Published in final edited form as:

Obstet Gynecol. 2010 February ; 115(2 0 1): 290–296. doi:10.1097/AOG.0b013e3181c9b8c3.

Fetal Anomalies in Obese Women: The Contribution of Diabetes

Joseph R. Biggio Jr., MD, Victoria Chapman, Cherry Neely, Suzanne P. Cliver, and Dwight J. Rouse, MD, MSPH

University of Alabama at Birmingham Center for Women's Reproductive Health

Abstract

Objective—To examine temporal changes in maternal weight and the association with major structural anomalies and other factors, such as diabetes, in our primary obstetric population.

Methods—We conducted a serial, cross-sectional study utilizing a perinatal database to identify all women with singletons who delivered in our system from 1991–2004. Three, 5-year time epochs were defined to compare patient cohorts. Maternal weight, body mass index (BMI), diabetes status, incidence of major anomalies, and demographic data were compared. Multiple logistic regression was performed to estimate factors contributing to anomaly rates.

Results—Forty-one thousand nine-hundred two pregnancies were included. In each time epoch, there was an increase in the mean maternal weight, the mean BMI, the proportion of women weighing in excess of 200 lb, the proportion with a BMI higher than 29, the prevalence of pregestational diabetes, and the prevalence of major anomalies (all $p < 0.0001$). There was no significant independent association between maternal obesity and the presence of a major anomaly. In a multivariable logistic model, the major factor contributing to the rising rate of congenital anomalies was the prevalence of pre-gestational diabetes (OR 3.8, CI 2.1 – 6.6). The population-attributable risk of anomalies related to obesity increased from essentially 0% in 1991–94 to 6.1% in 2000–04, while that related to diabetes increased from 3.3% to 9.2% during the same time periods.

Conclusion—Although in the prevalence of maternal obesity and anomaly have increased, maternal weight alone was not associated with an increase in congenital anomalies. Instead, diabetes was significantly associated with the increase in the rate of anomalies seen in our population. Identification of maternal weight as a risk factor in epidemiologic studies may be a surrogate for pregestational diabetes.

Introduction

The rate of obesity in adult women in the United State is 35.3%.⁽¹⁾ In addition to the decrement in overall health and well-being caused by obesity, a multitude of adverse pregnancy outcomes have been consistently associated with maternal obesity. Maternal obesity increases the risk for gestational diabetes, pre-eclampsia, fetal death, macrosomia,

Corresponding author: Joseph R. Biggio Jr., M.D., 619 19th St. South, OHB 457, Birmingham, AL 35249-7333, 205-934-6638 (office), 205-975-4375 (fax), jbiggio@uab.edu.

Presented in part at the 27th Annual Society for Maternal-Fetal Medicine Meeting, San Francisco, CA, February 5–10, 2007

Financial Disclosure: The authors did not report any potential conflicts of interest.

infection, cesarean delivery, thromboembolic events, surgical complications, early neonatal death, and birth trauma.(2–7) Whether or not maternal obesity is associated with an increased risk of fetal malformations remains controversial with case-control and cohort studies often yielding contrary results.(8–17)

We undertook the present investigation to estimate whether the increase in the prevalence of obesity in our obstetric population was associated with a corresponding increase in the prevalence of major congenital anomalies, and, if so, to evaluate whether other factors, particularly diabetes, could be contributory.

Materials and Methods

This study was approved by the University of Alabama Institutional Review Board. We utilized a computerized perinatal database to identify women who received prenatal care within the University of Alabama maternity care system from 1991 – 2004. We defined three time epochs—1991–94, 1995–99, 2000–04—to compare patient cohorts in a serial, cross-sectional fashion. In addition to data routinely available in our perinatal database, computerized records of prenatal ultrasound examinations on each patient were linked to the perinatal database to enhance the identification of infants with congenital anomalies. Our perinatal database has been in operation since 1979 and contains almost 1,000 coded antepartum, intrapartum and postpartum items per patient.(18) Immediately following delivery, physicians record the intrapartum and postpartum data on standardized forms. All antepartum data from the patient's clinical chart are entered by dedicated personnel and these data are subjected to scheduled audit. Neonatal outcome data are derived directly from the infant discharge summary and diagnoses and incorporated into the database. Our current ultrasound database has been in operation since 1991 and includes fields for sonographic findings and diagnoses. This database can be reliably linked to the perinatal database using a medical record number, a unique perinatal care number, and date of birth.

