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Original article

Preconception maternal gastric bypass surgery and the impact on fetal growth parameters

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Abstract

Background: Bariatric surgery is increasingly performed in women of reproductive age. As bariatric surgery will result in postoperative rapid catabolic weight loss which potentially leads to fetal malnutrition and directly related impaired intra-uterine growth, it is advised to postpone pregnancy for at least 12–18 months after surgery.

Objectives: To investigate the consequences of preconception gastric bypass surgery (pGB) on fetal growth parameters and maternal pregnancy outcome.

Setting: Maasstad Hospital, The Netherlands, general hospital and Erasmus Medical Center, The Netherlands, university hospital.

Methods: We included 97 pGB pregnancies (Maasstad hospital) and 440 non-bariatric pregnancies (Rotterdam Periconception cohort, Erasmus Medical Center). Longitudinal second and third trimester fetal growth parameters (head circumference, biparietal diameter, femur length, abdominal circumference, estimated fetal weight) were analyzed using linear mixed models, adjusting for covariates and possible confounders. Fetal growth and birthweight in pGB pregnancies were compared to non-bariatric pregnancies and Dutch reference curves. Maternal pregnancy outcome in the pGB group was compared to non-bariatric pregnancies.

Results: All fetal growth parameters of pGB pregnancies were significantly decreased at 20 weeks' gestation ($P < .001$) and throughout the remaining part of pregnancy ($P < .05$) compared with non-bariatric pregnancies (crude and adjusted models). In our cohort, gestational weight gain was not significantly associated with birthweight corrected for gestational age. Birthweight was significantly lower in pGB pregnancies (estimate –241 grams [95% CI, –342.7 to –140.0]) with a 2-fold increased risk of small-for-gestational-age (SGA) (adjusted odds ratio 2.053 [95% CI, 1.058 to 3.872]). Compared to the non-bariatric pregnancies, we found no significant differences in maternal pregnancy outcome.

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Conclusions: PGB is associated with overall reduced fetal growth trajectories and a 2-fold increased risk of SGA, without significant adverse consequences for maternal pregnancy outcome. We recommend close monitoring of fetal growth after pGB. (Surg Obes Relat Dis 2023;■:1–10.)

Keywords: Gastric bypass; Fetal growth; Birthweight; Ultrasonography; Body mass index

The global obesity epidemic also involves women of reproductive age. Obesity (defined as a body mass index [BMI] ≥30 kg/m^2) can influence fetal growth patterns and subsequent birthweight [1,2]. Fetal neuroendocrine and metabolic processes are affected by maternal obesity and associated low-grade inflammation, influencing fetal insulin levels and hereby regulating fetal growth [3,4]. Obesity increases the risk of adverse pregnancy outcomes for women and their offspring, not only during pregnancy but also later in life [5]. Offspring of women with obesity have an increased body fat percentage at birth, which is associated with obesity later in life, even when maternal glucose tolerance has been within the normal range during pregnancy [6].

Reducing obesity preconceptionally appears a promising treatment modality for optimizing maternal, fetal, and offspring health. Severe obesity is associated with a significantly increased risk of pregnancy complications compared to controls with a normal BMI, such as gestational diabetes (adjusted odds ratio [aOR] 11.01 [95% CI, 10.25–11.82]), high birth weight (>4.5 kg) (aOR 2.74 [95% CI, 2.55–2.95]), pre-eclampsia (aOR 4.44 [95% CI, 4.17–4.72]), emergency cesarean section (42–50 versus 9%), and failed induction of labor (29 versus 13%) [7,8].

The most effective long-term weight loss intervention for severe obesity (defined as a BMI ≥40 kg/m^2) is bariatric surgery. Since most postbariatric patients are women of reproductive age, the postoperative effects of bariatric surgery on fertility, pregnancy, and offspring are increasing [9–14]. It has been shown that prepregnancy bariatric surgery reduces the risk of gestational diabetes, large-for-gestational-age (LGA) infants, hypertensive disorders during pregnancy, postpartum hemorrhage, and cesarean delivery rates [13–15]. Additionally, when matched for presurgical BMI, an increased risk of intra-uterine growth restriction, small-for-gestational-age (SGA) infants, and preterm birth was observed compared to controls [16]. Although successful in achieving weight loss, preconception gastric bypass (pGB) is associated with an increased risk of nutritional deficiencies which may impact fetal outcome [17]. A recent meta-analysis has shown that preconception bariatric surgery and specifically gastric bypass (GB) surgery can lead to a reduced birthweight, which is associated with increased neonatal morbidity and mortality and adverse health during the life course [16,18]. The optimal time interval between bariatric surgery and conception has not been established yet, but postbariatric patients are internationally advised to wait before planning a pregnancy during the first 12–24 postoperative months [19–21].

The overall studied neonatal outcomes are mainly limited to birthweight, preventing detailed insight into the development of impaired fetal growth. One study found that estimated fetal weight was lower in postbariatric offspring, but little is known regarding intra-uterine adaption after bariatric surgery [22]. Our previous research showed that pGB is associated with lower vitamin serum levels [23]. Therefore, we hypothesized that the GB-related malnutrition and postsurgically adapted maternal metabolic and (neuro) endocrine balances will significantly hamper fetal growth potential in general and influence intra-uterine adaptation. Our study focuses on the specific associations between the currently most practiced type of bariatric surgery nationally (i.e. GB) and fetal growth parameters and birthweight.

