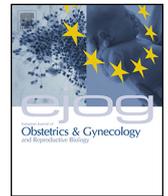




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Full length article

Maternal and neonatal outcomes according to gestational weight gain in twin pregnancies: Are the Institute of Medicine guidelines associated with better outcomes?



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ABSTRACT

Objective: The Institute of Medicine (IOM) recommended a gestational weight gain for full-term twin pregnancies of 17–25 kg for normal Body mass Index patients, and characterize its guidelines on during twin pregnancies as “provisional”. Indeed, they are exclusively based on observational epidemiological data.

The objective of this study was to investigate whether the IOM's gestational weight gain guidelines are optimal for maternal and neonatal.

Outcomes study design: We included all consecutive twin pregnancies delivering two live births retrospectively. Monoamniotic pregnancies, major congenital abnormalities, twin-to-twin transfusion syndrome, patients with missing gestational weight gain data in the last month before delivery, and patients with a body mass index (BMI) ≤ 18.5 were excluded. To control for gestational length, we divided the total weight gain by the gestational age in weeks at the last weight measurement to obtain the weight gain per week. Patients were classified as having low gestational weight gain, adequate gestational weight gain, or excessive gestational weight gain, with the results adjusted for BMI and tobacco use.

Results: There were 878 patients in our level-III university hospital maternity ward who met the inclusion criteria in 1997–2013. Excessive gestational weight gain women had greater rates of preeclampsia than adequate gestational weight gain women did. Low gestational weight gain women showed a lower rate of gestational hypertension than AGWG women did. Delivery before 37 weeks of gestation (26.9% vs. 17.3%, $p = 0.009$), birth weight < 2500 g, respiratory distress syndrome, and transfer to the neonatal intensive care unit were more frequent in the LGWG group compared with the AGWG group. Apgar score < 7 at 5 min were more frequent in the EGWG group.

Conclusion: Adequate gestational weight gain was associated with better outcomes. Our results suggest that the IOM guidelines for twin pregnancy are appropriate and therefore should be routinely used.

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Introduction

Twin gestations are a disproportionally significant factor in perinatal morbidity and mortality [1], as 60% of twins are born preterm and 25% have very low birth weight [2,3]. They are involved in high rates of preeclampsia, intrauterine growth restriction (IUGR), cesarean section delivery, and fetal [4] and neonatal death [3]. The number of twin gestations is dramatically

rising, especially with assisted reproductive technology [5]. Issues surrounding twins' antepartum care and risk reduction are becoming of paramount importance.

Inappropriate gestational weight gain (GWG) result in significant consequences for singletons, justifying a particular interest. Indeed, an excessive GWG is responsible of elevated rates of macrosomia and caesarean sections, and of long term weight retention for the mother and even the child [6–8]. At the opposite, an insufficient GWG increases preterm births, IUGR and early mortality [6–8].

GWG is higher for twin pregnancies than for singletons [9], thus this population require specific recommendations. After the Institute of Medicine (IOM) published its recommendations for GWG in twin pregnancies in 1990 [10], further studies have

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demonstrated that, similar to singletons, GWG depends on the prepregnancy body mass index (BMI) [11,12]. Therefore, the IOM revised its guidelines in 2009 [13]. The recommended GWGs for full-term twin pregnancies are 17–25 kg (37–54 lbs.) for women in the normal weight category (BMI 18.5–24.9), 14–23 kg for women in the overweight category (BMI 25.0–29.9), and 11–19 kg for obese women (BMI > 30) [13,14]. Nevertheless, the IOM referred to these guidelines as “provisional,” specifying that they are based only on observational epidemiological data (25th–75th percentiles of GWG per BMI group ≥ 37 weeks of amenorrhea with mean birth weight ≥ 2500 g); this means that they do not consider pregnancy outcomes.

