Cesarean section and risk of obesity in childhood, adolescence, and early adulthood: evidence from 3 Brazilian birth cohorts[1–3]

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ABSTRACT

Background: The number of cesarean sections (CSs) is increasing in many countries, and there are concerns about their short- and long-term effects. A recent Brazilian study showed a 58% higher prevalence of obesity in young adults born by CS than in young adults born vaginally. Because CS-born individuals do not make contact at birth with maternal vaginal and intestinal bacteria, the authors proposed that this could lead to long-term changes in the gut microbiota that could contribute to obesity.

Objective: We assessed whether CS births lead to increased obesity during childhood, adolescence, and early adulthood in 3 birth cohorts.

Design: We analyzed data from 3 birth-cohort studies started in 1982, 1993, and 2004 in Southern Brazil. Subjects were assessed at different ages until 23 y of age. Poisson regression was used to estimate prevalence ratios with adjustment for $\leq$15 socioeconomic, demographic, maternal, anthropometric, and behavioral covariates.

Results: In the crude analyses, subjects born by CS had ~50% higher prevalence of obesity at 4, 11, and 15 y of age but not at 23 y of age. After adjustment for covariates, prevalence ratios were markedly reduced and no longer significant for men or women. The only exception was an association for 4-y-old boys in the 1993 cohort, which was not observed in the other 2 cohorts or for girls.

Conclusion: In these 3 birth cohorts, CSs do not seem to lead to an important increased risk of obesity during childhood, adolescence, or early adulthood. *Am J Clin Nutr* 2012;95:465–70.

INTRODUCTION

Births by CS[4] have markedly increased in the past 2 decades in a large number of middle- and high-income countries in the world (1). In the United States, CSs reached an unprecedented level of 32.9% in 2009 (2), whereas in England, this proportion was 24% in 2008 (3). In Brazil, CSs overtook vaginal deliveries in 2009 (50.1%) to become the most common way of delivery for the country's ~3 million annual births (4).

Although these operations can be lifesaving, both for mother and the fetus, there is concern that increasing rates may have also short- and long-term deleterious effects. Recent studies suggested that children born by CS could have increased risk later in life of diseases such as atopy and allergies (5), asthma (6), celiac disease (7), and type 1 diabetes (8). The main explanation for possible increased risk is that the lack of contact at birth with maternal vaginal and intestinal flora would render these children more susceptible later in life to a number of diseases because of changes in the development of the immune system (9).

More recently, increased rates of obesity were reported in young Brazilian adults born by CS compared with young Brazilian adults born vaginally (10). The plausibility suggested by the authors (10) was, again, that of different gut microbiota composition, but it is also possible that the findings could be due to residual confounding, particularly by socioeconomic position, which is associated with the type of delivery and obesity in Brazil (11–15).

In this article, we examine the association of CSs with obesity in childhood, adolescence, and early adulthood by using data from 3 population-based Southern Brazilian birth cohorts.

SUBJECTS AND METHODS

During 1982, 1993, and 2004, birth-cohort studies were started in Pelotas, Southern Brazil, with primary data collection at all maternity hospitals of the city by using almost the same methodology. The proportion of home births in these years and the nonresponse rate at recruitment in the 3 cohorts were <1%. Each birth cohort was visited on several occasions, and details of the methodology of each visit were published elsewhere (16–20).

In relation to the data analyzed in this article, for the 1982 birth cohort, we used perinatal information and data collected at 4 and 23 y of age. At birth, all 5914 live babies from all maternity

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[4] Abbreviations used: BAZ, *z* score of BMI; CS, cesarean section; HAZ, *z* scores of height-for-age; WAZ, *z* score of weight-for-age.

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hospitals were initially recruited, their mothers were interviewed by using a pretested structured questionnaire, case notes of the hospitals were reviewed, and all babies were weighed and measured by especially trained interviewers under the supervision of a pediatrician by using standard techniques .

In 1986, when the children were ~4 y of age, we conducted a census of all the nearly 80,000 households in the city in search of all children born in 1982 because it had been shown in the first follow-up visit at 12 mo of age that the use of only the known address obtained during the perinatal interview had lead to substantial losses. With the use of this methodology, we were able to find and examine 4742 children, with a follow-up rate of 84.1%, with consideration that 237 children of the cohort had died. In this follow-up, the mean age of the children was 43.1 mo (range: 35.4–53.0 mo), and they were weighed and measured with standardized procedures.