Methods

Study design and participants

We performed a retrospective cohort study in which we compared 2 cohorts. Diagnosis Treatment Combination (DTC) codes were used to identify eligible pregnancies after pGB with a due date between 2009 and 2019 by searching the electronic medical record database for the combination of the DTC code for bariatric surgery and any pregnancy-related DTC code after bariatric surgery. An additional search on the appointment code referring to patients visiting the bariatric outpatient clinic for follow-up during pregnancy was performed. Only patients undergoing pGB were included at the bariatric expertise center of the Maasstad Hospital, Rotterdam, The Netherlands. At this expertise center, of the Maasstad Hospital, a standard gastric bypass is performed with a Roux-en-Y reconstruction, consisting of an alimentary limb of 150 cm and a biliopancreatic limb of 50 cm. To reduce potential bias of temporal and spatial confounding, the group of non-bariatric pregnancies was selected around the same time frame from the Rotterdam Periconception Cohort (the Predict study), a tertiary center prospective cohort study at the Erasmus Medical Center, Rotterdam, The Netherlands. All singleton pregnancies without preconception bariatric surgery included between 2010 and 2020 who received longitudinal second and third trimester ultrasound examinations were used as a comparison group.

The study protocol of the Predict study has been described previously [24,25].

Gestational age (GA) was determined by crown-rump length ultrasound measurement between 10^{+0} and 12^{+6} weeks' gestation after the last menstrual period, or by conception date plus 14 days if conception occurred following in vitro fertilization.

Details of ethical approval

This study has been approved by the medical ethical review committee of the Erasmus MC, The Netherlands (MEC-2019-0518) and the local board of the Maasstad Hospital, The Netherlands (MEC-2019-0792). A waiver has been issued for the Medical Research Act and therefore formal written consent was not required from the patients with pregnancies after GB surgery. All Rotterdam Periconception cohort participants provided written consent before participation (MEC 2004–227).

Clinical parameters

Maternal analyzed characteristics were age at conception, obstetric history, substance use, folic acid use, length (centimeters), weight (kilograms), GA at the ultrasound examination, smoking, parity, geographical background, fetal sex, booking BMI (kg/m^2), gestational weight gain (kilograms) between pregnancy intake and the day of delivery and time between surgery and conception (if applicable). Gestational weight gain was categorized into insufficient, adequate, and excessive weight gain according to the guidelines from the Institute of Medicine [26]. Regarding the main aims of this study, fetal growth parameters were measured by longitudinal ultrasound examinations (see below), whereas birthweight (grams) and pregnancy outcome (pregnancy-related hypertensive disorders, gestational diabetes, and preterm birth) were collected from medical records.

Ultrasound examinations

Longitudinal ultrasound examinations of fetal growth parameters in pGB pregnancies including head circumference (HC), biparietal diameter (BPD), abdominal circumference (AC), and femur length (FL) were collected between 19 and 38 weeks' gestation, as part of standard obstetrical care. The ultrasound examinations in pGB pregnancies were performed as part of the standard care according to the protocol for (clinical) antenatal care of the Dutch Society of Obstetrics and Gynecology.

In the non-bariatric pregnancies, longitudinal ultrasound examinations of fetal growth including HC, BPD, AC, and FL were performed at 22–24 weeks' gestation, 26 weeks' gestation, and 30–32 weeks' gestation according to study protocol. Estimated fetal weight (EFW) was calculated using the Hadlock IV formula [27].

To further validate the findings for clinical practice, fetal ultrasound measurements from the pGB pregnancies were also compared to the standard Dutch fetal reference curves used in routine obstetrical care [28]. All ultrasound examinations were performed by experienced fetal sonographers according to the International Society of Ultrasound in Obstetrics and Gynecology practice guidelines [29].

Statistical analysis

Continuous, normally distributed variables were presented as mean with standard deviation (SD), and variables with a skewed distribution as median with interquartile range (IQR). Categorical variables were presented as counts and proportions.

In order to investigate fetal growth trajectories, we used linear mixed models to analyze the ultrasound examinations of each pregnancy. To accurately model fetal growth we applied a logarithmic transformation of the fetal growth parameters.

When comparing fetal growth in the pGB pregnancies with non-bariatric pregnancies, average growth at 20 weeks' GA (expressed as the intercept) of the non-bariatric pregnancies was used as a reference.

The results of pGB pregnancies were also compared to Dutch standard reference curves for fetal growth used in general daily clinical practice [28]. To account for repeated measures compared to reference curves, multiple outputation was performed [30]. Multiple outputation is a standardized technique to analyze correlated data and involves creating new data sets by repeatedly discarding observations from a cluster to break the dependence. These data sets are then analyzed separately and the results are pooled.

Fetal growth parameters were adjusted for GA and converted into standard deviation scores (Z-scores). The association between time between surgery and conception and fetal growth parameters was also studied.

Multivariable regression analysis was used to investigate the association between pGB and birthweight, SGA (birthweight $<10^{th}$ percentile) and large-for-gestational-age (LGA) (birthweight $>90^{th}$ percentile). As GA, smoking, parity, booking BMI, geographic background, fetal sex, gestational weight gain, time between surgery and conception, and age at conception are all associated with birthweight, we decided to correct for these in the regression analysis.

When investigating the association of birthweight in pGB pregnancies with Dutch standard birthweight charts, referred to as "Hoftiezer percentiles", [31] no adjustments were performed for GA and fetal sex, as these percentiles are already adjusted for these factors. A one-sample Kolmogorov-Smirnov test was performed to investigate the association between pGB and Hoftiezer percentiles.

Multivariable logistic regression was applied to investigate the associations with pregnancy outcome, adjusted for BMI. Analyzed maternal pregnancy outcome included pregnancy-related hypertensive disorders (gestational hypertension or preeclampsia), gestational diabetes (glucose intolerance resulting in hyperglycemia with onset during pregnancy) [32], and preterm birth (defined as birth before 259 days' GA).

We considered a P value <.05 as statistically significant. The statistical analyses were performed using SPSS Statistics Version 28.0.1.0 (IBM) and R Statistical Software (Foundation for Statistical Computing, Vienna, Austria, Version 4.1.2).