Most of the available literature on this topic focuses on fetal growth and has shown a positive association between GWG and birth weight [11,15–21]. However, this effect has not shown constant statistical results, mainly due to small sample sizes, especially when the results are stratified by prepregnancy BMI. Likewise, the authors do not always control for gestational duration, which is a major confounding factor [12,22], and they sometimes choose to exclude preterm birth to avoid this issue, thereby excluding an important proportion of the patients [16,23], especially those with complications. In addition, there is a lack of data on the effects of excessive GWG (EGWG), as most studies have focused on the link between low GWG (LGWG) and low birth weight [15,24]. Moreover, only a few studies have examined other outcomes, such as preterm birth, gestational diabetes, or hypertensive disorders, and their findings are inconsistent. In addition, many studies were performed before 2009, and they did not specifically study outcomes regarding the IOM recommendations [12,25,26,26].

The points outlined above show that there is a lack of clinical evidence in the field [27], but GWG appears to be linked with obstetrics outcomes. Determination of the optimal GWG in twin pregnancies is an interesting topic, as it is a modifiable factor and has a high potential for intervention. Indeed, Phelan et al. reported that only 41.7% of women reported receiving weight gain advice from their practitioner [28], although for singleton pregnancies nutritional and activity interventions have been successful in prior trials in reducing the rate of excessive GWG [29,30].

The main objective of this work was to determine whether the IOM's current guidelines for weight gain in twin pregnancies, according to maternal prepregnancy BMI, have an impact on perinatal outcomes.

Material and methods

We retrospectively included all consecutive twin pregnancies who delivered in a level-III university hospital maternity ward between 1997 and 2013. The study protocol was approved by the Ethics Committee for Research in Obstetrics and Gynecology of the French National College of Obstetricians and Gynecologists (CNGOF; CEROG OBS 2014-04-02).

We considered all twin gestations with two live born infants delivered after 23 weeks and 6 days of amenorrhea where the mothers had a documented prepregnancy BMI, without twin-to-twin transfusion syndrome. The prepregnancy BMI was calculated using self-reported height and weight at the first antenatal visit and categorized according to the World Health Organization's definition. Normal BMI was defined as a BMI of 18.5–24.5, overweight as 25–29.5, and obesity as 30 or greater. The gestational weight change was calculated by subtracting the maternal prepregnancy weight from the weight at delivery, or if not available, the weight at the last prenatal visit. Exclusion criteria included pregnancies complicated by major fetal anomalies, and monoamniocity. We also excluded women with a pre-pregnancy BMI less than 18.5 kg/m² [2] (underweight), as the IOM has not yet made weight gain recommendations in this population, and

patients without any weight report less than a month before their delivery.

As suggested by many authors previously [15,17–19,33,34], and because the IOM weight gain recommendations are for women who deliver at 37 weeks or after, it would not be appropriate to compare the total GWG in women who delivered at earlier gestational ages. Therefore, to control for gestational age at delivery, we divided the total weight gain by the gestational age in weeks at the last weight measurement to obtain the weight gain per week. We then divided the IOM lower limit of adequate weight gain at 37–42 weeks by 37 to determine the IOM recommended weight gain per week. For normal-BMI women, this was 0.46–0.68 kg/week; for overweight women, it was 0.36–0.62 kg/week; and for obese women, it was 0.3–0.51 kg/week. Then, we compared obstetrical and neonatal outcomes between groups of women categorized according to the IOM guidelines' matched cutoffs. In fact, we compared the adequate GWG (AGWG) group with women who exceeded the recommended GWG (EGWG), and women in whom the weight gain was below the IOM guidelines (low GWG, LGWG).

Chorionicity was determined based on the first-trimester ultrasound assessment of the dividing membrane characteristics (absence of the “twin peak” sign and presence of a thin dividing membrane) and confirmed by postpartum examination of the placenta and intertwined membrane.

All twin pregnancies were monitored according to the French guidelines [35]. Accordingly, uncomplicated monochorionic pregnancies were delivered between 36 and 39 weeks of gestation and dichorionic ones between 38 and 40 weeks [35]. Obstetrical complications included gestational hypertension, preeclampsia (diagnosis made using standard criteria [36]), gestational diabetes mellitus (GDM), cholestasis, placenta previa, premature rupture of membranes, premature delivery threats, instrumental deliveries, cesarean sections, and severe (>1 L) postpartum hemorrhage.

