Table 3 summarises the odds of having an SGA or LGA infant with respect to normal weight women. Compared with normal pre-pregnancy BMI, pre-pregnancy underweight BMI was associated with increased odds of SGA but with lower odds of LGA infants. On the other hand, pre-pregnancy overweight and obese BMI were protective for SGA (OR 0.84, 95% CI 0.80, 0.89 and OR 0.73, 95% CI 0.66, 0.81, respectively) but was associated with increased odds of LGA infants (OR 1.44, 95% CI 1.37, 1.51 and OR 2.11, 95% CI = 1.97, 2.25, respectively).

We then investigated the association between GWG, stratified by pre-pregnancy BMI and all gestational outcomes (Table 4). For pre-pregnancy underweight, the odds of PTB or very PTB were not significant irrespective of GWG. However, in underweight and normal weight women, low GWG was associated with increased odds of SGA, whereas high GWG was associated with increased odds of LGA. On the other hand, low GWG in underweight and normal weight women was protective against LGA, whereas high GWG was protective against SGA. The odds of PTB were increased in normal weight and overweight women for both low (OR 1.25, 95% CI 1.15, 1.35 and OR 1.43, 95% CI 1.2, 1.69, respectively) and high GWG (OR 1.43, 95% CI 1.32, 1.55 and OR 1.24, 95% CI 1.1, 1.4, respectively). Low GWG in obese women was associated with increased odds of very PTB (OR 2.23, 95% CI 1.05, 1.99) and decreased odds of LGA (OR 0.8, 95% CI 0.65, 1.0). High GWG in obese women increased the risk for LGA (OR 1.48, 95% CI 1.28, 1.72).

Comment

Our results illustrate the risks of low and high pre-pregnancy BMI and weight gain for PTB and

Table 3. Unadjusted and adjusted odds ratios and 95% confidence intervals for the association of pre-pregnancy body mass index with small and large for gestational age (NCPNN 2001, 2012)

	Small for gestational age			Large for gestational age		
Pre-pregnancy body mass index	*N* (%)	Unadjusted OR (95% CI)	Adjusted OR[a] (95% CI)	*N* (%)	Unadjusted OR (95% CI)	Adjusted OR[b] (95% CI)
Normal	7376 (9.1)	1.00 (Reference)	1.00 (Reference)	7381 (9.1)	1.00 (Reference)	1.00 (Reference)
Underweight	789 (12.9)	1.47 (1.36, 1.59)	1.46 (1.33, 1.59)	354 (6.2)	0.66 (0.59, 0.73)	0.70 (0.62, 0.79)
Overweight	2199 (7.8)	0.84 (0.80, 0.88)	0.84 (0.80, 0.89)	3878 (12.9)	1.48 (1.42, 1.54)	1.44 (1.37, 1.51)
Obese	704 (7.5)	0.80 (0.74, 0.87)	0.73 (0.66, 0.81)	1844 (17.4)	2.10 (1.99, 2.22)	2.11 (1.97, 2.25)

[a]OR adjusted for maternal education, maternal age, paternal age, smoking during pregnancy, newborn sex, consanguinity, and parity.
[b]OR adjusted for maternal age, paternal age, smoking during pregnancy, newborn sex, and parity.

Table 4. Unadjusted and adjusted odds ratios and 95% confidence intervals for the association of gestational weight gain by pre-pregnancy body mass index with very preterm, preterm, small for gestational age and large for gestational age (NCPNN 2001, 2012)

Pre-pregnancy body mass index	Underweight		Normal		Overweight		Obese	
Weight gain	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Very preterm[a]								
Low	0.75 (0.41, 1.36)	0.60 (0.30, 1.21)	1.22 (0.99, 1.50)	1.15 (0.90, 1.46)	1.56 (1.01, 2.41)	1.42 (0.84, 2.39)	1.96 (1.02, 3.78)	2.23 (1.05, 1.99)
High	0.86 (0.44, 1.68)	0.72 (0.33, 1.55)	1.42 (1.15, 1.75)	1.20 (0.93, 1.54)	1.08 (0.79, 1.49)	0.88 (0.61, 1.29)	1.14 (0.63, 2.05)	1.02 (0.52, 1.99)
Preterm[b]								
Low	1.25 (1.02, 1.54)	1.21 (0.96, 1.53)	1.28 (1.20, 1.37)	1.25 (1.15, 1.35)	1.41 (1.21, 1.65)	1.43 (1.20, 1.69)	1.02 (0.80, 1.31)	1.14 (0.85, 1.52)
High	1.12 (0.88, 1.43)	1.09 (0.82, 1.43)	1.45 (1.35, 1.55)	1.43 (1.32, 1.55)	1.31 (1.17, 1.45)	1.24 (1.10, 1.40)	1.11 (0.92, 1.35)	1.11 (0.89, 1.39)
SGA[a]								
Low	1.45 (1.23, 1.71)	1.62 (1.34, 1.96)	1.54 (1.46, 1.63)	1.54 (1.44, 1.64)	1.11 (0.97, 1.27)	1.09 (0.93, 1.27)	1.21 (0.95, 1.55)	1.11 (0.82, 1.50)
High	0.65 (0.51, 0.83)	0.55 (0.42, 0.72)	0.87 (0.81, 0.93)	0.81 (0.75, 0.88)	0.74 (0.67, 0.82)	0.70 (0.63, 0.78)	0.99 (0.81, 1.22)	0.95 (0.75, 1.21)
LGA[c]								
Low	0.62 (0.46, 0.82)	0.58 (0.42, 0.81)	0.67 (0.63, 0.72)	0.64 (0.59, 0.69)	0.85 (0.74, 0.97)	0.80 (0.69, 0.93)	0.94 (0.78, 1.13)	0.80 (0.65, 1.00)
High	1.81 (1.41, 2.32)	1.96 (1.48, 2.59)	1.67 (1.58, 1.76)	1.73 (1.63, 1.85)	1.45 (1.34, 1.57)	1.51 (1.39, 1.65)	1.52 (1.33, 1.74)	1.48 (1.28, 1.72)

