DOI: 10.1111/1471-0528.12365
www.bjog.org

Risk for congenital malformations in offspring of women who have undergone bariatric surgery. A national cohort

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Accepted 21 May 2013. Published Online 9 August 2013.

Objective To study the risk for congenital anomalies in the first child of women after bariatric surgery compared with all other women giving birth to their first child and divided by maternal body mass index (BMI) groups.

Design Prospective, population-based register study.

Setting Sweden.

Sample All firstborn children to women born 1973–83 were studied to determine if they had a congenital anomaly and a mother who had undergone bariatric surgery before pregnancy.

Methods A total of 270 805 firstborns; of which 341 had mothers who had had bariatric surgery before delivery. We retrieved information on the women's marital or cohabitation status, smoking, BMI, diabetes and hypertension during pregnancy.

Main outcome measures Congenital malformations.

Results Of the firstborn children to mothers who had had bariatric surgery before pregnancy, 4.1% (95% confidence interval [95% CI] 2.2–6.0) were malformed compared with 3.4% (95% CI 3.3–3.5) of those whose mothers had *not* undergone bariatric surgery. The risk for congenital malformation in firstborn children increased with increasing maternal BMI. The adjusted odds ratio (OR) for congenital malformation among children whose mothers' BMI ranged between 25 and 29 kg/m^2 was 1.09 (95% CI 1.03–1.15), whose mothers' BMI ranged between 30 and 34 kg/m^2 was 1.14 (1.05–1.24) and whose mothers' BMI was ≥35 kg/m^2 was 1.30 (95% CI 1.16–1.45) compared with those whose mothers had a normal BMI. Bariatric surgery before pregnancy did not have any effect on the odds ratio for having congenital malformation (OR = 1.09, 95% CI 0.63–1.91).

Conclusions Preconception bariatric surgery does not seem to affect the risk for congenital malformations but a high to very high BMI does appear to increase the risk.

Keywords Bariatric surgery, birth defects, congenital malformations, obesity, pregnancy.

Please cite this paper as: Josefsson A, Bladh M, Wiréhn A, G Sydsjö. Risk for congenital malformations in offspring of women who have undergone bariatric surgery. A national cohort. BJOG 2013;120:1477–1482.

Introduction

Effective treatment of obesity has been available by surgical means since the 1990s. Gastric bypass and particularly laparoscopically performed bypass are the most widely used surgical methods, and they result in good long-term weight loss and acceptable side effects.[1–3] Among the women undergoing obesity surgery a great number are fertile women. In the USA over 50 000 individuals underwent bariatric surgery between 1998 and 2005, women in the age group 18–45 years accounted for about half of these women.[4]

Obesity in itself increases the risk for complications during pregnancy for both the mother and the infant.[5,6] There is also an increased risk of birth defects in the offspring of obese mothers, most pronounced for neural tube defects, congenital heart defects and orofacial clefts.[7] In a large prospective national cohort study, we found that Swedish women who had undergone bariatric surgery before pregnancy had a shorter gestational length and their children had a lower birthweight and were more often born small for gestational age compared with a reference population.[8] Similarly, in a recent review by Vrebosch et al.,[9] the authors conclude that laparoscopic adjustable gastric band-

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ing seemed to improve pregnancy outcomes in surgically corrected women, even when obesity was still present at the beginning of pregnancy.

A theoretical increased risk of congenital anomalies in the offspring of women giving birth after bariatric surgery is an ongoing concern.[10] The basis for the concern is the possible presence of nutritional deficiencies, particularly malabsorptive conditions. The objective of this study with a large prospective cohort from Swedish medical health registries was to study the risk for congenital anomalies in the first child of women after bariatric surgery compared with risk in all other women giving birth to their first child and divided by maternal body mass index (BMI) groups.

