CSP CADERNOS DE SAÚDE PÚBLICA
REPORTS IN PUBLIC HEALTH

ARTIGO
ARTICLE

Cesarean section and body mass index in children: is there a causal effect?

Parto cesáreo e índice de massa corporal em crianças: existe um efeito causal?

Operación de cesárea e índice de masa corporal en niños: ¿existe un efecto causal?

Lilian Fernanda Pereira Cavalcante [1]
Carolina Abreu de Carvalho [1]
Luana Lopes Padilha [2]
Poliana Cristina de Almeida Fonseca Viola [3]
Antônio Augusto Moura da Silva [1]
Vanda Maria Ferreira Simões [1]

doi: 10.1590/0102-311X00344020

Abstract

Obesity is considered a global public health problem. Cesarean section has been associated with high body mass index (BMI) and increased obesity throughout life. However, this association has been challenged by some studies. This study aims to assess the causal effect of cesarean section on the BMI of children aged 1-3 years. This is a cohort study of 2,181 children aged 1-3 years, born in 2010, obtained from the BRISA Birth Cohort, in São Luís, state of Maranhão, Brazil. Sociodemographic variables, maternal characteristics, type of childbirth, morbidity, anthropometric measurements, and BMI were assessed. Marginal structural models with a counterfactual approach were used to check the causal effect of the type of childbirth on obesity, weighted by the inverse probability of selection and exposure. Out of the 2,181 children assessed (52% female), 50.6% were born by cesarean section, 5.9% of the newborn infants were large for gestational age, and 10.7% of them had excess weight. No causal effect of cesarean section on BMI was observed (coefficient = -0.004; 95%CI: -0.136; 0.127; p = 0.948). Cesarean section did not have a causal effect on the BMI of children aged 1-3 years.

Cesarean Section; Child Obesity; Body Mass Index

Correspondence
L. F. P. Cavalcante
Universidade Federal do Maranhão.
Av. dos Portugueses s/n, São Luís, MA 65085-580, Brasil.
liliancavalcante03@gmail.com

[1] *Universidade Federal do Maranhão, São Luís, Brasil.*
[2] *Instituto Federal de Educação, Ciência e Tecnologia do Maranhão, São Luís, Brasil.*
[3] *Universidade Federal do Piauí, Teresina, Brasil.*

Introduction

The first 1,000 days of life are crucial; nutritional factors have an important impact during this time, influencing metabolic disorders throughout life [1,2,3]. Also, obesity has been regarded as a pandemic [4] and it is increasingly more prevalent among children [5]. Thus, obesity-related research and public health interventions have been focused at assessing the underlying causes of this problem [6]. In this context, cesarean section (C-section) has been considered a possible cause for the development of overweight and obesity [7,8,9].

C-sections have increased in the past decades in middle- and high-income countries. In 2009, the rate of C-section was 32.9% in the United States [10], 24% in England [11], and higher than 50% in Brazil [12]. C-section rates have increased considerably in Brazil, from 52%, in 2010, to 56%, in 2018. In the state of Maranhão, the rates increased from 34%, in 2010, to 48.2%, in 2018 [12].

This is an alarmingly dramatic scenario considering that the World Health Organization (WHO) [13] recommends a C-section rate of no more than 15%. Accordingly, a systematic review suggested that rates up to 16% were associated with lower maternal, neonatal, and child and infant mortality rates [14], whereas another review demonstrated that rates up to 19% were related to beneficial effects, reducing mother-child mortality [15].

In Brazil, C-section has been associated with non-clinical factors. High income and older mothers have higher C-section rate and, in the private healthcare sector, C-section is almost universal [16]. Furthermore, C-section rates are the highest in the most developed regions of Brazil [17].

Some studies indicate that C-section may have a lifetime effect on the risk of obesity [7,8,9]. This association can be explained by the hormonal theory and microbiota pathways, among other hypotheses. Differences in cortisol, interleukin 6, norepinephrine levels in infants born by cesarean section and vaginal delivery could lead to neuroimmunoendocrine and epigenetic changes that could interfere with long-term energy metabolism, predisposing those born by C-section to weight gain [18,19,20].