Results

Longitudinal second and third trimester ultrasound data were available in 97 pGB cases and 440 non-bariatric pregnancies.

Maternal baseline characteristics

The baseline characteristics of the included 97 pGB pregnancies and 440 non-bariatric pregnancies are shown in Table 1. The median surgery-to-conception interval was 18.3 months (IQR 9.4–28.5). Minimum time between pGB and conception was .2 months with a maximum of 94.7 months. The pGB group had a significantly higher booking BMI (29.8 versus 25.3 kg/m^2; P < .001), younger age (29.2 versus 32.0 yr; P < .001), and lower frequency of folic acid use (P = .008). The number of ultrasound examinations did not differ significantly between the groups.

Fetal growth parameters

Table 2 illustrates the difference in HC, BPD, AC, FL, and EFW trajectories between pGB cases (n = 97) and non-bariatric pregnancies (n = 440). After adjustment for GA, fetal sex, geographic background, age at conception, booking BMI, smoking, parity and folic acid use, pGB cases showed a significantly lower HC, BPD, AC, FL, and EFW at 20 weeks GA (P < .001), of which BPD, AC, and EFW remained significantly reduced until the end of pregnancy (P <.05). Figs. 1A–E show the trajectories of these different fetal growth parameters for cases (red) and non-bariatrics (blue). Time between pGB and conception did not significantly change the association between pGB and fetal growth parameters.

Table 1
Baseline characteristics of the post-gastric bypass pregnancies (n = 97) and the control pregnancies (n = 440)

	Post–gastric bypass pregnancies (n = 97)	Control pregnancies (n = 440)	P value
Age at conception (yr)			
Median	29.2 (26.0–32.2)	32.0 (28.9–35.1)	<.001*
Missing	0	0	
Geographic origin			<.001*
Caucasian	61 (62.9)	346 (83.4)	
African	7 (7.2)	22 (5.3)	
Asian	1 (1.0)	10 (2.4)	
Other/mixed	28 (28.9)	37 (8.9)	
Missing	0	25	
Parity			
Nulliparous	40 (41.2)	226 (51.4)	.071
Missing	0	0	
BMI before surgery (kg/m^2)			
Median	43.6 (40.8–46.4)	-	-
Missing	0		
BMI at conception (kg/m^2)			
Median	29.8 (26.2–32.4)	25.3 (22.2–29.4)	<.001*
Missing	10	34	
Time between gastric bypass surgery and conception (mo)			
Median	18.3 (9.4–28.5)	-	-
Missing	0		
Smoking			
Yes	12 (12.4)	56 (13.2)	.819
Missing	0	17	
Folic acid use			
Yes	88 (92.6)	415 (97.9)	.008*
Missing	2	16	
Fetal sex			
Female	48 (52.2)	217 (50.2)	.735
Missing	5	8	

BMI = body mass index.
Data are presented as number of cases (valid %) or median (interquartile range).
* Significant P values.

Table 2
The associations between gastric bypass surgery and second and third trimester fetal growth parameters

	Model 1			Model 2		
	Estimate[†]	95% confidence interval	*P* value	Estimate	95% confidence interval	*P* value
Head circumference (mm)						
Fetal growth at 20 weeks' GA (intercept)	173.001	172.242–173.747	<.001*	171.932	166.102–177.985	<.001*
GA	1.068	1.068–1.069	<.001*	1.068	1066–1.069	<.001*
Gastric bypass surgery	.984	.976–.992	<.001*	.982	.972–.992	<.001*
GA^2	.998	.998–.998	<.001*	.998	.998–.998	<.001*
GA × Gastric bypass surgery	1.001	1.001–1.002	<.001*	1.001	1.001–1.002	<.001*
Biparietal diameter (mm)						
Fetal growth at 20 weeks' GA (intercept)	48.086	47.780–48.395	<.001*	50.694	48.638–52.831	<.001*
GA	1.069	1.067–1.070	<.001*	1.069	1.067–1.071	<.001*
Gastric bypass surgery	.979	.967–.990	<.001*	.979	.966–.992	<.001*
GA^2	.998	.998–.999	<.001*	.998	.998–.999	<.001*
GA × Gastric bypass surgery	1.001	1.000–1.002	.100	1.001	1.001–1.002	.027*
Abdominal circumference (mm)						
Fetal growth at 20 weeks' GA (intercept)	156.335	155.462–157.213	<.001*	153.561	146.028–159.876	<.001*
GA	1.069	1.069–1.071	<.001*	1.069	1.069–1.069	<.001*
Gastric bypass surgery	.962	.962–.972	<.001*	.963	.953–.974	<.001*
GA^2	.999	.999–.999	<.001*	.999	.999–.999	<.001*
GA × Gastric bypass surgery	1.001	1.000–1.002	.009*	1.001	1.000–1.002	.039*
Femur length (mm)						
Fetal growth at 20 weeks' GA (intercept)	32.622	32.434–32.812	<.001*	32.295	30.932–33.717	<.001*
GA	1.076	1.075–1.077	<.001*	1.076	1.074–1.078	<.001*
Gastric bypass surgery	.967	.956–.978	<.001*	.964	.951–.977	<.001*
GA^2	.998	.998–.998	<.001*	.998	.998–.998	<.001*
GA	1.002	1.002–1.003	<.001*	1.002	1.001–1.003	<.001*
Gastric bypass surgery						
Estimated fetal weight (grams)						
Fetal growth at 20 weeks' gestation (intercept)	339.984	336.198–343.814	<.001*	325.610	292.598–355.704	<.001*
GA	1.207	1.204–1.210	<.001*	1.207	1.204–1.213	<.001*
Gastric bypass surgery	.953	.934–.974	<.001*	.954	.927–.973	<.001*
GA^2	.996	.996–.997	<.001*	.997	.996–.997	<.001*
GA	1.000	.998–1.001	.649	.999	.997–1.001	.348
Gastric bypass surgery						

GA = gestational age.
Difference in growth rate between post-gastric bypass pregnancies and control pregnancies; associations were investigated using linear mixed effect models. Model 1: corrected for gestational age. Model 2: corrected for gestational age, fetal sex, geographic background, age at conception, BMI at conception, smoking, parity, and folic acid use.
* Significant *P* values.
[†] Estimates were retransformed from a logarithmic to the original scale and are multiplicative.

