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Cesarean delivery is associated with an increased risk of obesity in adulthood in a Brazilian birth cohort study[1–3]

Helena AS Goldani, Heloisa Bettiol, Marco A Barbieri, Antonio AM Silva, Marilyn Agranonik, Mauro B Morais, and Marcelo Z Goldani

ABSTRACT

Background: Obesity is epidemic worldwide, and increases in cesarean delivery rates have occurred in parallel.

Objective: This study aimed to determine whether cesarean delivery is a risk factor for obesity in adulthood in a birth cohort of Brazilian subjects.

Design: We initiated a birth cohort study in Ribeirão Preto, southeastern Brazil, in 1978. A randomly selected sample of 2057 subjects from the original cohort was reassessed in 2002–2004. Type of delivery, birth weight, maternal smoking, and schooling were obtained after birth. The following data from subjects were collected at 23–25 y of age: body mass index (BMI; in kg/m^2), physical activity, smoking, and income. Obesity was defined as a BMI $\geq$30. A Poisson multivariable model was performed to determine the association between cesarean delivery and BMI.

Results: The obesity rate in adults born by cesarean delivery was 15.2% and in those born by vaginal delivery was 10.4% ($P = 0.002$). Adults born by cesarean delivery had an increased risk (prevalence ratio: 1.58; 95% CI: 1.23, 2.02) of obesity at adulthood after adjustments.

Conclusion: We hypothesize that increasing rates of cesarean delivery may play a role in the obesity epidemic worldwide. *Am J Clin Nutr* doi: 10.3945/ajcn.110.010033.

INTRODUCTION

Obesity and associated metabolic disorders are epidemic worldwide (1). The novel hypothesis for obesity-related research and public health interventions are targeting the understanding of the causal pathways of obesity in populations to identify where interventions that broadly affect the population can be implemented (2).

Increases in cesarean delivery rates have occurred in parallel with increasing obesity rates (3). Cesarean delivery rates in England, Sweden, and the United States have risen from 6%, 8%, and 10% in 1975 (4) to 19%, 12%, and 22% in 1999 (5) and further to 21%, 16%, and 24% in 2001 (6), respectively. In Southeastern Brazil, the cesarean delivery rate has increased from 30% in 1978 to 51% in 1994 (7) and further to ≈44% in 2007 (8, 9). Similarly, the prevalence rate of obesity in Brazil has increased from 4% in 1974 (10) to 11% in 2006 (11).

A possible mechanism that might be hypothesized to link the increasing rates of obesity and cesarean delivery could be related to environmental factors. Changes in the development or composition of the gut microbiota affect host metabolism and energy storage and consequently can affect the development of obesity (2, 12, 13). Changes in the gut microbiota may be linked to some chronic inflammatory conditions common in the Western world, among them obesity. This would be explained in part by the hygiene hypothesis (14), the main concept of which explains the rising incidence of immunoregulatory disorders such as allergies, Crohn disease, and type 1 diabetes in Western countries.

Cesarean delivery is associated with delayed acquisition of bifidobacteria, which might be due to lack of contact of infants with the maternal vaginal flora (15, 16). A recent case-control study found that the composition of gut flora in infancy predicted overweight later in childhood (14).

Given that infants born by cesarean delivery are more likely to have fewer *Bifidobacterium* spp. as the predominant microbiota and that the microbiota of obese patients is more related to fewer *Bifidobacterium* spp., we hypothesized that infants born by cesarean delivery are more likely to develop obesity in adult life. This study aimed to determine whether cesarean delivery is a risk factor for obesity in adulthood in a cohort of subjects born in southeastern Brazil.

SUBJECTS AND METHODS

This study was approved by the Research Ethics Committee of the Hospital das Clinicas de Ribeirão Preto, Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo.