Major congenital anomalies were defined as defects requiring medical or surgical intervention in the neonatal period as well as defects with the potential for significant physical or neurologic morbidity. The analysis was limited to patients delivering after 20 weeks to avoid potential failed ascertainment of anomalies in early second-trimester pregnancy losses or terminations. Women who terminated pregnancies due to prenatally-diagnosed major congenital anomalies after 20 weeks' gestation were included in this cohort. All anomalies on terminated fetuses were confirmed following delivery either by gross examination of the abortus or by autopsy. All neonates diagnosed with a major congenital anomaly prenatally or in whom a major defect was diagnosed by the examining pediatrician or neonatologist prior to discharge or death were considered to have a major anomaly.

We investigated an association between obesity and the presence of any anomaly involving single organ systems (central nervous, cardiovascular, pulmonary, genitourinary, and musculoskeletal) and ventral wall defects. This analysis was limited to singleton gestations in order to minimize the effect of any temporal changes in multiple gestations and their effect on anomaly rates. Women who delivered at or beyond 20 weeks' gestation and

received primary prenatal care in our system were eligible for inclusion in this analysis regardless of the time of antenatal care initiation.

Body mass index (BMI) was calculated from the maternal weight at the first visit and the maternal height from self-report. In the early time periods, up to 30% of patients did not have a height recorded. We therefore utilized a first prenatal visit weight in excess of 200 lb as our primary definition of obesity so as to include patients without a recorded height. Among women with a weight of at least 200 lb, only those with a height of at least 5 ft 9 in would have a BMI $<29 \text{ kg/m}^2$. As previously reported by our group, in our patient population, this height represents the 99th percentile, so our 200 lb threshold perforce includes few women with a BMI $<29 \text{ kg/m}^2$. (19) In secondary analyses, we used Institute of Medicine criteria for obesity: BMI of more than 29.0 kg/m^2 . (20) Women were considered to have pre-gestational diabetes if they had a diagnosis of medically-treated diabetes pre-dating pregnancy, or if they demonstrated evidence of glucose intolerance and were treated medically prior to 20 weeks of gestation. Because variation in practice patterns during the time studied made it difficult to accurately ascertain whether a women was a Type I or Type II diabetic, we collected data on White's classification and the proportion of women diagnosed with diabetes after the initiation of prenatal care but prior to 20 weeks' gestation. Throughout the time course of this study, our standard management policy was to place women with pre-gestational diabetes on split-mix regular and intermediate-acting insulin injections once pregnancy was recognized. Women were instructed to check pattern blood sugars with glucose goals of $<105 \text{ mg/dL}$ fasting and $<120 \text{ mg/dL}$ preprandial.

Comparisons between time epochs were made using ANOVA for continuous variables and the chi-square test for proportions. Multiple logistic regression was performed to examine the independent effect of maternal obesity, hypertension, pre-gestational diabetes, maternal age, parity, and race on the prevalence of congenital anomalies. A relative risk and 95% confidence interval for major congenital anomalies in obese women was calculated for each time epoch. Data were analyzed with SAS version 9.1 (SAS Institute, Cary, NC) Statistical significance was defined at the $\alpha=0.05$ level.