Figs. 2A–C and Figs. S1A–B visualize fetal growth patterns of the pGB cases converted into longitudinal Z-scores against the Dutch reference curves used for routine obstetrical care. Individual fetal parameters of HC and BPD were decreased at midgestation ($P = .01$ and $P < .001$; Fig. 2A and Fig S1A), which continued throughout pregnancy. The EFW and AC curves decreased progressively midthird trimester (Figs. 2B–C). In general, no clear effect on FL was observed ($P = .843$, Fig. S1B). The progressive worsening of the AC midtrimester with decreased but stable HC is suggestive of relative brain sparing mechanisms.

Birthweight and pregnancy outcome

The associations between pGB and birthweight are described in Table 3. There was no significant difference in length of gestation between both groups. Birthweight was significantly lower in the pGB pregnancies (adjusted estimate –241.4 grams [95% CI, –342.7 to –140.0]). In line with these findings, compared with the general Dutch birthweight charts, Hoftiezer percentiles were significantly lower after pGB (adjusted estimate –17.9 [95% CI, –25.1 to –10.6], $P < .001$), indicating that birthweight was almost 18 percentiles lower in the pGB group. The risk of SGA was significantly increased in pGB pregnancies (aOR 2.053 [95% CI: 1.058–3.872], $P = .029$), whereas the risk of LGA was significantly lower (aOR .099 [95% CI: .0055–.4821], $P = .025$) (Table S1). Maternal booking BMI was positively associated with the risk of LGA (aOR 1.1460 [95% CI: 1.0749–1.2235], $P < .001$), while it was not significantly associated with the risk of SGA (OR .9662 [95% CI: .9121–1.0199], $P = .226$). In addition, we found no significant associations between birthweight and