This was a prospective birth cohort study consisting subjects born in Ribeirão Preto-SP, southeastern Brazil, from 1 June 1978 to 31 May 1979. During this period, 9067 births were registered

[1] From the Department of Pediatrics, Hospital de Clínicas de Porto Alegre, Faculdade de Medicina, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil (HASG, MA, and MZG); the Department of Pediatrics, Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, Brazil (HB and MAB); the Department of Public Health, Faculdade de Medicina, Universidade Federal do Maranhão, Brazil (AAMS); and the Department of Pediatrics, Faculdade de Medicina, Universidade Federal de São Paulo, São Paulo, Brazil (MBM).

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[3] Address correspondence to HAS Goldani, Rua Ramiro Barcelos 2350, Hospital de Clínicas de Porto Alegre, CEP 900135-903, Porto Alegre-RS, Brazil. E-mail: hgoldani@hcpa.ufrgs.br.

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and 6973 newborns whose mothers were living in the city at the time of delivery were included in the study (6827 singletons and 146 twin deliveries). Of the 6827 singletons, 246 died during the first year of life and 97 died before the age of 20 y, for a total of 343 deaths. Trained personnel collected data from mothers and children, including medical histories and anthropometric measures at the time of birth.

Between April 2002 and May 2004, 2103 individuals were randomly selected and invited for further assessment. The subjects were given a detailed lifestyle questionnaire (including information on physical activity) and a socioeconomic questionnaire and underwent a physical examination and anthropometric assessment. A detailed description of the cohort methods and a comparison of this sample with the original population were published elsewhere (17, 18). Briefly, the 2002–2004 sample was comparable with the original population with regard to birth weight, birth length, and maternal age, although the sample was slightly wealthier. Only singletons were included in the analyses.

Economic, social, and maternal health care data were obtained from a standardized questionnaire completed by the mothers soon after delivery, and demographic information was collected from official records (17).

The subjects' data were obtained by using a standardized questionnaire at the time of their return for evaluation at 23–25 y of age. Physical activity was evaluated with the International Physical Activity Questionnaire (IPAQ)–Short Form (19), by using the metabolic cost or unit of resting metabolic rate (metabolic equivalent) and classifying the individuals as "active" or "sedentary," following guidelines for data processing and analysis of the IPAQ (19, 20). Subject smoking was considered to be any report of smoking during the past year. Weight and height were measured by trained personnel under the supervision of the principal investigators and all were blinded to birth data (21). Body mass index (BMI) was calculated by dividing weight (in kg) by height squared (in m^2) (22). Obesity was defined as BMI ≥ 30 (23). Income in minimum wages was considered as a measure of socioeconomic status (SES).

The following covariables were collected soon after birth: *1*) type of delivery (cesarean or vaginal delivery); *2*) birth weight, obtained from trained staff and defined as low birth weight (<2500 g) or normal birth weight (≥2500 g); *3*) maternal smoking status, defined as smoking at any time of pregnancy (yes) compared with never smoked (no); and *4*) maternal schooling (in y).

Categorical variables were expressed as absolute and relative frequencies. Continuous variables were expressed as means ± SDs. The chi-square test was performed to analyze categorical data. Multivariable analysis using a Poisson regression model was performed to assess the association between cesarean delivery and BMI in early adulthood. The model was adjusted for participant's sex, birth weight, income, smoking, schooling, and physical activity and for maternal factors (schooling and smoking during pregnancy). The covariables were selected considering known factors related to BMI in adulthood that were available in our database. The interaction between cesarean delivery and sex related to BMI was tested due to differences in BMI according to sex. Statistical significance was set at $P \leq 0.05$. SPSS (Statistical Package for the Social Sciences; SPSS Inc, Chicago, IL) version 18.0 was used for the statistical analysis.

RESULTS

A total of 2057 subjects were included in the analysis. The mean (±SD) age of the subjects was 23.9 ± 0.71 y and weight was 69.7 ± 16.40 kg. The cesarean delivery rate was 31.9%, performed mostly in higher SES groups. Cesarean delivery in the group of better-educated mothers reached 45.1% of all deliveries. In contrast, among less-educated mothers, the cesarean delivery rate was 26.8%. The mean (± SD) BMI of those born by cesarean delivery was 25 ± 5.27 and of those born by vaginal delivery was 24 ± 4.26 ($P < 0.001$).