For neonates, we considered premature birth before 37 and 34 weeks' gestation, birth weight, arterial blood cord pH < 7.10, Apgar score < 7 at 5 min, transfer to neonatal intensive care unit (NICU), respiratory distress, neonatal sepsis, and death. Small for gestational age was defined as birth weight < 10th centile according to the curves used in our department [37].

Data were collected using the CLINSIGHT software (Version 6.2.300, 2011). Qualitative variables were described in terms of frequency and percentage, categorical variables as the mean (standard deviation) for age and median (interquartile range) for BMI. The normality of the quantitative variables was graphically checked and tested using the Shapiro-Wilk test. Patients' characteristics and main complications were compared between the included and excluded patients using the chi-square test for categorical variables and Student *t*-test for age. The patients' characteristics were compared between the three GWG groups using chi-square tests for categorical variables and an analysis of variance for age. Pregnancy and neonatal outcomes were compared using unadjusted and adjusted tests. For unadjusted comparisons, the three GWG groups were compared using chi-square tests, and for adjusted comparisons, logistic regression analyses were performed. The multivariable model was adjusted for pregestational BMI and smoking. Post hoc pairwise comparisons with the reference group (AGWG) were performed using the Bonferroni correction. Statistical testing was done at a two-tailed α level of 0.05. Data were analyzed using the SAS software package, release 9.4 (SAS Institute, Cary, NC).

Results

We included 878 women (Fig. 1). According to the prepregnancy BMI categories, there were 621 normal weight women (71%), 168 overweight women (19%), and 88 obese women (10%).

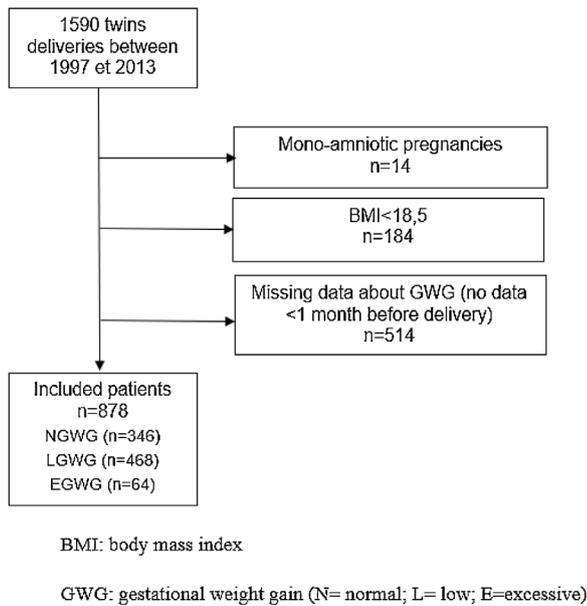


Fig. 1. Flow-chart of the study.

Among them, we counted 346 AGWG, 468 LGWG, and 64 EGWG patients.

In comparison with women from the AGWG reference group, women in the EGWG group were more likely smokers (23.4% in the EGWG group vs. 12.1% in the AGWG group), and they had a higher preconceptional BMI than women in the AGWG group did. Other patient characteristics were similar between the groups (Table 1). Table 3 (Supplementary material) shows that the included and excluded patients' characteristics were not statistically different.

Maternal and neonatal complications are reported in Table 2. Compared with AGWG women, LGWG women showed a lower rate of gestational hypertension (adjusted p value = 0.001). Likewise, EGWG women exhibited increased rates of preeclampsia compared with AGWG women. The LGWG group compared with the AGWG group showed more deliveries before 37 weeks of gestation (26.9% vs. 17.3%, $p = 0.009$), birth weight <2500 g (77.5% vs. 64.2%, $p < 0.0001$), respiratory distress syndrome, and transfer to the NICU. Nevertheless, neonates from EGWG patients more often showed Apgar scores <7 at 5 min (15.6% vs. 7.2%, $p = 0.049$).