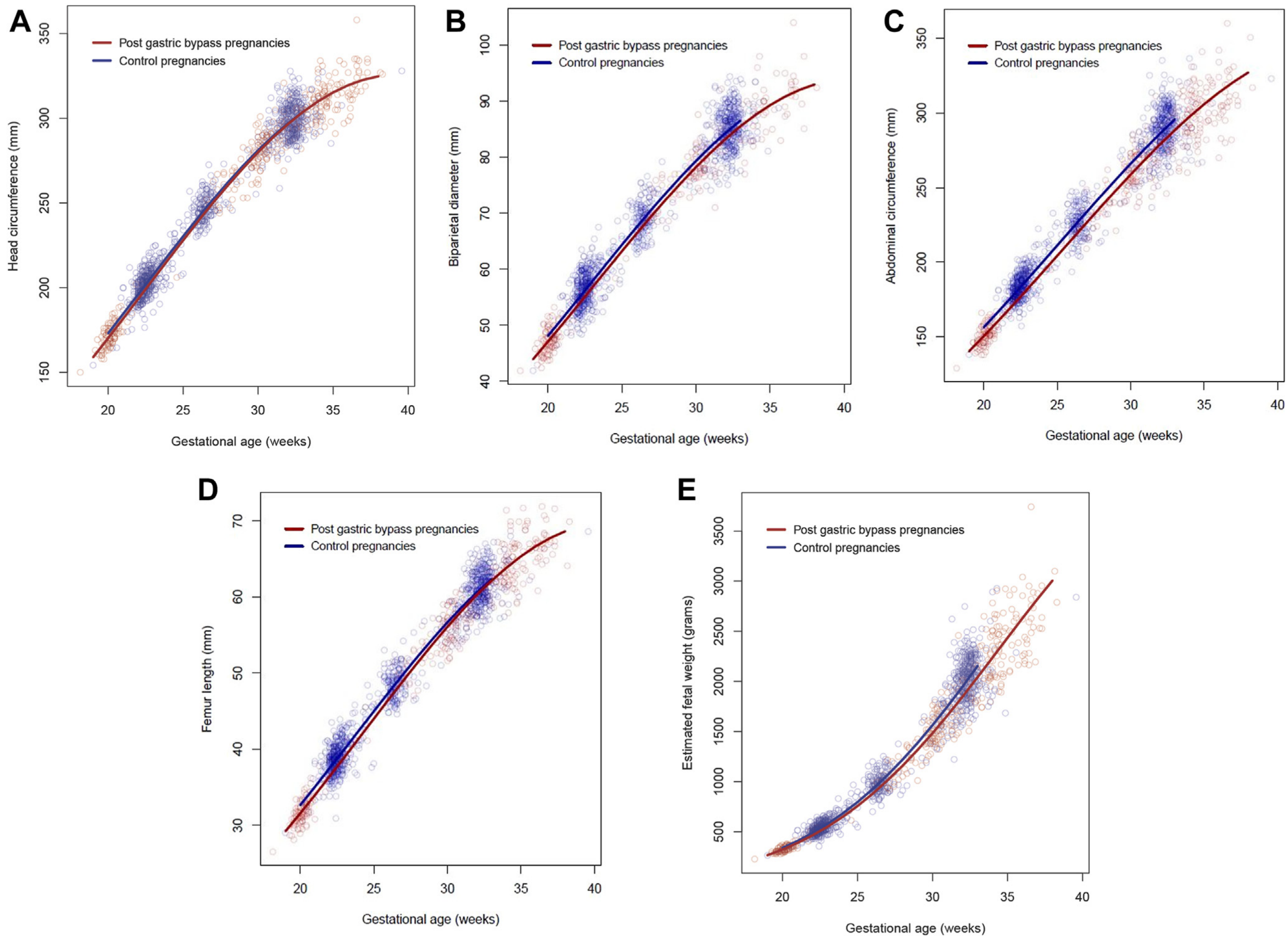

Fig.1. (A) Head circumference (mm) in post gastric bypass pregnancies (n = 97) and control pregnancies (n = 440). (B) Biparietal diameter (mm) in post gastric bypass pregnancies (n = 97) and control pregnancies (n = 440). (C) Abdominal circumference (mm) in post gastric bypass pregnancies (n = 97) and control pregnancies (n = 440). (D) Femur length (mm) in post gastric bypass pregnancies (n = 97) and control pregnancies (n = 440). (E) Estimated fetal weight (grams) in post gastric bypass pregnancies (n = 97) and control pregnancies (n = 440).

the effect of time interval between pGB and conception, maternal age, folic acid use, smoking, geographic background, or gestational weight gain (all $P > .05$, Table S2). We found no significant associations between pGB and pregnancy-related hypertensive disorders, gestational diabetes, and preterm birth (Table S1). The incidence of adverse maternal pregnancy outcome is illustrated in Table S3.

Discussion

Main findings

This study aimed to investigate the relationship between maternal factors, including BMI and gestational weight gain, pGB and fetal growth parameters, and birthweight. Our results show that fetal growth, determined by ultrasound measurements of individual fetal growth parameters and estimated fetal weight, is decreased from 20 weeks' gestation in pGB pregnancies. The significantly lower estimated fetal weight throughout pregnancy in pGB cases resulted in significantly more SGA and fewer LGA neonates as compared to the non-bariatric group.

Interpretation

This study found decreased intra-uterine growth in pGB pregnancies. The findings of decreased fetal growth potential after pGB are supported by the increased risk of SGA and the decreased risk of LGA. Our findings are in line with 2 previous cohort studies also reporting a higher risk of SGA after bariatric surgery and a lower risk of LGA infants [33,34]. Multiple mechanisms may underlie the significantly reduced fetal growth and resulting lower birthweight in pGB cases. Factors involved in fetal growth restriction in postbariatric patients described in the literature include intermittent hypoglycemia, caloric restriction, the release of persistent organic pollutions after major weight loss, hormonal changes such as an improved insulin sensitivity, and

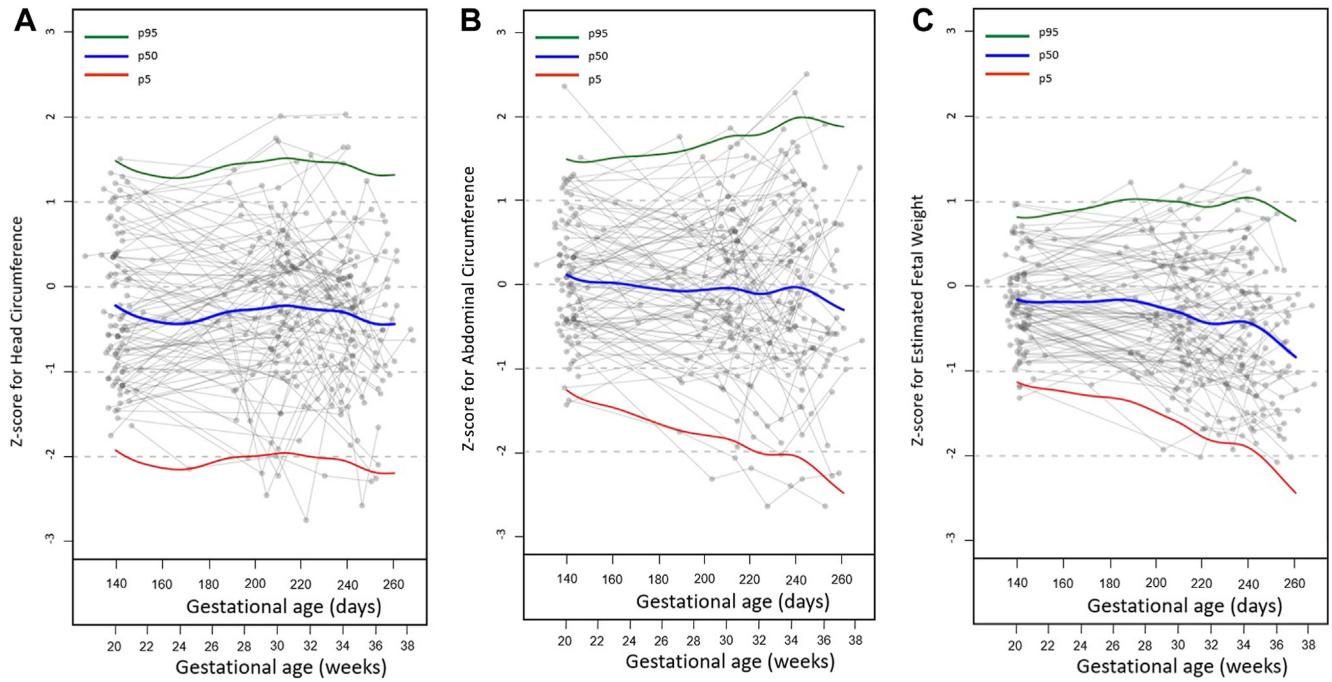

Fig. 2. (A) Z-scores for head circumference (HC) of pregnancies after gastric bypass surgery (n = 97). The dotted lines correspond with the Z-scores. Z-score -1 corresponds with the 15.9th percentile, Z-score +1 corresponds with the 84.1st percentile. (B) Z-scores for abdominal circumference of pregnancies after gastric bypass surgery (n = 97). The dotted lines correspond with the Z-scores. Z-score -1 corresponds with the 15.9th percentile, Z-score +1 corresponds with the 84.1st percentile. (C) Z-scores for estimated fetal weight (EFW) of pregnancies after gastric bypass surgery (n = 97). The dotted lines correspond with the Z-scores. Z-score -1 corresponds with the 15.9th percentile, Z-score +1 corresponds with the 84.1st percentile.

increased incretin levels during the second half of pregnancy [35–39].