With the increase in the rate of obesity over the last two decades, we suspected that there might be a concomitant escalation in the rate of pre-gestational diabetes. Given the association between poorly-controlled maternal diabetes and fetal anomalies, we examined the magnitude of the effect of diabetes on anomaly rates in the face of rising prevalence of obesity by considering the etiologic fraction and the population attributable risk for obesity and pre-gestational diabetes. The etiologic fraction, also known as the proportion of the attributable risk among the exposed, was calculated to estimate the proportion of anomalies due to either obesity and/or pre-gestational diabetes. It is derived by dividing the difference in the incidence rates between exposed and unexposed groups by the incidence rate of the exposed group. The population attributable risk estimates the proportion of **all** cases in the population that arise due to the exposure and is calculated by dividing the difference between the incidence in the total population and the incidence in the non-exposed by the incidence in the total population. It serves as a measure of the impact of the exposure on the population as a whole and represents the proportion of outcomes that could be eliminated in the population if it were possible to eliminate the exposure. (21)

Results

A total of 41,902 singleton gestations were included in this analysis. Over the three 5-year epochs of this study there was an increase in the proportion of patients receiving care in our health system who were Hispanic (1.3%; 4.2%; 17.0%, respectively; $P<0.0001$). Because these patients were underrepresented during the earlier epochs, we limited our analysis to Caucasians and African Americans. Key demographic data are displayed in Table 1. In each subsequent time epoch there was an increase in the mean maternal weight, the mean BMI, the proportion of women weighing in excess of 200 lb, the proportion with a BMI >29 , and the prevalence of pre-gestational diabetes. ($P<0.0001$) In univariable analysis, the rate of major anomalies increased at each time period with the greatest relative increases in the cardiac and pulmonary systems. (Table 2)

During each time period, there was no significant independent association between maternal obesity by either definition and the presence of a major congenital anomaly. (Table 2) Moreover, even considering the entire time course of the study as one unit, obesity was not independently associated with an increase in the risk of major congenital anomalies. The adjusted OR (95% CI) for major anomalies using the 200 lb threshold was 0.9 (0.6 – 1.3) and for BMI >29 it was 1.3 (0.3 – 5.1).

In both obese and normal weight women, the prevalence of pre-gestational diabetes increased across time periods (Table 3). In a multivariable logistic model, the major factor contributing to the rising rate of congenital anomalies was the prevalence of pre-gestational diabetes (OR 3.8, CI 2.1 – 6.6) (Table 4).

Although there was no direct association between maternal obesity and major congenital anomalies, the proportion of anomalies in obese women related to obesity increased from 0 to 23% during the time course of our study (Table 3). Among diabetic women, the fraction of anomalies attributable to diabetes ranged from 58 to 76% during the time periods studied. In obese, diabetic women the proportion of anomalies related to diabetes rose dramatically from 48% in 1991–94 to 74% in 2000–04. For our obstetric population as a whole, the population-attributable risk of anomalies related to obesity increased from essentially 0% in 1991–94 to 6.1% in 2000–04, while that related to diabetes increased from 3.3% to 9.2% during the same time periods (Table 3).

Discussion

From 1991 to 2004, in our obstetric population there was a nearly 15 lb increase in the mean maternal weight at the first prenatal visit and greater than a 30% increase in the proportion of women with a BMI greater than 29 kg/m². During this time, we also noted a nearly two-fold increase in the rate of major congenital anomalies. There was not, however, an independent association between maternal obesity and major congenital anomalies. Interestingly, we saw a 250% increase in the prevalence of pre-gestational diabetes during this time period, and its presence, either with or without associated obesity, appears to be a major contributor to the increasing rate of anomalies in our population.

Our results, derived from an inner-city population receiving primary obstetric care in our facilities, differ from many other reports in the literature. Naeye was the first to report an increase in the prevalence of congenital malformations from 4.0% in thin patients to 5.5% in obese patients. Although the rate of congenital anomalies was 4.5 % in normal weight women, this group was not compared to the obese women.(11) Furthermore, those data were derived from a cohort followed from 1959–1966; the rates and management of diabetes have changed dramatically since that time and the contribution of diabetes to the occurrence of congenital anomalies was not considered. Cedergren and Kallen reported a 30% increase in orofacial clefts in the offspring of obese Swedish women, however, diabetic status was not considered in their analysis.(8) Waller and colleagues were the first to report an association between maternal weight and neural tube defects. In this case-control study, the reported an OR of 1.8 for a neural tube defect, and several other groups have reported a similar magnitude of risk.(12, 13, 16, 17) An increased risk of cardiac defects in non-diabetic, obese women has also been reported in several case control studies but varying definitions of obesity have been utilized.(9, 14, 22) Excluding women with known preexisting diabetes, Watkins et al reported an increased risk of not only neural tube defects and heart defects, but also omphalocele and multiple anomalies in the Atlanta Birth Defects Risk Factor Surveillance Study.(15) Although the point estimates are similar, analyses were based on maternal interview after delivery and were therefore susceptible to selection and recall bias. Two recent meta-analyses demonstrated small obesity-associated increases in the risk of neural tube defects, some cardiac defects, and cleft lip, however, many of the primary sources evaluated in these systematic reviews either excluded diabetics or based the classification only on maternal recall. Furthermore, several lumped pre-gestational and gestational diabetics together for the purpose of analysis. No assessment of the magnitude of the contribution of diabetes to the occurrence of fetal anomalies in the setting of obesity is provided.(23, 24)