There were no other statistically significant differences between the groups.

Table 1
Patients' characteristics according to their gestational weight gain.

	Total (n = 878)	AGWG (n = 346)	LGWG (n = 468)	EGWG (n = 64)	p
Age, mean (SD) (years)	30.5 (4.9)	30.7 (4.5)	30.5 (5.1)	29.2 (4.6)	0.07
Chorionicity					0.39
Bichorial	728 (83.0)	293 (84.7)	385 (82.4)	50 (78.1)	
Monochorial diamniotic	149 (17.0)	53 (15.3)	82 (17.6)	14 (21.9)	
Pregestational hypertension	3 (2.0)	1 (1.8)	1 (1.8)	1 (7.7)	NA
Pregestational diabetes mellitus	3 (2.1)	1 (1.8)	2 (2.6)	0	NA
Nulliparity	444 (50.6)	180 (52.0)	232 (49.6)	32 (50.0)	0.78
Smoking	118 (13.5)	42 (12.1) ^b	61 (13.1)	15 (23.4) ^b	0.049
Medically Assisted Reproduction	340 (38.8)	134 (38.8)	190 (40.7)	16 (25.0)	0.054
History of cesarean	77 (9.7)	21 (6.7)	50 (11.9)	6 (10.0)	0.060
BMI, median (IQR)	22.5 (20.6 to 25.7)	22.6 (20.8 to 25.5) ^b	22.2 (20.2 to 25.4)	25.0 (22.0 to 29.0) ^b	0.001
<25	621 (70.8)	246 (71.1)	344 (73.7)	31 (48.4)	
25–30	168 (19.2)	73 (21.1)	77 (16.5)	18 (28.1)	
>30	88 (10.0)	27 (7.8)	46 (9.9)	15 (23.4)	

Values are number (percentage) unless otherwise indicated.

a, b identify the significant pairwise post-hoc comparisons with reference group (NGWG) after Bonferroni's correction.

AGWG: adequate gestational weight gain; LGWG: low gestational weight gain; EGWG: excessive gestational weight gain; SD: standard deviation; NA: non-applicable; BMI: body mass index; IQR: interquartile range.

Discussion

We sought to investigate the effects of inadequate GWG on twin pregnancies according to the IOM classification (2009), considering the gestational age at delivery. In summary, we found more preeclampsia with EGWG and less gestational hypertension for LGWG compared with AGWG. IUGR, preterm birth and its usual complications were more frequent for LGWG women.

We observed that a high majority of AGWG and LGWG patients were included in the study; only 7.3% of the women were EGWG patients, who are supposed to constitute the full upper quartile. This may partly be due to our integration of preterm births and birth weights <2500 g, as the IOM recommendations were generated from the 25th–75th percentile of GWG for term pregnancies delivering twins >2500 g. However, this was not the case in other published studies [17,18,33,34]. Because most of the studies are from North America, this difference in the distribution could reflect European patients' characteristics. We also observed that only 10% of our patients were obese before pregnancy, a lower rate than expected. Indeed, 38% of the women worldwide are obese [39], but only 15% in France [40]. McKeating et al., about pregnant women, reported a 8.6% obese rate in the 13 European Union Accession countries and a 15.4% rate of the Original European Union countries, according [38], thus our rate is in between. It would be interesting to know if obese women are less likely to get a twin pregnancies, because of fertility issues maybe.

One of the main strengths of our study is that we adjusted our results according to the prepregnancy BMI. We also controlled our results for gestational duration, dividing the total GWG by gestational duration, to avoid bias due to the strong correlation between GWG and gestational duration. Indeed, the IOM recommendations were established for "total weight gain". However, women with longer pregnancies have more time to gain weight, and GWG is not linear throughout pregnancy. GWG during the first half of pregnancy is usually lower than in the second half [41]. Assumption of a linear weight gain pattern may have resulted in the incorrect conclusion that women delivering preterm will have lower rates of gain overall than those who deliver at a later gestational age [42].