The effect via microbiota is based on the assumption that newborns have contact with bacteria in the vaginal canal during vaginal delivery and their intestines are predominantly colonized by bacteria that absorb less fat and fewer nutrients, that could predispose to overweight [9]. On the other hand, some studies suggest that infants born by C-section could have an intestinal microbiota that would tend to extract more nutrients from the diet, predisposing them to overweight or obesity [21,22,23].

Nevertheless, the association between cesarean section and increased risk of overweight in children shows no agreement in the literature. Barros et al. [16], showed no association between C-section and body composition, which estimates fat tissue better than the body mass index (BMI). Sutharsan et al. [24], in a meta-analysis of children, adolescents, and adults, as well as other studies suggest that the associations between C-section and overweight/obesity likely result from confounding biases that were not properly controlled during analysis [9,20,25,26].

Accordingly, our study used graphic and counterfactual approaches to assess the causal effect between C-section and BMI of children aged 1-3 years from the BRISA Birth Cohort.

Materials and methods

Study design

This cohort study was part of the project *Etiologic Factors of Preterm Birth and Effects of Perinatal Factors on Child Health: Birth Cohorts from Two Brazilian Cities – São Luís (MA) and Ribeirão Preto (SP)* (BRISA) [27], developed by the Federal University of Maranhão (UFMA) and by the Ribeirão Preto Medical School, University of São Paulo (USP).

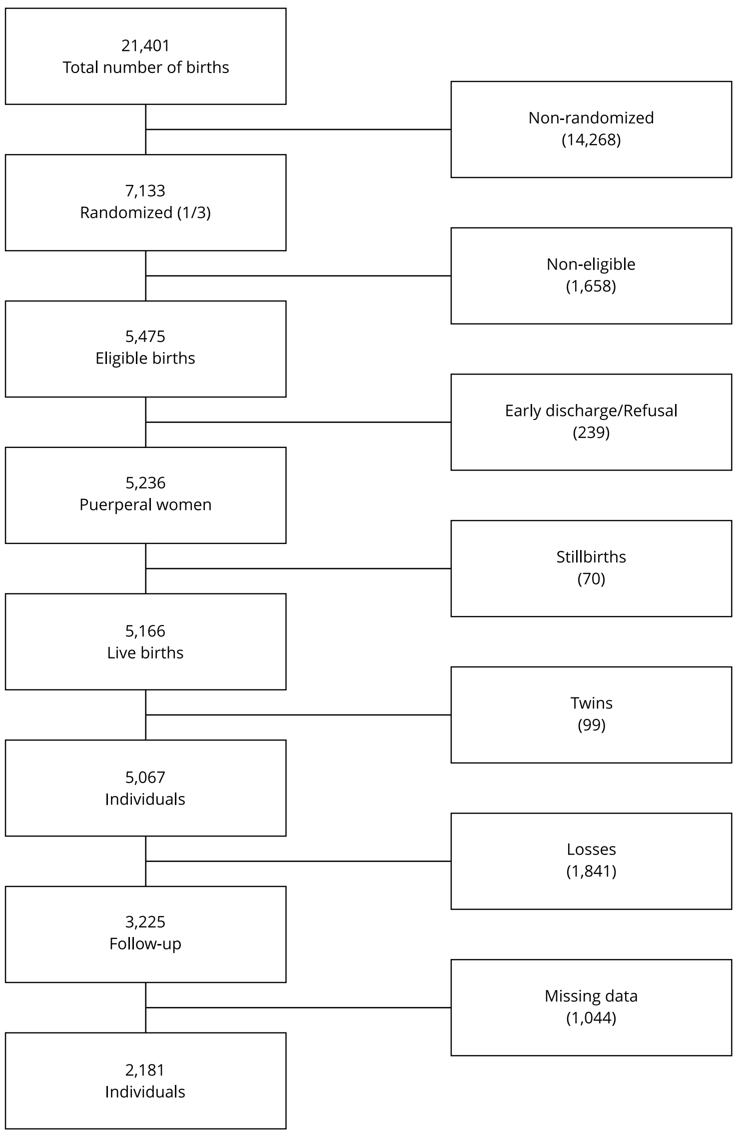
This study used data from the BRISA Birth Cohort in São Luís (Maranhão State), carried out in two stages: at birth, from January to December 2010, and during follow-up visits, from April 2011 to January 2013. Each child was evaluated only once when they were aged 1-3 years.