In one of the few prospective, population-based cohort studies examining this issue, Moore et al examined risk factors and outcomes of nearly 23,000 women undergoing midtrimester maternal serum screening. These investigators interviewed women during the second trimester of pregnancy regarding medical history and risk factor exposure. Infant outcomes were obtained from physician and patient questionnaires. In the absence of diabetes, obese women had no higher risk of having offspring with a major defect, but women who were diabetic and obese had a 3-fold risk compared to non-obese, non-diabetics.(10) These findings parallel ours in that the risk in obese women is concentrated in those with diabetes. More recently, a case-control study by Shaw and Carmichael of more than 650 cases of neural tube defects and heart defects failed to demonstrate an association with obesity.(25)

Although one of the goals of our study was to examine temporal changes in the incidence of anomalies and obesity, standard medical practice also changed over the time period of investigation. In the early time periods, BMI was not routinely recorded; therefore, this parameter could not be reliably used or calculated. We relied instead on an alternative definition of obesity for our primary analysis. However, results were similar when only women with available BMI were included, thus we feel that our definition allows for reasonable representation of this group of women.

Changes also occurred in the reliability with which congenital anomalies are diagnosed prenatally. Ultrasound technology improved dramatically from 1991 to 2004, so it is possible that even major congenital anomalies could have been missed more in the early time periods. However, a recent study by Dashe and colleagues showed a persistently lower detection rate for fetal anomalies in obese women even during the last 6 years.(26) To minimize a potential for ascertainment bias, we limited our investigation to congenital anomalies that would be significant enough to require treatment in the neonatal period or would be recognized in the neonatal period. Furthermore, we included all neonates who had defects diagnosed in the neonatal period and did not limit inclusion to only infants with prenatally diagnosed anomalies. With prenatal ultrasound findings and an examination of each child by a pediatrician and/or neonatologist prior to discharge, it is unlikely that major congenital malformations would go undetected. Prenatal ultrasound findings were particularly important in ascertainment of visceral malformations, such as cystic adenomatoid malformations of the lung, which might otherwise be undetected during a neonatal examination. The prevalence of the anomalies we report was similar to the prevalence reported in the EUROCAT survey, a European congenital anomaly surveillance program, for livebirths and fetal deaths.(27) The relatively low prevalence of anomalies in our study is likely a reflection of limiting our analysis to patients delivered beyond 20 weeks' gestation. Despite the low prevalence of some types of anomalies, given our sample size a post hoc power analysis demonstrated that we had greater than 90% power to detect a doubling in the prevalence of anomalies in obese women compared to the rates seen in non-obese women.

Among the strengths of our clinical database study are the size of the study group and the availability of individual patient clinical data that are not subject to recall bias. One of the weaknesses of this type of study, however, is the limitation of investigation to datapoints that were collected during the course of clinical care. In our case, detailed data regarding individual patient glycemic control are not available in the database and therefore we cannot comment on the association between glycemic control and anomaly rates.