We observed a lower risk of LGA. Since preconception BMI is positively associated with birthweight, the large decrease in BMI after pGB could explain why the risk of LGA decreases after pGB. Our results suggest that the combination of postsurgical reduction in maternal BMI before pregnancy and the maternal booking BMI play a major role in fetal growth potential and final birthweight.

The incidence of adverse maternal pregnancy outcome was not significantly different between pGB cases and the non-bariatric group. However, compared with 120 pregnant non-postbariatric women with a comparable pre-surgical BMI studied by Lapolla et al., the incidence of gestational diabetes and pregnancy-related hypertensive disorders is lower in pGB pregnancies, without a difference in the occurrence of preterm birth [40]. A meta-analysis of observational studies matching patients on presurgical BMI also showed a reduction in gestational diabetes and gestational

Table 3
The associations between gastric bypass surgery and perinatal outcomes

	Model 1			Model 2		
	Estimate	95% confidence interval	*P* value	Estimate	95% confidence interval	*P* value
Birthweight (grams)						
Gastric bypass surgery	–168.0	–262.2 to –73.7	.001*	–241.4	–342.7 to –140.0	<.001*
Hoftiezer percentiles						
Gastric bypass surgery	–12.47	–19.18 to –5.76	<.001*	–17.9	–25.1 to –10.6	<.001*
Gestational age (d)						
Gastric bypass surgery	1.3	–2.0 to 4.5	.456	3.0	–.8 to 6.8	.118

Associations were evaluated using linear regression analysis. Model 1: birthweight: adjusted for gestational age. Hoftiezer percentiles and gestational age: unadjusted. Model 2: birthweight: adjusted for gestational age, smoking, parity, BMI at conception, folic acid use, geographic background, fetal sex, and age at conception. Hoftiezer percentiles and gestational age: adjusted for smoking, parity, BMI at conception, folic acid use, geographic background, fetal sex, and age at conception.

* Significant *P* values.

hypertension, which is likely caused by postbariatric weight loss [16]. A retrospective case-control study matched for preoperative BMI performed by Rottenstreich et al. researched pregnancy outcome after sleeve gastrectomy and found comparable results regarding a similar risk of pregnancy-related hypertensive disorders, fewer LGA and more SGA infants [41]. Contrary to our study results, Rottenstreich et al. did find a decreased risk of gestational diabetes, which can be explained by the use of a control group matched for preoperative BMI [41]. Pregnancies in women with (persisting) severe obesity have a higher risk of pregnancy complications. In line with this, several studies indicate that in cases of prepregnancy obesity, weight loss due to bariatric surgery will improve maternal pregnancy outcome [16,40]. In view of long-term maternal health, maternal weight loss before achieving a pregnancy should therefore be encouraged and recommended.

Strengths and limitations

Strengths of this study include the longitudinal follow-up with serial ultrasound monitoring of only singleton pregnancies after pGB. Even in comparison to nonbariatric pregnancies of a tertiary cohort (the Predict study), in which more adverse pregnancy outcome including fetal growth restriction are expected, fetal growth in pGB cases was reduced. Fetal growth is even more decreased compared to standard Dutch curves for fetal growth used in standard obstetrical clinical practice, highlighting the robustness of the negative associations between pGB and fetal growth.

Limitations of this study include the retrospective study design, missing placental weights and lack of histopathology and the use of aspirin, missing information on socioeconomic status which can influence nutritional status, and the lack of routine Doppler measurements of fetal middle cerebral and umbilical artery. As the incidence of pregnancy complications was low in both the pGB cases and the non-bariatric pregnancies, the power to detect differences between the groups may have been too low.

Practical implications

Ultrasound examination should also include simultaneous assessment of placental growth and development, including uterine and umbilical artery Doppler measurements. The most optimal moment and BMI after pGB to conceive and support fetal growth still need to be determined. However, focusing on maternal outcome, weight loss before achieving a pregnancy should be advised. This study emphasizes the importance of preconception counselling of postbariatric women contemplating pregnancy. Also, pregnancies after GB should be considered as high-risk pregnancies, with the need for regularly performed fetal growth assessment by serial ultrasound examination to detect fetal growth restriction and monitor fetal growth more frequently. If necessary, induction of labor can be contemplated.

Research implications

First trimester embryonic and placental growth in women with bariatric surgery have hardly been investigated. Nørgaard et al. reported delayed fetal growth between the first and second trimester [42], indicating reduced growth potential is initiated before the second trimester of pregnancy. This is supported by our findings of significantly lower HC, BPD, EFW, AC, and FL at 20 weeks' gestation. Our results suggest that to identify the initiating moment of reduced fetal growth potential, ultrasound assessment should be initiated earlier than mid-pregnancy. For example, the recent implementation of the 12-to-13-week fetal anomaly scan could be of added value in this matter [43]. Moreover, the use of aspirin as a prophylaxis for fetal growth restriction could be studied in postbariatric pregnancies. In addition, when possible, the effect of nonsurgical prepregnancy weight loss on fetal and maternal pregnancy outcome should be investigated.

The pathophysiological mechanisms behind fetal growth restriction in general are largely unexplained. Previous research has shown that several demographic, physiologic, and obstetric factors that are associated with fetal growth only explain 36.3% of birthweight variability [44]. The prospective BEYOND study investigates postbariatric women using 3-dimensional ultrasounds to assess embryonic and placental development from early gestation and should provide more inside into this issue [44].