The prevalence rate of obesity in young adults was 15.2% in those born by cesarean delivery compared with 10.4% in those born by vaginal delivery ($P = 0.002$). The obesity rate was higher in less-privileged SES groups, considering maternal schooling, subject's schooling, and income. No differences in prevalence rates of obesity were found according to birth weight, maternal smoking during pregnancy, and subject's physical activity, sex, and smoking (**Table 1**).

The prevalence rate of obesity at 23–25 y of age was ≈46% higher in those born by cesarean delivery than in those born by vaginal delivery ($P = 0.002$) in the nonadjusted analysis. The effect remained statistically significant after adjustment. Subjects born by cesarean delivery had a 58% higher risk of obesity in adulthood than did those born by vaginal delivery (**Table 2**). Because no significant interaction between cesarean delivery and sex in relation to BMI was detected (*P* interaction in the fully adjusted model = 0.196), the models were not stratified by sex.

DISCUSSION

To our knowledge, this is the first population-based study to show an association between type of delivery and obesity in a cohort of subjects at 23–25 y of age. The main finding was that subjects who were born by cesarean delivery had a significantly increased risk of obesity in adulthood. The risk was 58% higher after control for the participant's sex, birth weight, income, smoking, schooling, and physical activity and maternal factors (schooling and smoking during pregnancy).

In previous studies using the same database, birth weight, physical activity, and SES have been correlated with BMI, although low birth weight was not associated with obesity in adulthood (24, 25). In contrast with the current literature (26), maternal smoking was not related to BMI.

The rationality and sequence of possible events linking type of delivery with obesity in adulthood was derived by the recent determination that adiposity is characterized by low-grade inflammation. Early intestinal colonization that might occur in infants born by cesarean delivery has been associated with an increase in circulating soluble CD14—a marker of systemic inflammation. Infants receive their first microbial inoculation at the time of delivery, which is further reinforced during breastfeeding by breast-milk–derived galactooligosaccharides and bacteria in breast milk (27). Likewise, a recent meta-analysis showed that cesarean delivery is associated with an increased risk of childhood-onset type 1 diabetes mellitus (3). A difference in gut microbiotic composition could increase the risk of type 1 diabetes, and the hygiene hypothesis might suggest that children with reduced or delayed exposure to infection in early life may have an increased risk of type 1 diabetes (28).

TABLE 1
Differences in prevalence rates of obesity [BMI (in kg/m^2) ≥30] in 2057 subjects aged 23–25 y age according to type of delivery and other covariables

Variables	BMI ≥30	P^1
	%	
Type of delivery		0.002
Vaginal (*n* = 1400)	10.4	
Cesarean (*n* = 657)	15.2	
Physical activity		0.681
Active (*n* = 1034)	11.7	
Sedentary (*n* = 1017)	12.3	
Birth weight		0.634
≥2500 g (*n* = 1929)	11.9	
<2500 g (*n* = 128)	13.3	
Maternal schooling		0.005
0–4 y (*n* = 916)	11.6	
5–8 y (*n* = 555)	15.5	
9–11 y (*n* = 331)	9.1	
≥12 y (*n* = 215)	7.9	
Maternal smoking during pregnancy		0.644
No (*n* = 1505)	12.1	
Yes (*n* = 512)	11.3	
Subject's income (minimum wage)[2]		0.003
<3 (*n* = 217)	14.7	
3–4.9 (*n* = 461)	15.6	
5–9.9 (*n* = 629)	12.2	
10–19.9 (*n* = 404)	8.9	
≥20 (*n* = 196)	6.6	
Sex		0.255
Male (*n* = 992)	12.8	
Female (*n* = 1065)	11.2	
Subject's schooling		0.004
<8 y (*n* = 316)	16.8	
≥8 y (*n* = 1741)	11.1	
Subject's smoking status		0.781
Nonsmoker (*n* = 1550)	11.7	
Ex-smoker (*n* = 152)	12.5	
Smoker (*n* = 355)	13.0	

[1] *P* values were derived by using the chi-square test (excluding missing values).
[2] In Brazilian currency.