The 1982 birth cohort was visited in 2004–2005, with the same methodology of conducting a city census of all households (~98,000 households). We were able to locate 4297 members of the cohort (mean age: 22.8 y; range: 21.9–23.7 y), which represented a follow-up rate of 77.4%, given that 282 cohort members were known to have died. All located individuals were weighed and measured with standardized techniques.

In regards to the 1993 birth cohort, in this article we used information collected at birth and ages 4, 11, and 15 y. At birth, the methodology used was the same as the one described the 1982 birth cohort, and 5249 babies were recruited. Mothers were interviewed by using a structured questionnaire, hospital case notes were reviewed, and babies were weighed and measured with standard techniques. In 1997, when the children were ~4 y of age, we tried to locate all children who were born with low birth weight (<2500 g) and a systematic sample of 20% of the remaining children with birth weights ≥2500 g. The eligible number of children for this visit was 1363 children, and we were able to locate 1273 children, which represented a response rate of 87.2%. The different sampling fractions for low birth weight and other children required weighted analyses of this data set.

In 2004, when the children were ~11 y of age, we used several strategies to locate all cohort members, including a census of all 98,000 urban household and a school census, in which the registries of >100 schools in the city were reviewed. We were able to locate 4452 children, which, with the addition of the 141 children known to have died since birth, lead to a follow-up rate of 87.5% of the original birth cohort of 5249 children. Children were weighed and measured, and subscapular and triceps skinfold thicknesses were also measured 3 times with Cescorf scientific calipers, and the mean value was used in the analyses (21).

In 2008, a new city census was conducted in search of all adolescents born in 1993. Nearly 100,000 households were visited, and from the 5249 individuals initially recruited in the perinatal study, we were able to find 4349 individuals, which, with the addition of the 148 cases already deceased, corresponded to a follow-up rate of 85.7%. From the located adolescents, 4110 adolescents (94.5%) were weighed and measured, including the measurement of subscapular and triceps skinfold thicknesses.

In relation to the 2004 birth cohort, in this article we used information collected at birth and 4 y of age. As in the previous cohorts, the perinatal study comprised all births to mothers who were living in urban areas of the city that occurred in all maternity hospitals. There were 4232 births, and mothers were interviewed with structured questionnaires, and babies were weighed and measured with standardized techniques and equipment. In 2008, when the children were ~4 y of age, we undertook the same methodology of the previous cohorts and conducted a city census of all households looking for children born in 2004. With this methodology, we were able to find 3799 children from the 4137 children who were still alive, which corresponded to a follow-up rate of 91.8%.

In all follow-up visits of the 3 cohorts, children were weighed with digital scales and measured with aluminum stadiometers according to standardized techniques within the margins of error of the National Center for Health Statistics (22). Standardization sessions for anthropometric measurements were carried out before and during data collection.

Physical measurements were converted into WAZs, HAZs, and BAZs (BMI was calculated as weight in kilograms divided by the square of height in meters) by using the WHO Growth Standards (23).

The definition of obesity varied according to age; at 4 y of age, obesity was defined as a BAZ ≥2 SDs from the median of the WHO reference curve; at 11 and 15 y of age, obesity was defined according to WHO criteria (24) (BMI of at least the 85th percentile of NHANES I and the sum of tricipital and subscapular skinfold thicknesses of at least the 90th percentile); at 23 y of age, obesity was defined as BMI ≥30.

All analyses were conducted for the whole population and were also separately by sex. The exposure variable was the type of delivery (ie, whether the baby was delivered by CS or vaginally). Several covariates were included in the analyses. Potential confounders measured at birth in the 3 cohorts included family income at birth (divided into quintiles), maternal schooling at birth (divided into 4 groups), type of payment for delivery (covered by the National Health System, private practice, private health insurance), maternal skin color (white or black, mixed, or other), birth order (continuous), maternal age (continuous), maternal prepregnancy weight (4 groups), maternal height (continuous), smoking during pregnancy (yes or no), and birth weight (continuous). In addition, the following other covariates measured at the time of anthropometric examinations were included: family income (at 4, 11, 15, or 23 y of age), schooling (at 11, 15, or 23 y of age), physical activity (at 11 or 23 y of age), and smoking and alcohol consumption (at 15 or 23 y of age).

The analyses were performed with Stata version 10.1 software (Stata Statistical Software Release 10; StataCorp). Standard descriptive techniques were used with chi-square tests for trends and 95% CIs for comparing proportions. A Poisson model (25) was used to explore the independent effect of CSs on obesity at different ages and to estimate adjusted prevalence ratios.