Moreover, we decided to adjust the birth weight for gestational age. Using absolute birth weights is problematic because this cannot separate the neonates who are small due to IUGR and those who are small due to preterm birth.

We found more deliveries before 37 and 34 weeks, and birth weights <2500 g and <10th percentile for the LGWG patients. The evident correlation between GWG and birth weight/prematurity

Table 2
Included and excluded patients' characteristics.

	AGWG (n = 346)		LGWG (n = 468)		EGWG (n = 64)		P-value*
	n (%)	n (%)	OR (95% CI)	n (%)	OR (95% CI)		
Gestational hypertension	26 (7.5)	11 (2.4)	0.28 (0.14 to 0.59) ^a	9 (14.3)	1.67 (0.71 to 3.90)	0.001	
Preeclampsia	21 (6.1)	14 (3.0)	0.48 (0.24 to 0.97)	10 (15.6)	2.60 (1.14 to 5.96) ^b	0.001	
Cholestasis	5 (1.5)	19 (4.3)	NA	0	NA	NA	
Gestational diabetes mellitus	94 (30.6)	151 (36.9)	1.33 (0.97 to 1.83)	22 (39.3)	1.43 (0.78 to 2.61)	0.18	
Placenta praevia	3 (2.6)	2 (1.2)	NA	0	NA	NA	
Post-partum hemorrhage >1000cc	35 (11.2)	39 (9.2)	0.82 (0.50 to 1.32)	10 (17.2)	1.80 (0.82 to 3.97)	0.13	
Premature delivery threat	209 (60.6)	327 (70.0)	1.55 (1.16 to 2.08) ^a	37 (57.8)	0.97 (0.56 to 1.67)	0.009	
Delivery <37 weeks	60 (17.3)	126 (26.9)	1.73 (1.22 to 2.44) ^a	15 (23.4)	1.31 (0.68 to 2.53)	0.009	
Delivery <34 weeks	18 (5.2)	48 (10.3)	2.07 (1.18 to 3.64) ^a	6 (9.4)	1.54 (0.57 to 4.12)	0.040	
PROM	61 (17.7)	95 (20.5)	1.22 (0.86 to 1.75)	12 (18.8)	1.03 (0.51 to 2.07)	0.53	
Instrumental delivery	171 (58.7)	235 (58.5)	0.99 (0.73 to 1.35)	37 (67.3)	1.26 (0.68 to 2.36)	0.73	
Cesarean delivery	108 (31.3)	149 (31.8)	1.02 (0.75 to 1.38)	22 (34.4)	1.04 (0.58 to 1.84)	0.99	
Birth weight <2500 g	222 (64.2)	362 (77.5)	1.92 (1.41 to 6.62) ^a	40 (62.5)	0.87 (0.50 to 1.54)	<0.0001	
Birth weight <10th percentile	165 (48.3)	235 (50.8)	1.11 (0.84 to 1.57)	22 (34.4)	0.54 (0.31 to 0.95)	0.038	
Respiratory distress	53 (15.5)	106 (23.0)	1.63 (1.13 to 2.36) ^a	15 (23.4)	1.50 (0.77 to 2.91)	0.032	
pH <7.10 (arterial blood cord)	7 (8.1)	13 (9.8)	1.23 (0.46 to 3.24)	1 (7.1)	0.75 (0.08 to 7.07)	0.86	
Apgar <7 at 5 minutes	25 (7.2)	41 (8.8)	1.25 (0.74 to 2.10)	10 (15.6)	2.74 (1.22 to 6.14) ^b	0.049	
NICU admission	84 (24.3)	148 (31.6)	1.42 (1.04 to 1.95)	20 (31.3)	1.28 (0.70 to 2.32)	0.091	
Sepsis	53 (15.5)	57 (12.4)	0.79 (0.53 to 1.19)	11 (18.0)	1.20 (0.58 to 2.49)	0.36	
Death	3 (0.9)	6 (1.3)	NA	0	NA	NA	

a, b identify the significant pairwise post-hoc comparisons with reference group (NGWG) after Bonferroni's correction.