Methods

The study population comprised all live firstborn children born before 2010 as offspring to women born between 1973 and 1983 (n = 270 805). These children were separated into two groups, one group consisting of children with and the other without congenital malformations. Information on whether the mother had or had not undergone bariatric surgery before pregnancy was linked to the information on the children. Information on the children's malformations was categorised by the mothers' status, i.e. bariatric surgery or not, and the mothers were also divided into five BMI categories (BMI < 20, 20–24, 25–29, 30–34 and ≥ 35 kg/m^2). Socio-economic data and other health-related factors such as diabetes, hypertension/pre-eclampsia and smoking prevalence at the time of each mother's first pregnancy were also collected. Data on the obstetric outcome of the women's first childbirth were also collected.[8]

Bariatric surgery was defined as gastroplasty, gastric banding or gastric bypass, performed with either a laparascopic or an open technique. These surgical procedures formed the vast majority of the procedures reported; individual cases in which other methods were used, such as intragastric balloon or duodenal shunt with biliopancreatic diversion, were also identified. None of these individual cases was included in the analysis as they were too few and there was also some uncertainty about the coding for these procedures.

Data collection

The Swedish Medical Birth Register was established in 1973 and covers approximately 99% of all births. The register contains information on birth outcomes as well as certain maternal characteristics.[11] Almost all pregnant women in Sweden regularly visit antenatal clinics, usually from the 6th to the 9th week of gestation; from these records data on pregestational weight, BMI and smoking habits, for example, can be retrieved. The Total Population Register contains information on births, deaths and marital status, as well as information on migrations, and country of origin for Swedish residents born abroad.[12]

The National Patient Register has been in use since 1964 and from 1987 onwards it covers all inpatient care in Sweden.[13] The diagnoses in the National Patient Register are based on the Swedish version of the World Health Organization international classification of diseases (ICD). ICD-8[14] was used until 1986, ICD-9[15] was used between 1987 and 1996, and ICD-10[16] was used from 1997 and onwards. The ICD-10 codes (and their corresponding ICD-9 codes) used to identify bariatric surgery include JDF00, JDF10–JDF21.

The Causes of Death Register records information on all deceased persons registered in Sweden at the time of death.[17]

The Swedish Register of Birth Defects (previously the Register of Congenital Malformations) contains data on congenital anomalies. It was started in 1964 and from 1973 covers all births in Sweden as part of the Swedish Medical Birth Register. The congenital malformations are reported with verbatim descriptions and include all infants where a malformation has been diagnosed within 6 months after birth.[11,18] Any congenital malformations were defined as ICD-9, codes 740.0–759.9 or ICD-10 codes beginning with Q.

From a study cohort of all females born in 1973–83 who were alive and still living in Sweden at 13 years of age (n = 494 692) we extracted all 'women–firstborn children pairs'. The 494 692 women were then individually linked to the maternal personal identification numbers for births occurring in the Swedish Medical Birth Register before 2010 (the first birth occurred in 1987).

A total of 270 805 mother–firstborn offspring pairs were identified and available for analysis; of this total, 341 had had bariatric surgery before the delivery of their firstborn child and 269 887 women had either no bariatric surgery before pregnancy or surgery before pregnancy. After removal of individuals with missing data on BMI a total of 244 612 women were included in the study. Figure 1 displays the selection procedure.

We also retrieved information on the women's marital or cohabitation status, smoking, diabetes and hypertension during pregnancy.

Statistical analyses

Background characteristics and information on the mothers and the firstborn children's congenital malformations are presented as numbers and proportions. Information on maternal age and BMI is also presented as mean values. Differences in maternal categorical characteristics between mothers who had and had not undergone gastric bypass surgery were analysed using the Pearson's chi-square test.