Inclusion and exclusion criteria

In 2010, there were 21,401 births at public and private maternity wards in São Luís. One-third (7,133) of these births were randomly selected and 5,574 of the selected children had been living in São Luís for at least three months and were, therefore, eligible. The sample consisted of 5,166 live births after the exclusion of 70 stillbirths, 99 twins, and 239 early hospital discharges or refusals to participate in the study. A total of 5,067 children were invited to participate in the follow-up assessments, but only 3,225 showed up (36.3% loss). Out of these, 1,044 were excluded due to lack of information on birth weight (54), maternal race/skin color (2), socioeconomic background (86), maternal education (28), BMI measurement during follow-up (14), and pregestational maternal BMI (860). Hence, the final sample included 2,181 individuals (Figure 1).

Figure 1

Flow chart of the BRISA Birth Cohort. São Luís, Maranhão State, Brazil, 2010.



Weight and height measurements during the follow-up period and information on the type of delivery were used as inclusion criteria. Abnormal BMI (z-scores < -5 and > 5) was used as exclusion criterion [28].

The sample of 2,181 individuals was estimated to have a 98% power to detect differences between the groups (born by vaginal delivery – G1; and born by C-section – G2), with α = 5%; mean 0.44 (± 1.18 standard deviation – SD) in G1 and mean 0.63 (±1.20 SD) in G2, and 1:1 ratio between the groups in the bilateral testing.

Maternal and perinatal variables

At birth, the mothers answered a questionnaire, from which the following variables were used: type of delivery (vaginal or cesarean); maternal age in years (continuous variable); socioeconomic background assessed by the Brazilian Economic Classification Criteria (CCEB) [29] (A/B, C, D/E, in which class A represent the wealthiest and more educated and class E the poorest and less educated) and maternal schooling years (1-8; 9-11, and ≥ 12); gestational hypertension (yes or no); number of children per mother, including the child from the current pregnancy (1; 2-4, and ≥ 5 children), and race/skin color (white, black, and mixed-race/yellow/Asian/indigenous).

Additionally, prenatal care adequacy (yes or no) was determined based on the date of the first prenatal visit, gestational age, and the number of visits during pregnancy [14]. Self-reported information was also obtained, such as weight before pregnancy (kg), height before pregnancy (cm), and weight at the end of pregnancy. Weight (kg) and height (m) were used to calculate pregestational BMI (underweight ≤ 18.5, normal weight 18.5-24.9, and excess weight ≥ 25) [30].

Weight gain during pregnancy (continuous variable) was calculated by the difference between weight at the end of pregnancy and weight before pregnancy. Initially, all women with weight gain inferior to 3kg (271 women) were left out. For those women with insufficient information for the calculation of gestational weight gain (994 women), weight values were imputed in a regression model. Weight gain was predicted by the following maternal variables: schooling, socioeconomic background, parity, skin color, age, and BMI. One mother was excluded due to excess weight gain (114kg).

Data on the newborns were obtained from the neonatal questionnaire and included the following variables: sex (male or female), age in months, weight (g), length (cm), and gestational age (weeks of gestation).

Weight for gestational age – based on weight measurements and gestational age – was calculated in z-score using the International Fetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH-21st) application. Nutritional status was determined by weight for gestational age, in z-score, considering the following cutoff points: small for gestational age (z-score < -2); appropriate for gestational age (-2 ≤ z score ≤ +2); and large for gestational age (z-score > +2) [31].

The data were typed in duplicate into a Microsoft Office Access 2007 spreadsheet (https://products.office.com/). The duplicated data were compared and the errors were corrected.

In the follow-up period, the mothers were contacted by phone and invited to participate in the study. The data were collected by a team of trained researchers and interviewers. Anthropometric measurements were checked during data collection. Weight (kg) was measured using a digital scale (Filizola; https://www.oswaldofilizola.com.br/), and height (cm) was verified by an infantometer (Alturexata; Belo Horizonte, Brazil) following WHO guidelines [28]. The WHO Antro software, version 3.2.2 (http://www.who.int/childgrowth/software/en/) was used to calculate BMI-for-age, in z-score (continuous variable), based on sex- and age-specific weight and height measurements. In the statistical analysis, BMI-for-age was used as a continuous variable. For the sake of sample description, nutritional status was classified according to BMI-for-age using the following cutoff points: underweight (z-score < -2); normal (-2 ≤ z-score ≤ +2); and overweight (z-score > +2) [32].