All phases of the cohort studies were approved by the Research Ethics Committee of the Federal University of Pelotas, which is affiliated with the Brazilian Federal Medical Council.

RESULTS

The prevalence of CSs and obesity at 4, 11, 15, and 23 y of age for male and female subjects stratified by family income and maternal schooling is shown in **Table 1**. Male subjects comprised 50.8% of the sample, and female subjects comprised

TABLE 1

Distribution of exposure and outcome variables by sex across categories of family income and maternal education[1]

Socioeconomic indicators	Percentage of cesarean sections in 1982 cohort (n = 5914)		Percentage of cesarean sections in 1993 cohort (n = 5249)		Percentage of cesarean sections in 2004 cohort (n = 4231)		Percentage of obesity in 4-y-olds in 1982 cohort (n = 4742)		Percentage of obesity in 4-y-olds in 1993 cohort (n = 1237)		Percentage of obesity in 4-y-olds in 2004 cohort (n = 3756)		Percentage of obesity in 11-y-olds in 1993 cohort (n = 4100)		Percentage of obesity in 15-y-olds in 1993 cohort (n = 4349)		Percentage of obesity in 23-y-olds in 1982 cohort (n = 4297)	
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Total	27.2	27.3	30.4	30.7	46.9	43.9	8.9	6.7	12.8	9.8	12.7	12.0	13.2	8.2	10.2	7.2	7.5	9.1
Family income at birth																		
1 (poorest)	19.0	14.7	21.8	25.6	41.1	35.8	6.1	4.4	8.1	3.7	9.8	7.6	6.8	6.6	4.2	6.6	6.0	9.9
2	23.2	24.9	22.9	22.8	36.3	34.2	8.9	4.0	14.2	6.9	10.5	9.9	10.3	9.8	11.0	7.4	4.9	13.5
3	21.7	21.9	26.5	27.7	44.2	40.3	6.7	4.9	7.1	11.7	11.7	13.6	12.0	6.3	10.0	6.0	7.6	8.9
4	32.9	30.5	36.0	30.1	46.4	47.3	9.2	10.9	16.1	9.5	16.3	13.4	17.9	10.2	12.3	9.9	10.7	9.0
5 (wealthiest)	43.4	43.3	47.4	47.0	65.9	63.3	14.0	9.0	16.3	17.0	15.0	15.5	19.9	7.2	13.0	5.7	8.2	4.1
P	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.011	<0.001	0.021	0.009	<0.001	0.701	<0.001	0.859	0.009	<0.001
Maternal schooling																		
0 y	17.9	13.6	19.0	11.1	22.2	32.0	10.3	3.6	0.0	10.2	6.3	—	4.8	0.0	4.8	2.0	0.0	14.7
1–4 y	21.1	20.2	22.5	23.9	32.0	30.4	6.5	5.8	7.5	6.0	6.6	9.4	8.4	7.9	8.5	7.6	6.9	11.2
5–8 y	26.6	25.6	26.1	28.6	40.3	35.4	8.3	6.2	13.7	9.2	10.8	10.8	13.9	8.2	10.3	7.7	8.0	9.7
≥9 y	40.2	40.2	46.4	43.5	57.9	56.3	12.7	9.0	15.7	14.8	16.6	14.4	17.1	9.3	12.4	6.3	9.0	4.8
P	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.003	0.009	0.003	0.043	<0.001	0.026	<0.001	0.094	0.022	0.867	0.007	<0.001

[1] P values refer to chi-square tests for trends.

49.2% of the sample. In the 3 perinatal studies, CS rates were strongly and directly associated with income and education. As regards obesity, prevalence rates at 4 y of age were higher for boys and girls from better-off families. This trend was maintained for male subjects at 11, 15, and 23 y of age. However, for female subjects, no socioeconomic differences were observed at 11 or 15 y of age, and by the age of 23 y, the pattern was reversed, with women from low socioeconomic groups presenting higher prevalence of obesity than did women of better-off families.

The crude prevalence of obesity according to type of delivery at different ages is shown in **Table 2**. Obesity was significantly more prevalent in the CS group at 4, 11, and 15 y of age for both male and female subjects, with the only exception being for 4-y old girls in the 1993 cohort. However, at 23 y of age, no significant differences were observed in the prevalence of obesity for men or women.