Our findings are noteworthy for a number of reasons. First, while much attention has been given to population-based, epidemiologic data linking maternal obesity with all birth defects, including some organ specific defects, the pathophysiologic basis and underlying cause of the association has been poorly investigated due to limited data. Lower levels of folic acid, increased serum insulin, chronic hypoxia and increased inflammatory mediators have all been postulated to contribute to the occurrence of malformations. (5, 13, 15–17) Our study provides evidence that the defects may not be due solely to the maternal obesity *per se* but may be due to undiagnosed diabetes. Second, from a public health standpoint, these findings highlight the need to consider refocusing attention on interventions that can best decrease the rate of adverse pregnancy outcomes. Although obesity alone has been associated with myriad poor outcomes, the coexistence of diabetes further increases the risk. Interventions to decrease the prevalence of maternal obesity require high levels of patient motivation and goal attainment is often delayed. In contrast, diagnosis and treatment of diabetes can readily achieve desired aims as long as a patient is reasonably compliant. In our population, during the 2000–2004 period, over 9% of all major congenital anomalies and

71% of those in obese women were attributable to diabetes. If euglycemia could be achieved prior to pregnancy, or at least embryogenesis and organogenesis, then the vast majority of these anomalies could potentially be avoided. This suggests a role not only for weight reduction strategies, but also consideration of screening for diabetes in obese women contemplating pregnancy and at presentation for antenatal care in those already pregnant. Moreover, given the lack of an independent effect of obesity, it may be that even women who are not overtly obese, but have other risk factors for diabetes, may be at increased risk for fetal anomalies and could benefit from attention to glycemic control.

We conclude that the association between obesity and fetal anomalies may be due to underlying diabetes, which if uncontrolled can lead to hyperglycemia. Since hyperglycemia is a major contributor to developmental malformations, interventions to address obesity and identify women at risk for diabetes and hyperglycemia should be considered in efforts to reduce the occurrence of congenital anomalies.

Acknowledgments

Supported in part by NICHD Women's Reproductive Health Research Grant K12 HD001258-06 (JRB)

References

1. Ogden, CL.; Carroll, MD.; McDowell, MA.; Flegal, KM. NCHS data brief No1. Vol. 2007. Hyattsville, MD: National Center for Health Statistics; 2007. Obesity among adults in the United States--no change since 2003--2004.
2. Cnattingius S, Bergstrom R, Lipworth L, Kramer MS. Prepregnancy weight and the risk of adverse pregnancy outcomes. *N Engl J Med*. 1998 Jan 15; 338(3):147-52. [PubMed: 9428815]
3. Hall LF, Neubert AG. Obesity and pregnancy. *Obstet Gynecol Surv*. 2005 Apr; 60(4):253-60. [PubMed: 15795633]
4. Cedergren MI. Maternal morbid obesity and the risk of adverse pregnancy outcome. *Obstet Gynecol*. 2004 Feb; 103(2):219-24. [PubMed: 14754687]
5. Waller DK, Dawson TE. Relationship between maternal obesity and adverse pregnancy outcomes. *Nestle Nutr Workshop Ser Pediatr Program*. 2005; (55):197-207. discussion -11.
6. Castro LC, Avina RL. Maternal obesity and pregnancy outcomes. *Curr Opin Obstet Gynecol*. 2002 Dec; 14(6):601-6. [PubMed: 12441699]
7. Dietl J. Maternal obesity and complications during pregnancy. *J Perinat Med*. 2005; 33(2):100-5. [PubMed: 15843256]
8. Cedergren M, Kallen B. Maternal obesity and the risk for orofacial clefts in the offspring. *Cleft Palate Craniofac J*. 2005 Jul; 42(4):367-71. [PubMed: 16001917]
9. Cedergren MI, Kallen BA. Maternal obesity and infant heart defects. *Obes Res*. 2003 Sep; 11(9):1065-71. [PubMed: 12972676]
10. Moore LL, Singer MR, Bradlee ML, Rothman KJ, Milunsky A. A prospective study of the risk of congenital defects associated with maternal obesity and diabetes mellitus. *Epidemiology*. 2000 Nov; 11(6):689-94. [PubMed: 11055631]
11. Naeye RL. Maternal body weight and pregnancy outcome. *Am J Clin Nutr*. 1990 Aug; 52(2):273-9. [PubMed: 2375293]
12. Shaw GM, Velie EM, Schaffer D. Risk of neural tube defect-affected pregnancies among obese women. *JAMA*. 1996 Apr 10; 275(14):1093-6. [PubMed: 8601928]
13. Waller DK, Mills JL, Simpson JL, Cunningham GC, Conley MR, Lassman MR, et al. Are obese women at higher risk for producing malformed offspring? *Am J Obstet Gynecol*. 1994 Feb; 170(2):541-8. [PubMed: 8116710]