Directed acyclic graph

A directed acyclic graph (DAG) was used to organize knowledge by mapping out cause and effect relationships. DAG codifies a qualitative theory – or assumptions – about the causal structure of a problem. A priori, it does not assume any distribution, and it is hinged upon nonparametric structural equations. Its use in causal modeling underscores the notion that causality implies directionality of influence. By graphical models, the backdoor criterion was used to identify the minimum set of variables to adjust for confounding [33].

The DAG was created using the DAGitty 2.2 software (http://www.dagitty.net/). Unmeasured variables were also included in the DAG: intestinal microbiota, hormones of labor, and infant's food intake. Controlling was made for confounding factors, avoiding adjustment for colliders and their descendants, as false associations could be induced (collider bias) [33].

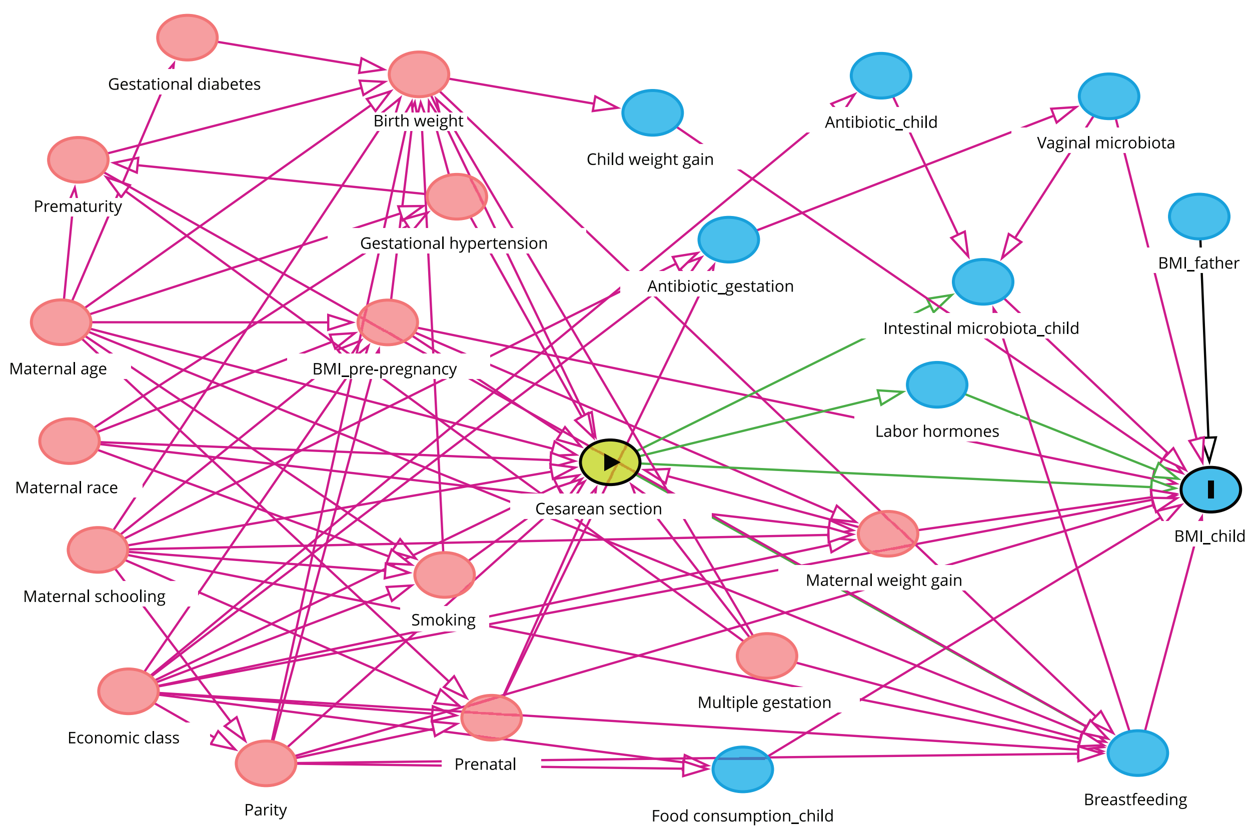
Type of delivery (dichotomous variable) was the exposure variable and BMI-for-age (continuous variable) was the outcome variable. The variables indicated for the minimum adjustment for confounding were pregestational BMI (categorical variable), CCEB (categorical variable), schooling years (categorical variable), maternal age (categorical variable), number of children (categorical variable), prenatal care adequacy (dichotomous variable), weight gain during pregnancy (continuous variable), and birth weight for gestational age (categorical variable) (Figure 2).