Head circumference is known to be correlated with fetal brain volume and neurocognitive development later in life, while lower birthweight is considered a risk factor for cardiovascular disease. Our study and other findings of significantly reduced fetal head parameters and lower birthweight in pGB cases warrant close follow-up and scientific research of neurocognitive outcome during childhood.

We recommend future research to closely monitor and support maternal homeostasis after pG1B, (re)evaluate the optimal moment for conception, standardized longitudinal assessments of fetal and placental growth, and initiate active follow-up of offspring health during the life course.

Conclusion

This study shows that there is an increased risk of overall stunted growth already detectable at midpregnancy and until the end of gestation, independent of time interval between surgery and conception. Compared to women with severe obesity, pGB reduces the risk of gestational diabetes, macrosomia, and pregnancy-related hypertensive disorders, and therefore improves maternal pregnancy outcome. We also found significantly more SGA neonates after pGB, which is associated with adverse health outcomes later in life. Therefore, we conclude that any pregnancy after GB should be perceived as a high-risk pregnancy and advise strict postnatal follow-up focusing on neurodevelopmental and endocrine status of these offspring.

Disclosures

The authors have no commercial associations that might be a conflict of interest in relation to this article.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.1016/j.soard.2023.08.015.

References

[1] El Rafei R, Abbas HA, Charafeddine L, et al. Association of pre-pregnancy body mass index and gestational weight gain with preterm births and fetal size: an observational study from Lebanon. Paediatr Perinat Epidemiol 2016;30(1):38–45.

[2] Spann MN, Scheinost D, Feng T, et al. Association of maternal prepregnancy body mass index with fetal growth and neonatal thalamic brain connectivity among adolescent and young women. JAMA Network Open 2020;3(11):e2024661.

[3] Parisi F, Milazzo R, Savasi VM, Cetin I. Maternal low-grade chronic inflammation and intrauterine programming of health and disease. Int J Mol Sci 2021;22(4):1732.

[4] Westermeier F, Sáez PJ, Villalobos-Labra R, Sobrevia L, Farías-Jofré M. Programming of fetal insulin resistance in pregnancies with maternal obesity by ER stress and inflammation. BioMed Res Int 2014;2014:917672.

[5] Aune D, Saugstad OD, Henriksen T, Tonstad S. Maternal body mass index and the risk of fetal death, stillbirth, and infant death: a systematic review and meta-analysis. JAMA 2014;311(15):1536–46.

[6] Sewell MF, Huston-Presley L, Super DM, Catalano P. Increased neonatal fat mass, not lean body mass, is associated with maternal obesity. Am J Obstet Gynecol 2006;195(4):1100–3.

[7] Ovesen P, Rasmussen S, Kesmodel U. Effect of prepregnancy maternal overweight and obesity on pregnancy outcome. Obstet Gynecol 2011;118(2 Pt 1):305–12.

[8] Hood DD, Dewan DM. Anesthetic and obstetric outcome in morbidly obese parturients. Anesthesiology 1993;79(6):1210–8.

[9] Young MT, Phelan MJ, Nguyen NT. A decade analysis of trends and outcomes of male vs female patients who underwent bariatric surgery. J Am Coll Surg 2016;222(3):226–31.

[10] The International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) [Internet]. Napoli (Italy): IFSO; 2018 [cited 2023 Sep 3]. 4th IFSO Global Registry Report 2018; [about 84 screens]. Available from: https://www.ifso.com/pdf/4th-ifso-global-registry-report-last-2018.pdf.

[11] Maggard MA, Yermilov I, Li Z, et al. Pregnancy and fertility following bariatric surgery: a systematic review. JAMA 2008;300(19):2286–96.

[12] Welbourn R, Hollyman M, Kinsman R, et al. Bariatric surgery worldwide: baseline demographic description and one-year outcomes from the Fourth IFSO Global Registry Report 2018. Obes Surg 2019;29(3):782–95.

[13] Puzziferri N, Roshek TB, Mayo HG, Gallagher R, Belle SH, Livingston EH. Long-term follow-up after bariatric surgery: a systematic review. JAMA 2014;312(9):934–42.

[14] Oteng-Ntim E, Mononen S, Sawicki O, Seed PT, Bick D, Poston L. Interpregnancy weight change and adverse pregnancy outcomes: a systematic review and meta-analysis. BMJ Open 2018;8(6):e018778.

[15] Schenkelaars N, Rousian M, Hoek J, Schoenmakers S, Willemsen S, Steegers-Theunissen R. Preconceptional maternal weight loss and hypertensive disorders in pregnancy: a systematic review and meta-analysis. Eur J Clin Nutr 2021;75(12):1684–97.

[16] Kwong W, Tomlinson G, Feig DS. Maternal and neonatal outcomes after bariatric surgery; a systematic review and meta-analysis: do the benefits outweigh the risks? Am J Obstet Gynecol 2018;218(6):573–80.

[17] Snoek KM, Steegers-Theunissen RPM, Hazebroek EJ, et al. The effects of bariatric surgery on periconception maternal health: a systematic review and meta-analysis. Hum Reprod Update 2021;27(6):1030–55.

[18] Malhotra A, Allison BJ, Castillo-Melendez M, Jenkin G, Polglase GR, Miller SL. Neonatal morbidities of fetal growth restriction: pathophysiology and impact. Front Endocrinol (Lausanne) 2019;10:55.

[19] O'Kane M, Pinkney J, Aasheim E, et al. British Obesity and Metabolic Surgery Society Guidelines on perioperative and postoperative biochemical monitoring and micronutrient replacement for patients undergoing bariatric surgery. Obes Rev 2020;21(11):e13087.