14. Watkins ML, Botto LD. Maternal prepregnancy weight and congenital heart defects in offspring. *Epidemiology*. 2001 Jul; 12(4):439–46. [PubMed: 11428386]
15. Watkins ML, Rasmussen SA, Honein MA, Botto LD, Moore CA. Maternal obesity and risk for birth defects. *Pediatrics*. 2003 May; 111(5 Part 2):1152–8. [PubMed: 12728129]
16. Watkins ML, Scanlon KS, Mulinare J, Khoury MJ. Is maternal obesity a risk factor for anencephaly and spina bifida? *Epidemiology*. 1996 Sep; 7(5):507–12. [PubMed: 8862982]
17. Werler MM, Louik C, Shapiro S, Mitchell AA. Prepregnant weight in relation to risk of neural tube defects. *JAMA*. 1996 Apr 10; 275(14):1089–92. [PubMed: 8601927]
18. Wirtschafter DD, Blackwell WC, Goldenberg RL, Henderson SA, Peake MN, Huddleston JF, et al. A county-wide obstetrical automated medical record system. *J Med Syst*. 1982 Jun; 6(3):277–90. [PubMed: 7119616]
19. Lu GC, Rouse DJ, DuBard M, Cliver S, Kimberlin D, Hauth JC. The effect of the increasing prevalence of maternal obesity on perinatal morbidity. *Am J Obstet Gynecol*. 2001 Oct; 185(4):845–9. [PubMed: 11641663]
20. Subcommittee on Nutritional Status And Weight Gain During Pregnancy. Institute of Medicine. *Nutrition During Pregnancy*. Washington D.C: National Academy Press; 1990. Assessment of Gestational Weight Gain; p. 63-95.
21. Gordis, L. *Epidemiology*. 2. Philadelphia: W B Saunders; 2000. More on Risk: Estimating the Potential for Prevention; p. 172-6.
22. Mikhail LN, Walker CK, Mittendorf R. Association between maternal obesity and fetal cardiac malformations in African Americans. *J Natl Med Assoc*. 2002 Aug; 94(8):695–700. [PubMed: 12152925]
23. Stothard KJ, Tennant PW, Bell R, Rankin J. Maternal overweight and obesity and the risk of congenital anomalies: a systematic review and meta-analysis. *JAMA*. 2009 Feb 11; 301(6):636–50. [PubMed: 19211471]
24. Rasmussen SA, Chu SY, Kim SY, Schmid CH, Lau J. Maternal obesity and risk of neural tube defects: a metaanalysis. *Am J Obstet Gynecol*. 2008 Jun; 198(6):611–9. [PubMed: 18538144]
25. Shaw GM, Carmichael SL. Prepregnant obesity and risks of selected birth defects in offspring. *Epidemiology*. 2008 Jul; 19(4):616–20. [PubMed: 18552593]
26. Dashe JS, McIntire DD, Twickler DM. Effect of maternal obesity on the ultrasound detection of anomalous fetuses. *Obstet Gynecol*. 2009 May; 113(5):1001–7. [PubMed: 19384114]
27. WHO Collaborating Centre for the Epidemiologic Surveillance of Congenital Anomalies. EUROCAT: European Surveillance of Congenital Anomalies. Available at: <http://www.eurocat.ulster.ac.uk> Retrieved May 7 2008