Statistical analysis and data processing

The Shapiro-Wilk test was used to check the normality of data. Normally distributed variables were described as mean and SD and those without normal distribution were presented as median and interquartile range. The qualitative variables were described as frequencies and percentages.

Figure 2

Directed acyclic graph: theoretical association model for cesarean delivery and body mass index (BMI) of children.



The assumptions about causal inference are the following: the intervention has to be well defined; there should be exchangeability between the exposed and unexposed groups (measured by the balance of the observed variables); there should be a single treatment version (cesarean section is a single technique); there should be observations in all subgroups (positivity); and there should not be contamination (the option for cesarean section in one woman cannot interfere in the probability of cesarean section in another woman) [34].

Using the counterfactual approach, the final sample was weighted by the inverse probability of treatment (birth by C-section) considering the minimum set of confounding variables by *teffects ipwra* (inverse probability weighted linear regression adjustment) routine, a doubly robust method.

Moreover, the sample was weighted by the inverse probability of participation in the follow-up assessments. Losses to follow-up were assessed and baseline variables were compared between those infants who showed up for the follow-up visits and those who did not. Chi-square test was used for this comparison and a p-value < 0.05 was considered as statistically significant. Type of delivery, gestational hypertension, maternal BMI, schooling years, maternal age, parity, and maternal skin color influenced the compliance with the follow-up assessments and were included in the regression model from which the weight was abstracted.

The final weight used in the model was obtained by multiplying the inverse probability of participation in the follow-up assessments by the inverse probability of treatment (birth by C-section). Balancing between the groups was checked by the *tebalance sum* routine, to evaluate whether conditional exchangeability could be assumed by the difference in standardized means and the variance ratio between groups. The ideal difference in standardized means is zero (in which < 0.2 is acceptable) and the ideal variance ratio is 1 (values from 0.8 to 1.2 are acceptable). The significance level was set at 5% (p < 0.05). All analyses were carried out using Stata, version 14.0 (https://www.stata.com).

Ethical and legal aspects

This study was approved by the Research Ethics Committee of the Presidente Dutra University Hospital (HUUPD), affiliated to the UFMA (process n. 223/09 and record n. 350/08), in compliance with *Resolution n. 196/1996* and complementary guidelines established by the Brazilian National Health Council/Ministry of Health. After receiving information about the study, the mothers who agreed to participate in the study signed a informed consent form.

Results

Our study included 2,181 mothers and infants. C-section births accounted for 50.6% of all births (data not shown). More than 50% of the mothers belonged to socioeconomic class C (57.4%); 64.9% had 9-11 schooling years; and 66.7% were of mixed-race. Primiparous women accounted for 51.7% of the sample and 17.3% reported having gestational hypertension. Regarding the pregestational maternal nutritional status, 17.5% had excess weight. Prenatal care adequacy was as high as 99.6% (Table 1).

Childbirth in the private sector, socioeconomic classification A/B, high schooling, white skin color, gestational hypertension, having one child and high pregestational BMI were associated with high C-section (p < 0,001) (Table 1).

Girls accounted for 52% of the children. Children whose weight for gestational age was high (large for gestational age) represented 5.9% of the sample. The nutritional status, based on BMI-for-age in the follow-up period, indicated that 10.7% had overweight (Table 2). The mean and SD for this variable was 0.54 ± 1.20.

The infants' sex was not associated to either BMI z-score or C-section nor was it an effect modifier of the association between C-section and BMI z-score (data not shown). Thus, results were not stratified by sex.

Balance statistics showed exchangeability between the groups regarding the observed variables included in the minimum set of adjustment for confounding (Table 3). No causal effect was observed for C-section on the BMI of the infants (coefficient = -0.004; 95% confidence interval – 95%CI: -0.136; 0.127; p-value = 0.948) (data not shown).

Table 1

Demographic, socioeconomic, perinatal, and nutritional characteristics of the mothers enrolled in the BRISA Birth Cohort. São Luís, Maranhão State, Brazil, 2010/2011-2013.