Some studies have shown that the newborn's intestinal bacteria during the first 3 d of life is influenced by the mode of delivery. Fecal samples from infants born by cesarean delivery have shown a substantial absence of *Bifidobacteria* spp., whereas samples from infants born by vaginal delivery have been characterized by subject-specific microbial profiles (29, 30).

In light of evidence of differences in intestinal microbiota between infants born by cesarean delivery and those born by vaginal delivery, Huurre et al (31) showed that the mode of delivery might, possibly via gut microbiota development, have significant effects on the immunologic function of infants. Obese children and adults have shown a higher proportion of *Firmicutes* in the feces (32).

TABLE 2
Prevalence ratio for obesity in subjects aged 23–25 y according to type of delivery obtained by the Poisson regression model

	Prevalence ratio	95% CI	*P*
Cesarean delivery (nonadjusted)	1.46	(1.15, 1.85)	0.002
Cesarean delivery (adjusted)[1]	1.58	(1.23, 2.02)	<0.001

[1] Adjusted for subject's birth weight, sex, physical activity, smoking, schooling, and income and maternal schooling and smoking during pregnancy.

Kalliomäki et al (14) showed in a study of 25 overweight and obese children from a cohort study at 7 y of age that early differences in fecal microbiota composition in children may predict overweight. The number of bifidobacteria in fecal samples during infancy at 6 mo and 1 y of age were ≈2-fold higher in children continuing to be of normal weight than in children becoming overweight at 7 y of age. Likewise, our cohort study showed that infants born by cesarean delivery had a higher risk of obesity at 23–25 y of age.

Breastfeeding has been recognized as a source of bifidobacteria for infant gut development and maturation (33). We lacked breastfeeding data during infancy, which was a limitation of our study. Recent studies in Brazil have reinforced cesarean delivery as a risk factor for early weaning (34, 35). However, a Brazilian study carried out at the same time as ours by Victora et al (36) showed little effect of type of delivery on breastfeeding rates in 6-mo-old infants. If type of delivery had a small effect on breastfeeding rates, it would have changed little the estimates presented here. Furthermore, the breastfeeding rate has been shown to be strongly associated with SES, which was controlled in our study (37).

Other limitations of our study included the lack of information about cesarean delivery indication and maternal BMI. Premature rupture of fetal membranes is known to be a risk factor for perinatal infection (38, 39) because of the exposure to vaginal flora. A cesarean procedure performed after rupture of fetal membranes and a long labor (especially a prolonged second stage) involves plenty of exposure to the vaginal milieu. This cohort lacks data regarding premature rupture of fetal membranes. Regarding maternal BMI, the obesity rate among Brazilian women around the time of this study in 1975 was 7.5%, which increased to 13% in 2003 (40). In 1975, the highest rates of obesity were found among the better-off social groups (41). Because we controlled for maternal schooling at the time of delivery, this adjustment may have partially accounted for the possible confounding effect of maternal BMI.

In conclusion, subjects who were born by cesarean delivery had a significantly increased risk of obesity in adulthood. Given that intestinal colonization could have a long-lasting effect on general health and considering the difference in intestinal flora between infants born vaginally and those born by cesarean delivery, we hypothesize that increasing rates of cesarean delivery may play a role in the obesity epidemic worldwide.

The authors' responsibilities were as follows—HASG, MBM, and MZG: designed the research; HB and MAB: provided essential materials (database); MA and AAMS: analyzed the data; HASG, MBM, and MZG: wrote the manuscript; and MZG: had primary responsibility for the final content. All authors read and approved the final manuscript. None of the authors declared a conflict of interest.

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