[20] Mechanick JI, Apovian C, Brethauer S, et al. Clinical practice guidelines for the perioperative nutrition, metabolic, and nonsurgical support of patients undergoing bariatric procedures–2019 update: cosponsored by American Association of Clinical Endocrinologists/American College of Endocrinology, The Obesity Society, American Society for Metabolic & Bariatric Surgery, Obesity Medicine Association, and American Society of Anesthesiologists. Surg Obes Relat Dis 2020;16(2):175–247.

[21] ACOG practice bulletin no. 105: bariatric surgery and pregnancy. Obstet Gynecol 2009;113(6):1405–13.

[22] Maric T, Kanu C, Muller DC, Tzoulaki I, Johnson MR, Savvidou MD. Fetal growth and feto-placental circulation in pregnancies following bariatric surgery: a prospective study. BJOG 2020;127(7):839–46.

[23] Snoek K, van de Woestijne N, Willemsen S, et al. The impact of preconception gastric bypass surgery on maternal micronutrient status before and during pregnancy: a retrospective cohort study in the Netherlands between 2009 and 2019. Nutrients 2022;14(4):736.

[24] Steegers-Theunissen RPM, Verheijden-Paulissen JJFM, van Uitert EM, et al. Cohort profile: the Rotterdam periconceptional cohort (predict study). Int J Epidemiol 2016;45(2):374–81.

[25] Rousian M, Schoenmakers S, Eggink AJ, et al. Cohort Profile Update: the Rotterdam Periconceptional Cohort and embryonic and fetal measurements using 3D ultrasound and virtual reality techniques. Int J Epidemiol 2021;50(5):1426–1427l.

[26] Institute of Medicine (US) and National Research Council (US) Committee to Reexamine IOM Pregnancy Weight Guidelines. Weight gain during pregnency: reexamining the guidelines. Rasmussen KM, Yaktine AL, eds. Washington (DC): National Academies Press (US); 2009.

[27] Hadlock FP, Harrist RB, Martinez-Poyer J. In utero analysis of fetal growth: a sonographic weight standard. Radiology 1991;181(1):129–33.

[28] Verburg BO, Steegers EAP, De Ridder M, et al. New charts for ultrasound dating of pregnancy and assessment of fetal growth: longitudinal data from a population-based cohort study. Ultrasound Obstet Gynecol 2008;31(4):388–96.

[29] Salomon LJ, Alfirevic Z, Da Silva Costa F, et al. ISUOG Practice Guidelines: ultrasound assessment of fetal biometry and growth. Ultrasound Obstet Gynecol 2019;53(6):715–23.

[30] Follmann D, Proschan M, Leifer E. Multiple outputation: inference for complex clustered data by averaging analyses from independent data. Biometrics 2003;59(2):420–9.

[31] Hoftiezer L, Hof MHP, Dijs-Elsinga J, Hogeveen M, Hukkelhoven CWPM, van Lingen RA. From population reference to national standard: new and improved birthweight charts. Am J Obstet Gynecol 2019;220(4):383.e1–383.e17.

[32] Metzger BE, Coustan DR, Organizing C. Summary and recommendations of the fourth international workshop-conference on gestational diabetes mellitus. Diabetes Care 1998;21(Suppl 2):B161–7.

[33] Johansson K, Cnattingius S, Näslund I, et al. Outcomes of pregnancy after bariatric surgery. N Engl J Med 2015;372(9):814–24.

[34] Roos N, Neovius M, Cnattingius S, et al. Perinatal outcomes after bariatric surgery: nationwide population based matched cohort study. BMJ 2013;347:f6460.

[35] Deleus E, Van der Schueren B, Devlieger R, Lannoo M, Benhalima K. Glucose homeostasis, fetal growth and gestational diabetes mellitus in pregnancy after bariatric surgery: a scoping review. J Clin Med 2020;9(9):2732.

[36] Bonis C, Lorenzini F, Bertrand M, et al. Glucose profiles in pregnant women after a gastric bypass. Obes Surg 2016;26(9):2150–5.

[37] Jansen A, Lyche JL, Polder A, Aaseth J, Skaug MA. Increased blood levels of persistent organic pollutants (POP) in obese individuals after weight loss—A review. J Toxicol Environ Health B Crit Rev 2017;20(1):22–37.

[38] Ouidir M, Louis GMB, Kanner J, et al. Association of maternal exposure to persistent organic pollutants in early pregnancy with fetal growth. JAMA Pediatr 2020;174(2):149–61.

[39] Bradley D, Magkos F, Klein S. Effects of bariatric surgery on glucose homeostasis and type 2 diabetes. Gastroenterology 2012;143(4):897–912.

[40] Lapolla A, Marangon M, Dalfrà MG, et al. Pregnancy outcome in morbidly obese women before and after laparoscopic gastric banding. Obes Surg 2010;20(9):1251–7.

[41] Rottenstreich A, Elchalal U, Kleinstern G, Beglaibter N, Khalaileh A, Elazary R. Maternal and perinatal outcomes after laparoscopic sleeve gastrectomy. Obstet Gynecol 2018;131(3):451–6.

[42] Nørgaard LN, Gjerris ACR, Kirkegaard I, et al. Fetal growth in pregnancies conceived after gastric bypass surgery in relation to surgery-to-conception interval: A Danish national cohort study. PLoS One 2014;9(3):e90317.

[43] Bardi F, Smith E, Kuilman M, Snijders RJM, Bilardo CM. Early detection of structural anomalies in a primary care setting in the Netherlands. Fetal Diagn Ther 2019;46(1):12–9.

[44] Bukowski R, Uchida T, Smith GCS, et al. Individualized norms of optimal fetal growth: fetal growth potential. Obst Gynecol 2008;111:1065–76.