Variables	Total		C-section		Vaginal birth		p-value
	n	%	n	%	n	%	
Sector							< 0.001
Public	1,788	82.0	1,069	59.8	719	40.2	
Private	393	18.0	385	98.0	8	2.0	
Socioeconomic classification *							< 0.001
A/B	462	21.1	356	77.1	106	22.9	
C	1,251	57.4	579	46.3	672	53.7	
D/E	468	21.5	169	36.1	299	63.9	
Schooling (years)							< 0.001
0-4	39	1.8	15	38.5	24	61.5	
5-8	328	15.0	112	34.1	216	65.9	
9-11	1,414	64.9	667	47.2	747	52.8	
> 12	400	18.3	310	77.5	90	22.5	
Skin color/Race							< 0.001
White	406	18.7	260	64.0	146	36.0	
Black	291	13.3	144	49.5	147	50.5	
Mixed-race	1,454	66.7	683	47.0	771	53.0	
Yellow/Asian	26	1.2	17	65.4	9	34.6	
Indigenous	2	0.1	0	0.0	2	100.0	
Gestational hypertension							< 0.001
No	1,804	82.7	850	47.1	954	52.9	
Yes	376	17.3	254	67.6	122	32.5	
Prenatal care							0.457
Adequate	2,173	99.6	1,101	50.7	1,072	49.3	
Inadequate	8	0.4	3	37.5	5	62.5	
Number of children							< 0.001
1	1,128	51.7	612	54.3	516	45.7	
2-4	1,001	45.9	478	47.8	523	52.3	
≥ 5	52	2.4	14	26.9	38	73.1	
Pregestational BMI *							< 0.001
Underweight	511	23.4	190	37.2	321	62.8	
Normal weight	1,289	59.1	678	52.6	611	47.4	
Excess weight	381	17.5	236	61.9	145	38.1	

BMI: body mass index.

Note: numbers may not add up to total (2,181) because of missing values.

* Socioeconomic classification: A is the most affluent and E comprises those with the lowest schooling and purchasing power;

** Pregestational BMI: underweight ≤ 18.5kg/m^2; normal weight 18.5-24.9kg/m^2; excess weight ≥ 25kg/m^2.

Table 2

Anthropometric measurements and sex of the children from the BRISA Birth Cohort. São Luís, Maranhão State, Brazil, 2010/2011-2013.

Variables	n	%
Sex		
Male	1,048	48.0
Female	1,133	52.0
Weight for gestational age – birth weight		
Small for gestational age	49	2.2
Appropriate for gestational age	2,004	91.9
Large for gestational age	128	5.9
Children's BMI		
Underweight	47	2.2
Normal weight	1,900	87.1
Overweight	234	10.7

BMI: body mass index.

Discussion

Our study did not show a causal effect between C-section and BMI among children. C-section births accounted for 50.6% – three times higher than the limit recommended by WHO [13]. The prevalence of overweight among children was 10.7%.

One of the limitations of this study was the use of self-reported weight and height information, which is prone to recall bias, for the calculation of the pregestational maternal BMI. The estimated value could have been overestimated by short women and underestimated by overweight women [35,36]. However, this is a common practice [37] due to the lack of planned pregnancy in most cases. Another limitation was follow-up losses. However, inverse probability weighting based on variables collected at birth was used to minimize this limitation. Even though children aged from 1 to 3 years were included, 90% were 14- to 28-month-old and BMI-for-age z-score was used to allow comparisons of children from different ages.

The strengths of this study include the use of data from a birth cohort of Brazilian children, with a large sample size, wide variety of perinatal information, and weight and height measurements made by trained researchers during the follow-up visits. Moreover, the children's BMI was classified according to international standards, allowing comparison with other studies and populations. The main confounding variables – including pregestational maternal BMI – were included in the adjustment.

Another strength was the selection of adjustment variables using a DAG, based on the theoretical plausibility of the relationships between variables, contributing to reducing the confounding bias. We also highlight the use of a method based on the counterfactual approach, the inverse probability of treatment weighting, and the statistical methods that assessed exchangeability of observed variables between the groups.

Cesarean section was associated with high maternal schooling and purchasing power [38,39], attendance in the private health facilities [39,40], old maternal age, and primiparity as reported by others [40].