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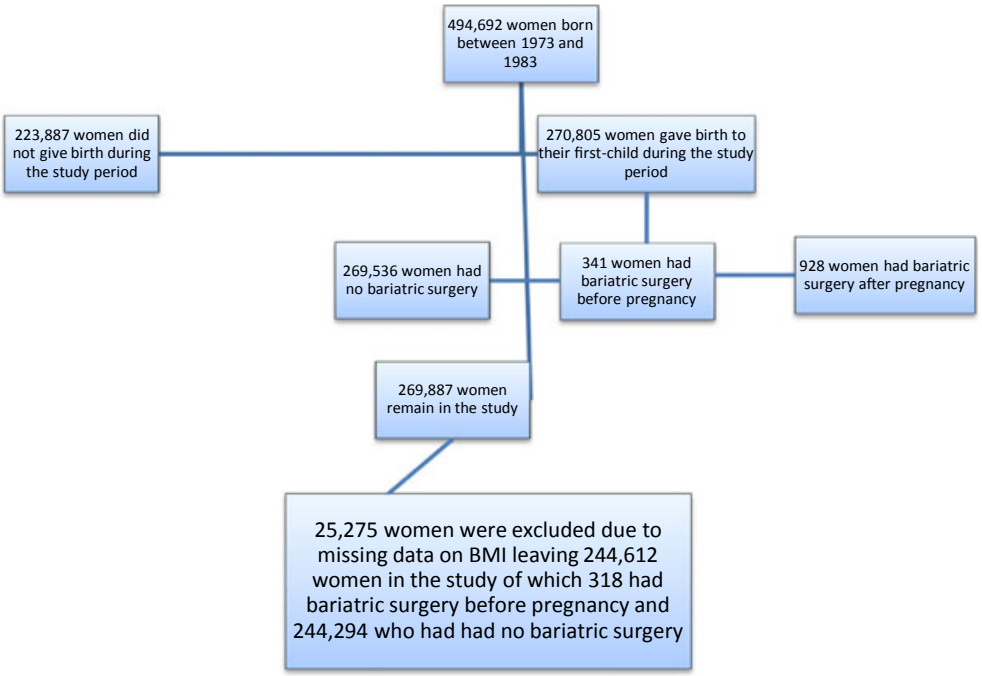

Figure 1. Flow chart of build-up of the study population.

Simple and multiple logistic regression analyses were performed to analyse group differences. In these analyses congenital malformation was set as a dependent variable and surgery before pregnancy, maternal age, marital status, smoking, prepregnancy BMI, hypertension and diabetes were used as independent variables. A P-value < 0.05 was considered statistically significant. All statistical analyses were performed using IBM SPSS version 19 (Armonk, NY, USA).

Results

Up to 2010, 270 805 women (54.8%) born between 1973 and 1983 had given birth to their firstborn child. Among all first-time mothers with no bariatric surgery, the mean age was 26.1 (SD = 4.9) years and the mean BMI at start of the pregnancy was 24.2 (SD = 4.4) kg/m^2. Analogous figures among mothers who had undergone surgery before pregnancy were 25.4 (SD = 5.4) years and mean BMI 34.4 (SD = 6.1) kg/m^2.

In Table 1, maternal characteristics are presented and these show that the surgically corrected mothers were younger, more often smokers, more likely to have diabetes and had a higher BMI (all $P \leq 0.05$). Around 11% of these mothers had reached a normal BMI in early pregnancy. Of the firstborn children to mothers who had had bariatric surgery before pregnancy, 4.1% (95% confidence interval [95% CI] 2.2–6.0) were malformed compared with 3.4% (95% CI 3.3–3.5) of those whose mothers had not undergone bariatric surgery. The odds ratio for having a congenital malformation in children born to mothers who had undergone surgery versus not was 1.22 (95% CI 0.70–2.12; $P = 0.492$). This nonsignificant difference remained when adjusting for age, marital status, smoking, BMI and clinical outcomes and resulted in an odds ratio of 1.09 (95% CI 0.63–1.91; $P = 0.747$) (Table 2).

Moreover, the adjusted analysis showed significantly higher odds ratios for having malformations in children born to mothers who had a BMI ≥ 25 kg/m^2 compared with those whose mothers were in the BMI category 20–24 kg/m^2 at the start of pregnancy (reference category). Odds ratio increased by increasing BMI category and was 1.09 (95% CI 1.03–1.15) for children whose mothers had a BMI of 25–29 kg/m^2 and was 1.14 (95% CI 1.05–1.24) and 1.30 (95% CI 1.16–1.45) for the BMI categories 30–34 and >35 kg/m^2 respectively (Table 2).