Corresponding crude and adjusted prevalence ratios are shown in **Table 3**. When potential confounding variables were added to the model, prevalence ratios were substantially reduced and no longer significant, except for the association for 4-y-olds in the 1993 cohort, in which the adjusted prevalence ratio for boys was 2.03. However, the corresponding prevalence ratios at the age of 4 y in the other 2 cohorts were considerably smaller at 1.25 in 1982 (P = 0.14) and 1.13 in 2004 (P = 0.36). The only association that apparently increased after adjustment for confounding was that for women at 23 y of age in the 1982 cohort from 1.08 in the crude analyses (P = 0.59) to 1.33 (P = 0.10) after adjustment.

All analyses were repeated with adjustment for early life confounders only, with contemporary variables left out. The results were virtually unchanged.

DISCUSSION

The strengths of these analyses included their longitudinal design with low attrition rates and the ability to compare 3 large birth cohorts starting 11 y apart at different ages that ranged from 4 to 23 y. A limitation was the lack of data on the timing of the rupture of membranes, which could have provided important insights regarding the exposure of the fetus to microorganisms.

In accordance with all previous studies conducted in Brazil, we showed a strong positive relation between CS prevalence and socioeconomic status (11–14). In contrast, the prevalence of obesity by socioeconomic status showed different patterns for men and women in early adulthood, with a higher prevalence observed in rich men and poor women. Those findings have also been described in other studies (15, 26, 27).

Recent analyses of the Brazilian Ribeirão Preto 1978–799 birth cohort showed an adjusted prevalence ratio for obesity of 1.58 (95% CI: 1.23, 2.02; P < 0.001) at 23–25 y of age for subjects born through CSs (10). Sex-stratified results are not shown, but the authors (10) reported that there was no interaction with sex. Their study included statistical adjustment for the subject's sex, birth weight, physical activity, smoking, schooling, and income, as well as for maternal schooling and smoking during pregnancy. Our analyses adjusted for all these factors and, in addition, for maternal family income, type of payment for delivery, skin color, parity, age, prepregnancy weight, and height.

TABLE 2
Prevalence of obesity at different ages according to type of delivery[1]

	All			M			F		
Follow-up visit/cohort	Vaginal delivery	Cesarean section	P	Vaginal delivery	Cesarean section	P	Vaginal delivery	Cesarean section	P
4 y/1982 cohort (n = 4742)	7.0 (5.0, 7.7)	10.4 (8.8, 12.1)	<0.001	7.8 (6.6, 9.1)	11.8 (9.4, 14.3)	0.002	5.8 (4.7, 6.9)	9.0 (6.8, 11.3)	0.005
4 y/1993 cohort (n = 1237)	9.1 (6.9, 11.2)	16.3 (12.1, 20.5)	<0.001	8.7 (5.7, 11.7)	22.0 (15.4, 28.7)	<0.001	9.4 (6.4, 12.4)	10.5 (5.6, 15.4)	0.710
4 y/2004 cohort (n = 3756)	10.0 (8.7, 11.4)	15.2 (13.5, 17.0)	<0.001	10.3 (8.5, 12.3)	15.5 (13.2, 18.0)	0.001	9.7 (8.0, 11.7)	14.9 (12.5, 17.5)	0.001
11 y/1993 cohort (n = 4100)	9.4 (8.4, 10.4)	13.6 (11.7, 15.4)	<0.001	11.5 (9.9, 13.1)	17.3 (14.4, 20.2)	<0.001	7.3 (6.1, 8.6)	10.0 (7.7, 12.2)	0.035
15 y/1993 cohort (n = 4349)	7.6 (6.6, 8.6)	11.1 (9.4, 12.9)	<0.001	8.8 (7.3, 10.3)	13.5 (10.8, 16.2)	0.002	6.4 (5.1, 7.7)	8.9 (6.7, 11.1)	0.043
23 y/1982 cohort (n = 4297)	8.1 (7.1, 9.0)	8.9 (7.3, 10.5)	0.374	7.3 (6.0, 8.5)	8.2 (6.0, 10.3)	0.460	8.9 (7.5, 10.4)	9.7 (7.3, 12.1)	0.591

[1] All values are percentages of obese subjects; 95% CIs in parentheses. P values refer to chi-square tests.