AGWG: adequate gestational weight gain; LGWG: low gestational weight gain; EGWG: excessive gestational weight gain; OR: odds-ratio; CI: confidence interval; NA: non-applicable; PROM: premature rupture of membranes (>12 h; at any gestational age); IUGR: intra uterine growth restriction; NICU: neonatal intensive care unit.

* P-value for global comparison between the three groups adjusted for pre-gestational BMI and smoking.

confirmed the findings of previous studies [11,15,17,18,24]. Nevertheless, it is uncertain why pre-pregnancy underweight and insufficient GWG could provoke preterm birth. Chronic nutritional deficiency and gestational anemia lead to placenta dysfunction, which is considered to lead to the production of stress hormones, thus promoting uterine contractions. Deficiencies in nutrients involved in the immune system (iron, zinc), could also be involved in an enhancement of infections, known to carry for preterm births.

We found that hypertensive gestational disorders were associated with excessive GWG, as demonstrated for singletons [43]. The mechanisms are poorly understood, but they may involve hypertriglyceridemia, elevation of fatty acids, and increased fraction of low density lipoprotein-cholesterol, making women atherogenic and bringing about endothelial dysfunction [44]. It is difficult to specify whether weight gain induces the occurrence of vascular complications or if, conversely, weight gain is the consequence of a frequent fluid-sodium retention in the case of preeclampsia or pregnancy-induced hypertension.

We did not find a link between GWG and gestational diabetes. Past studies have reported contradictory associations, and only in specific BMI subgroups [18,19,31,32], making their results difficult to interpret. For singletons, the IOM concluded in 2009 that the available data (11 studies) provided weak evidence of a link between GWG and development of an abnormal glucose metabolism [13].

The main interest of our study was the detailed report of neonatal outcomes and the highlighting of a statistically significant impact of GWG on those outcomes (more respiratory distress in LGWG group and more Apgar scores <7 at 5 min in EGWG group), which has been poorly reported to date. Transfer to the NICU was also more frequent LGWG group, even if the difference did not reach the statistical significance (31.6% vs. 24.3%).

Indeed, among the available studies on GWG and twin gestations according to the IOM guidelines, only a small body of data is available. Fox et al. and Lal et al. reported on NICU admissions [16,31], while Gavard et al. reported on Apgar scores and first-year mortality [23]. None of these studies found any significant difference. For Gavard et al., this can be attributed to the exclusive inclusion of obese women, as obesity is a major

overwhelming factor. For the 2 other studies, we cannot exclude practice differences. Indeed, Lal et al. found that around 45% of the pregnancies resulted in NICU admissions, which is more than in our cohort, while Fox et al. found around 3%, mostly because they did not include preterm births.

The limitations of this study mainly related to its retrospective design and the rate of excluded patients. The exclusion rate was high (32%) because we decided to exclude all the patients for whom we did not have any GWG data from less than 1 month before delivery, and even if these data are part of the recommended monthly prenatal consultation, they were often missing. The advantage is that we are showing these data; we did not choose to avoid including them, leaving the data unavailability rate unknown. In addition, we showed that the included and excluded patient characteristics were not statistically different (Table 3, Supplementary material). Finally, we decided not to adjust for chorionicity, as suggested in the literature [26], but we showed in Table 1 that chorionicity was equally distributed in the different groups.

Conclusion

Our results suggest that the 2009 IOM guidelines for twin pregnancy are appropriate and therefore should be routinely used to improve twin pregnancies outcomes. The finding that a focus on nutrition and adequate weight gain may prolong twin gestations is exciting. Even if there is no prospective trial in this field yet, all the retrospective data are tending toward the same results.

In any case, nutritional assessment and counseling need to be part of twin pregnancies' prenatal care, as gestational weight gain is a modifiable factor.

Declaration of interests

The authors report no conflict of interest.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.ejogrb.2019.01.010>.

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