Discussion

Main findings

In this prospective large cohort we found that first-born children of women who had undergone bariatric surgery before giving birth did not have an increased risk for a congenital malformation compared with children from an unselected pregnant population. Maternal obesity, however, did increase the child's risk of being born with congenital malformations, a risk that may be seen as small for each individual but important in a population in which obesity is a growing problem.[7] Therefore we compared all first-

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Table 1. Maternal characteristics divided on mothers who had and had not undergone gastric bypass surgery before pregnancy with firstborn child

	No bariatric surgery (n = 244 294)		Bariatric surgery (n = 320)		*P*-value*
	n	%	*n*	%	
Age (years)					
13–19	9142	3.7	20	6.3	0.022
20–24	59 002	24.2	72	22.6	
25–29	111 558	45.7	129	40.6	
30–36	64 592	26.4	97	30.5	
Marital status					
Married/cohabiting	218 541	89.5	262	82.4	
Other family situation	25 753	10.5	58	17.6	
Smoking					
No	189 919	77.7	184	57.9	<0.001
Yes	54 375	22.8	134	42.1	
BMI at start of pregnancy (kg/m^2)					
< 20	26 107	9.7	2	0.6	<0.001
20–24	133 929	49.5	36	10.6	
25–29	57 852	21.4	110	32.3	
30–34	18 676	6.9	87	25.5	
>35	8504	3.1	83	24.3	
Hypertension/Pre-eclampsia**					
No	232 732	95.3	292	91.8	0.004
Yes	11 562	4.7	26	8.2	
Diabetes**					
No	24 078	98.6	301	94.1	<0.001
Yes	3514	1.4	17	5.9	

*Pearson's chi-square test.
**Chronic and pregnancy induced.

born children, whose mothers underwent surgical correction before becoming pregnant, with children whose mothers had not had bariatric surgery but divided into classes by mothers' BMI in early pregnancy and found no increased risk for congenital malformation among children whose mothers had undergone bariatric surgery. Instead, it appears that obesity itself or circumstances related to obesity are the factors that contribute to an increased risk. One possibility is that the elevated risk for birth defects among children with obese mothers could be explained by difficulties faced in performing satisfactory prenatal ultrasound examinations with resulting suboptimal diagnostics leading to low detection rates and therefore fewer abortions of fetuses with serious malformations. Another potential explanation for the increase of birth defects among children with obese mothers is untreated diabetes with associated insulin resistance and hyperglycaemia.[19]

Interpretation

Our finding that bariatric surgery does not increase risk may be seen as a positive result because some studies have highlighted a potential risk for an increase of birth defects following childbirth after bariatric surgery mainly on the basis of malabsorption and nutritional deficiencies.[10,20] However, women who are surgically corrected because of obesity continue to be vulnerable during pregnancy because the majority are still obese, smoke and more often suffer from diabetes and hypertension.

Strengths and weaknesses

To our knowledge, this is the first population-based study covering a national cohort with prospectively collected data of first-time mothers including those having undergone bariatric surgery.

An advantage of a national register study is the large number of women, which gives a high statistical power, and the possibility of incorporating data from different sources, i.e. presumed confounders. The quality of Swedish registers in general is also good.

Still, in register studies there are always limitations, and this study is no exception, for instance, weight and height measurements in early pregnancy are not always registered

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Table 2. Maternal characteristics for firstborn children with and without congenital malformations and odds ratio (OR) for having congenital malformation.