TABLE 3
Obesity of individuals born through cesarean section relative to individuals born through vaginal delivery at different ages: crude and adjusted analyses[1]

	All				M				F			
Follow-up visit/cohort	Crude	P	Adjusted	P	Crude	P	Adjusted	P	Crude	P	Adjusted	P
4 y/1982 cohort (n = 4742)	1.53 (1.25, 1.87)	<0.001	1.22 (0.97, 1.53)	0.084	1.51 (1.16, 1.96)	0.002	1.25 (0.93, 1.68)	0.144	1.56 (1.14, 2.13)	0.005	1.17 (0.83, 1.66)	0.374
4 y/1993 cohort (n = 1237)	1.80 (1.27, 2.54)	0.001	1.31 (0.90, 1.92)	0.158	2.54 (1.61, 4.01)	<0.001	2.03 (1.20, 3.42)	0.008	1.11 (0.63, 1.96)	0.710	0.78 (0.46, 1.34)	0.373
4 y/2004 cohort (n = 3756)	1.52 (1.28, 1.81)	<0.001	1.21 (0.99, 1.48)	0.062	1.51 (1.19, 1.91)	0.001	1.13 (0.86, 1.49)	0.368	1.53 (1.19, 1.97)	0.001	1.30 (0.97, 1.74)	0.080
11 y/1993 cohort (n = 4100)	1.44 (1.22, 1.72)	<0.001	1.06 (0.86, 1.30)	0.575	1.51 (1.22, 1.88)	<0.001	1.11 (0.85, 1.43)	0.452	1.36 (1.02, 1.81)	0.035	1.00 (0.71, 1.40)	0.984
15 y/1993 cohort (n = 4349)	1.47 (1.20, 1.79)	<0.001	1.23 (0.98, 1.54)	0.073	1.53 (1.18, 1.99)	0.002	1.24 (0.92, 1.66)	0.151	1.39 (1.01, 1.90)	0.044	1.17 (0.82, 1.65)	0.391
23 y/1982 cohort (n = 4297)	1.10 (0.89, 1.37)	0.374	1.10 (0.87, 1.41)	0.428	1.13 (0.82, 1.55)	0.460	0.94 (0.60, 1.31)	0.713	1.08 (0.81, 1.46)	0.591	1.33 (0.94, 1.89)	0.106

[1] All values are prevalence ratios; 95% CIs in parentheses. Conducted by using Poisson regression analyses. P values refer to Wald's test. Adjusted analyses were adjusted for family income at birth, maternal schooling at birth, maternal skin color, birth order, maternal age, maternal prepregnancy weight, maternal height, smoking during pregnancy, type of payment for delivery (National Health System, private practice, private health insurance), birth weight, family income (at 4, 11, 15, or 23 y of age), schooling (at 11, 15, or 23 y of age), physical activity (at 11, 15, or 23 y of age), and smoking and alcohol consumption (at 15 or 23 y of age).

Our adjusted results did not confirm such a high risk of obesity in subjects delivered by cesarean delivery. No significant associations of CSs and obesity at any age were shown in women. For male subjects, we showed a significant association at 4 y of age but only in the 1993 cohort; this significant association was not present in the same cohort at later ages or in the 2004 cohort at the same age. Most prevalence ratios for men and women remained above unity.

Residual confounding and self-selection may have played a role in these results because, despite adjustment for several socioeconomic variables, there may be other sociocultural patterns associated with CS delivery and childhood obesity that may be difficult, if not impossible, to adjust for. Ethnographic research carried out during the early phases of the 1993 cohort showed that a distinct group of mothers had a particular propensity toward actively seeking medicalization (28, 29). These women were more likely to deliver through cesarean delivery, less likely to breastfeed, more likely to use private rather than public health care (30), and also highly concerned about the need for their babies to put on weight rapidly (31). This type of self-selection is difficult to control in quantitative analyses such as the present one and may lead to an association between CSs and obesity despite statistical control for measureable confounding factors.

Residual confounding may also explain why the associations in the earlier Brazilian study were stronger than in our study because the list of confounders in the earlier Brazilian study did not include maternal height and weight or the variety of socioeconomic variables available in our data sets. In terms of statistical power, the Ribeirão Preto analyses were based on 2057 subjects, whereas our analyses included ~4000 subjects in each cohort (except for in the 4-y-old follow up of the 1993 cohort, which was restricted to a stratified, systematic subsample of 1237 subjects).

In conclusion, the raising rates of CSs in Brazil and in many other countries are a reason for great concern because of the increased maternal and child morbidity associated with these procedures (32). Additional studies are necessary to assess potential long-term effects. However, our results do not confirm earlier findings of an important increase in risk of obesity, at least until early adulthood.

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