Table 1

Descriptive variables for cohort in each time period

	1991–94 (n=14,673)	1995–99 (n=16,458)	2000–04 (n=10,771)
Mean Age (yr) *	22.7 ± 5.4	22.8 ± 5.5	23.4 ± 5.3
Mean Weight (lb) *	156 ± 44	167 ± 55	170 ± 51
Mean BMI (kg/m ²) *	26.6 ± 6.8	27.7 ± 7.5	28.2 ± 8.1
African American Race (%) *	74.4	76.8	83.5
Smoker (%) *	23.3	15.8	28.3
Fewer than 12 yrs education (%) §	41.8	41.8	43.4
Funding Status (%) *			
Government	93	86	90
Private	4	7	7
Uninsured	3	7	3
Weight 200 lb (%) *	14.5	21.2	23.4
BMI 29 (%) *	29.1	35.1	40.8
Pre-gestational diabetes (%) *	1.3	1.7	3.2
White's Classification (%) #			
B	78	69	72
C	12	20	15
D or higher	10	11	13
Diabetes diagnosed prior to 20 wks, but after antenatal care initiated (%) #	21	24	14

* p<0.0001 for each variable between time periods by ANOVA and Chi-square

§ p=0.025

Reflects percentage of all diabetics who fall into category; p>0.05 for each comparison

Table 2

Anomaly Prevalence and Risk in each time period

	1991–94 (n=14,673)	1995–99 (n=16,458)	2000–04 (n=10,771)	p
Any major anomaly(%)	0.43	0.47	0.84	<0.0001
<i>Obese</i>	0.4	0.5	1.0	0.01
<i>Non-obese</i>	0.4	0.5	0.8	0.001
CNS	0.1	0.16	0.14	0.28
<i>Obese</i>	0.05	0.29	0.08	0.06
<i>Non-obese</i>	0.1	0.13	0.16	0.55
Cardiac	0.07	0.12	0.23	0.0004
<i>Obese</i>	0.05	0.11	0.36	0.03
<i>Non-obese</i>	0.07	0.12	0.19	0.046
Pulmonary	0.01	0.04	0.14	<0.0001
<i>Obese</i>	0	0	0.24	0.03
<i>Non-obese</i>	0.01	0.05	0.11	0.006
Ventral Wall	0.06	0.04	0.07	0.74
<i>Obese</i>	0.05	0.06	0.04	1
<i>Non-obese</i>	0.06	0.04	0.08	0.39
GI	0.01	0.01	0.02	0.38
<i>Obese</i>	0.05	0.03	0.04	1
<i>Non-obese</i>	0	0	0.01	0.21
GU	0.20	0.17	0.23	0.60
<i>Obese</i>	0.14	0.11	0.32	0.21
<i>Non-obese</i>	0.21	0.18	0.21	0.91
Musculoskeletal	0.03	0.03	0.1	0.02
<i>Obese</i>	0.05	0.11	0.16	0.58
<i>Non-obese</i>	0.03	0.01	0.08	0.01
RR for any anomaly in obese women	0.85 (0.41 – 1.8)	1.1 (0.64 – 1.8)	1.3 (0.83 – 2.0)	

Table 3

Variations in diabetes and its impact on anomaly rates across study periods

	1991–94 (n=14,673)	1995–99 (n=16,458)	2000–04 (n=10,771)	p
Prevalence of pre-gestational diabetes				
<i>Obese (%)</i>	4.4	4.9	7.9	<0.0001
<i>Non-obese (%)</i>	0.79	0.81	1.7	<0.0001
Etiologic fraction of anomalies related to:				
<i>Obesity</i>	0	0.08	0.23	
<i>Diabetes</i>				
<i>All diabetic women</i>	0.74	0.58	0.76	
<i>Obese diabetic women</i>	0.67	0.13	0.71	
Population Attributable Risk of Anomalies				
<i>Obesity</i>				
<i>All women (%)</i>	0	1.8	6.1	
<i>Diabetes</i>				
<i>All women (%)</i>	3.3	2.1	9.2	

Table 4

Multivariable Logistic Model for Congenital Anomalies

Effect	OR	95% CI
Diabetes	3.80	2.1–6.6
Weight >200lb	0.92	0.6–1.3
Age group	1.27	0.9–1.8
White	2.05	1.5–2.7
Primiparous	1.50	1.1–2.0
Hypertension	1.30	0.8–1.9