Maternal characteristics	Congenital malformations (*n* = 8295)		No congenital malformations (*n* = 236 317)		Odds ratio (OR) for having congenital malformation					
	n	%	*n*	%	Crude OR	(95% CI)	*P*-value	Adjusted* OR	(95% CI)	*P*-value
Bariatric surgery before pregnancy										
No	8282	99.8	236 012	99.9	1.00			1.00		0.747
Yes	13	0.2	305	0.1	1.22	(0.70–2.12)	0.493	1.09	(0.63–1.91)	
Age (years)										<0.001***
13–19	369	4.4	8793	3.7	1.00			1.00		
20–24	2657	32.0	56 417	23.9	1.12	(1.00–1.25)	0.042	1.19	(1.06–1.34)	0.002
25–29	3903	47.1	107 784	45.6	0.86	(0.77–0.96)	0.008	0.94	(0.84–1.05)	0.256
30–36	1366	26.8	63 323	26.8	0.51	(0.46–0.58)	<0.001	0.56	(0.49–0.63)	<0.001
Marital status										
Married/cohabiting	7211	86.9	211 592	89.5	1.00			1.00		
Other family situation	1084	13.1	24 725	10.5	1.29	(1.21–1.37)	<0.001	1.20	(1.12–1.29)	<0.001
Smoking										
No	6254	75.4	183 849	77.8	1.00			1.00		<0.001***
Yes	2041	24.6	52 468	22.2	1.14	(1.09–1.20)	<0.001	0.99	(0.94–1.05)	0.783
BMI at start of pregnancy										
<20	826	10.0	25 282	10.7	0.98	(0.91–1.06)	0.620	0.95	(0.88–1.02)	0.178
20–24	4317	52.0	129 630	54.9	1.00			1.00		
25–29	2073	25.0	55 807	23.6	1.12	(1.06–1.18)	<0.001	1.09	(1.03–1.15)	0.003
30–34	720	8.7	17 856	7.6	1.21	(1.12–1.31)	<0.001	1.14	(1.05–1.24)	0.002
≥35	359	4.3	7742	3.3	1.39	(1.25–1.55)	<0.001	1.30	(1.16–1.45)	<0.001
Hypertension/Preeclampsia**										
No	7902	95.3	225 122	95.3	1.00			1.00		
Yes	393	4.7	11 195	4.7	1.00	(0.90–1.11)	0.998	0.99	(0.89–1.10)	0.811
Diabetes**										
No	8132	98.0	232 949	98.6	1.00			1.00		
Yes	163	2.0	3368	1.4	1.39	(1.18–1.63)	<0.001	1.32	(1.13–1.55)	0.001

*Adjusted for all variables in the table.
**Chronic or pregnancy-induced.
***Overall *P*-value for age.
****Overall *P*-value for BMI.

by the midwife at the antenatal care clinic. Also, the registrations and scales are not standardised. However, in validation studies, the errors on ICD-chapter levels were estimated to be 4% in 1990; we found no recent validation in the register and have therefore chosen to analyse the bariatric surgical procedure as one entity.

Another possible limitation is the exclusion of women corrected with intragastric balloon or duodenal shunt with biliopancreatic diversion, because these techniques were very few and with an ambiguity about the correctness of the coding.

Conclusion

In this study we have shown that there seems to be no increased risk for birth defects after bariatric surgery. Together with earlier positive findings on obstetric outcomes after bariatric surgery,[8,9] we conclude that preconception bariatric surgery may be of value for obese women and their offspring. However, to verify this finding there is a need for future studies with a greater number of surgically corrected women of childbearing age.

Disclosure of interest

The authors have no conflicts of interest to disclose.

Contribution to authorship

AJ and GS had the original idea for the study. All authors planned the study. MB and ABW analysed the data and drafted the paper. All authors contributed to the interpretation of the data, revisions and gave input at all stages of the study. All authors have approved the final version of the manuscript.

Details of ethics approval

This study was approved by the Human Research Ethics Committee; Faculty of Health Sciences, Linköping University.

Funding

This study was supported by grants from The County Council of Ostergotland, Sweden.

Acknowledgement

We are grateful to the County Council of Ostergotland, Sweden, for their support. ■

References

1 Colquitt JL, Picot J, Loveman E, Clegg AJ. Surgery for obesity. *Cochrane Database Syst Rev* 2009;:CD003641.

2 Jaunoo SS, Southall PJ. Bariatric surgery. *Int J Surg* 2010;8:86–9.

3 Picot J, Jones J, Colquitt JL, Gospodarevskaya E, Loveman E, Baxter L, et al. The clinical effectiveness and cost-effectiveness of bariatric (weight loss) surgery for obesity: a systematic review and economic evaluation. *Health Technol Assess* 2009;13:1–190, 215–357, iii–iv.

4 Shekelle PG, Newberry S, Maglione M, Yermilov I, Hilton L, Suttorp M, et al. Bariatric surgery in women of reproductive age: special concerns for pregnancy. *Evid Rep Technol Assess* 2008;169:1–51.