[a]OR adjusted for body mass index (kg/m^2), maternal education, maternal age, paternal age, smoking during pregnancy, newborn sex, consanguinity, and parity.
[b]OR adjusted for body mass index (kg/m^2), maternal education, maternal age, paternal age, smoking during pregnancy, newborn sex, and consanguinity.
[c]OR adjusted for body mass index (kg/m^2), maternal age, paternal age, smoking during pregnancy, newborn sex, and parity.

sub-optimal fetal size. Low and high GWG were both associated with increased odds of PTB in normal weight and overweight women. Low GWG also increased the odds for SGA, whereas high GWG decreased the odds of SGA in underweight and normal weight women. Low GWG was protective against LGA, whereas high GWG increased the odds of LGA across all pre-pregnancy BMI categories. Interestingly, in normal pre-pregnancy BMI mothers, high GWG increased the risk of very PTB and PTB but was protective against SGA.

To our knowledge, this is the first study from the Middle East and North Africa (MENA) region covering a large population size to assess birth outcomes with respect to GWG and pre-pregnancy BMI. The lack of large studies from the MENA region hinders our understanding of potential regional differences or similarities in the associations between pre-pregnancy BMI and GWG and PTB and gestational size. However, based on genetic similarities and obesity rates in the region, we expect that our results would be more similar to Jordan, Iraq, and Syria than Saudi Arabia, Kuwait, and Bahrain.[18] In the Lebanese community, there is a misconception about the extent of weight gain during gestation and healthy pregnancy. Other strengths of our analysis include the use of the classification of gestational size (SGA or LGA) according to a previously published study pertaining to the Lebanese population and the adjustment by several possible confounding factors.[4]

Yet, our study has several limitations. One of the shortcomings is the inability to differentiate between spontaneous and medically induced PTB. Reporting bias also constituted a limitation because most pre-pregnancy BMI were self-reported and not measured in a clinical examination. It has been shown that self-reported BMI is sufficient for most epidemiologic studies, but it may not be accurate for estimating the prevalence of obesity.[19] In addition, GWG was not available by trimester, and it was not possible to study more categories such as very low and low GWG because of the limited number of cases specifically when studying very PTB (0.8%).

The underlying causes of spontaneous PTB are still largely unknown despite extensive research. The process of PTB is multifactorial with evident contribution of maternal nutritional status and parental consanguinity.[2,11,20–23] Nutritional status affects pre-pregnancy BMI, GWG as well as utero-placental blood flow, obstetrical complications, and infection rates, which impact the gestational size and age. A few studies have shown that very PTB and PTBs were significantly less likely in the obese population, whereas a systemic review by McDonald *et al*. showed that obesity increased the risk of PTB.[24–27] Our study also showed that there is increased odds of PTB in obese women and the odds of very PTB are even higher with low GWG (Tables 2,4). Similar to other studies we also demonstrated an increased risk for SGA in underweight women.[24,25,28–30] Pre-pregnancy overweight or obesity increases the risk of gestational diabetes, which could have contributed to the increased odds of LGA.[25,27,31,32] Contrary to one study in the Korean population, pre-pregnancy underweight in our population was protective against LGA births irrespective of weight gain degree.[25]

Similar to other studies, our findings suggest that obese women can benefit from low GWG to decrease the risk of LGA, but that this may cause an increased risk of very PTB (Table 4).[33–35] However, a more recent study identified obesity and GWG as two independent risk factors for fetal outcome, specifically macrosomia, with no significant association between the two variables.[22] On the other hand, high GWG in underweight women was not associated with PTB similar to the study by Savitz *et al*., but in contrast to the study by Carnero *et al*. where GWG was linearly correlated with a decreased risk of PTB in underweight Peruvian women.[11,36,37] Our study is in agreement with Carnero *et al*. with respect to the relationship between PTB and high GWG but not GWG and obesity.[11] In most studies, mothers with high GWG consistently have increased risk for LGA offspring, indicating that mothers should be advised to avoid high GWG.[10,15,38]

Careful review of the literature indicates that the effect of pre-pregnancy BMI and GWG on pregnancy outcomes varies significantly among different groups.[26] These differences could be attributed to population-specific genetic determinants,[25] variable definitions of GWG categories in addition to the lack of information regarding nutritional adequacy during gestation. Moreover, most studies, including ours, do not differentiate between spontaneous and medically induced PTB.[17,29,39]

Unlike other causes of PTB and gestational size aberrations, GWG and pre-pregnancy BMI may be prevented with appropriate awareness and guidance. In fact, there is a misconception in the Lebanese culture that increased GWG can be beneficial for the newborn's health and growth. Because high GWG increases the risk of LGA for all pre-pregnancy BMI, increasing awareness to monitor GWG can be beneficial. Similarly, underweight women should be advised to have adequate GWG to decrease the risk of SGA and prematurity. Thus, attaining an optimal pre-pregnancy BMI and following strict guidelines for GWG are highly recommended in planning for pregnancy and should be reinforced by obstetricians.

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