5 Weiss JL, Malone FD, Emig D, Ball RH, Nyberg DA, Comstock CH, et al. Obesity, obstetric complications and cesarean delivery rate—a population-based screening study. *Am J Obstet Gynecol* 2004; 190:1091–7.

6 Robinson HE, O'Connell CM, Joseph KS, McLeod NL. Maternal outcomes in pregnancies complicated by obesity. *Obstet Gynecol* 2005;106:1357–64.

7 Blomberg MI, Källén B. Maternal obesity and morbid obesity: the risk for birth defects in the offspring. *Birth Defects Res A Clin Mol Teratol* 2010;88:35–40.

8 Josefsson A, Blomberg M, Bladh M, Frederiksen SG, Sydsjö G. Bariatric surgery in a national cohort of women: sociodemographics and obstetric outcomes. *Am J Obstet Gynecol* 2011;205:206.e1–8.

9 Vrebosch L, Bel S, Vansant G, Guelinckx I, Devlieger R. Maternal and neonatal outcome after laparoscopic adjustable gastric banding: a systematic review. *Obes Surg* 2012;22:1568–79.

10 Hezelgrave NL, Oteng-Ntim E. Pregnancy after bariatric surgery: a review. *J Obes* 2011;2011:501939.

11 Centre for Epidemiology, National Board of Health and Welfare. *The Swedish Medical Birth Register; A Summary of Content and Quality* (Article no. 2003-112-3). Stockholm: National Board of Health and Welfare; 2003 [http://www.socialstyrelsen.se/publikationer2003/2003-112-3]. Accessed 15 April 2013.

12 Statistics Sweden. *A New Total Population Register System. More Possibilities and Better Quality*. (Serial no. 2002:2). Örebro: Statistics Sweden; 2002.

13 Centre for Epidemiology, National Board of Health and Welfare. The National Patient Register. (Article no. 2003-42-8). Stockholm: National Board of Health and Welfare; 2003 [http://www.socialstyrelsen.se/register/halsodataregister/patientregistret/inenglish]. Accessed 15 April 2013.

14 Centre for Epidemiology, National Board of Health and Welfare. *The Swedish version of 8th revision of WHO International Classification of Diseases*. Stockholm: National Board of Health and Welfare; 1968 [http://www.socialstyrelsen.se/klassificeringochkoder/Documents/KS68.pdf]. Accessed 15 April 2013.

15 Centre for Epidemiology, National Board of Health and Welfare. *The Swedish Version of 9th Revision of WHO's International Classification of Diseases*. Stockholm: National Board of Health and Welfare; 1987 [http://www.socialstyrelsen.se/klassificeringochkoder/Documents/KLASS87.pdf]. Accessed 15 April 2013.

16 Centre for Epidemiology, National Board of Health and Welfare. *The Swedish Version of 10th Revision of WHO's International Classification of Diseases*. Stockholm: National Board of Health and Welfare; 1997 [http://www.socialstyrelsen.se/klassificeringochkoder/diagnoskoder#4]. Accessed 15 April 2013.

17 Centre of Epidemiology, National Board of Health and Welfare. *Causes of Death 2003*. Stockholm: National Board of Health and Welfare; 2005 [http://www.socialstyrelsen.se/publikationer2005/2005-42-7/Summary]. Accessed 15 April 2013.

18 Centre for Epidemiology, National Board of Health and Welfare. *The Swedish Register of Birth Defects*. Stockholm: National Board of Health and Welfare [www.socialstyrelsen.se/register/halsodataregister/medicinskafodelseregistret/inenglish]. Accessed 15 April 2013.

19 Towner D, Kjos SL, Leung B, Montoro MM, Xiang A, Mestman JH, et al. Congenital malformations in pregnancies complicated by NIDDM. *Diabetes Care* 1995;18:1446–51.

20 Guelinckx I, Devlieger R, Vansant G. Reproductive outcome after bariatric surgery: a critical review. *Hum Reprod Update* 2009; 15:189–201.

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