The association between C-section and increased BMI during childhood is controversial, and reported by some studies [41,42,43], however, some recent studies have not found this association [44,45,46,47,48,49,50]. A meta-analysis carried out by Sutharsan et al. [24] reveals that the associations observed between C-section and obesity likely result from several biases, especially from confounding bias. Another meta-analysis suggests an association between C-section and obesity, more consistently perceived in a young population, but possible confounding bias was detected [43]. A study by Masukume et al. [20] on 3-year-old Irish children did not find data that could confirm the association

Table 3

Balance of variables in the exposed and non-exposed groups before and after inverse probability of selection weighting of the BRISA Birth Cohort. São Luís, Maranhão State, Brazil, 2010/2011-2013.

Variables	Differences in standardized means		Variance ratio	
	Raw	Weighted	Raw	Weighted
Maternal BMI				
Underweight	Reference			
Normal weight	0.113	-0.002	0.953	1.001
Excess weight	0.241	0.000	1.616	1.001
Weight for gestational age				
Small for gestational age	Reference			
Appropriate for gestational age	-0.026	-0.009	1.084	1.032
Large for gestational age	0.055	0.007	1.230	1.029
Maternal socioeconomic classification *				
A/B	Reference			
C	-0.210	0.007	1.065	0.997
D/E	0.582	-0.009	2.460	0.986
Maternal age (years)				
< 20	Reference			
20-34	0.071	-0.017	0.918	1.022
> 35	0.333	0.036	2.840	1.114
Maternal schooling (years)				
0-4	Reference			
5-8	-0.268	-0.002	0.558	0.994
9-11	-0.235	0.018	1.161	0.988
> 12	0.556	-0.021	2.655	0.967
Number of children				
1	-0.015	-0.006	0.986	1.006
2-4	-0.116	0.006	0.788	1.012
≥ 5	-0.130	-0.016	0.410	1.109
Weight gain during pregnancy	0.238	-0.005	1.069	0.975
Prenatal care adequacy	-0.001	0.011	0.959	1.271

* Socioeconomic classification: A is the most affluent and E comprises those with the lowest schooling and purchasing power.

between C-section and increased risk of overweight. A similar result was obtained for English children aged 3, 5, 7, 11, and 14 years [20].

The use of a DAG for the identification of a set of variables helps minimize the possibility of confounding and selection biases in the estimation of the causal effect investigated herein [51]. Its use in our study prevented us from unnecessarily adjusting for some variables that are commonly included in the multivariate model in studies on the association between C-section and BMI or overweight, such as diabetes mellitus, smoking during pregnancy, among others. Therefore, this leads to the potential interpretation of our finding as causal effect.

Environmental factors can interfere with BMI throughout the life course, especially within the first 1,000 days of life. It is widely known that the diet can modulate the intestinal microbiota of children and adults, and studies have demonstrated that the intestinal microbiota is modulated by environmental factors and, more robustly, by diet formulation [52,53,54,55,56]. Nevertheless, for the assessment of the causal effect between C-section and BMI in children, the diet is not a confounding factor, but a mediator variable instead, as indicated by the DAG developed herein; and, therefore, this variable does not need to be included in the adjustment.

This study did not make any distinction as to whether C-section was elective/planned or emergency/unplanned. Studies that separately assess the types of indication for C-section are controversial since emergency C-section is not associated with a lower incidence of overweight or change in BMI than an elective C-section [20,49,50].

Recent studies have suggested that the contact of the newborn with the maternal vaginal microbiota during an emergency C-section does not reduce the risk of obesity when compared with that of newborns born by a planned C-section, as expected. These findings contrasts with the assumption that contact with the vaginal microbiota could be accountable for the increased risk of childhood obesity [49,50]. Hence, determining exposure by the type of indication for C-section does not seem to change the outcomes of this association.

The prevalence of C-section in our study was slightly lower than the 52% reported in a Brazilian study carried out in 2011/2012. However, interestingly, the Northeastern Region, from which the sampled population in our study was taken, has lower rates of C-section than the Central-Western and Southern regions [57].

Conclusion

No causal effect was observed between C-section and BMI among children aged 1-3 years using graphical and counterfactual approaches to minimize confounding and selection biases.

There was a high rate of C-section in this study, in line with what has been observed in Brazil and in other countries. Even though no causal effect of C-section on the BMI of children could be found, it is important that the type of delivery be chosen based on medical criteria, since C-section may harm both mother and child, with high rates of perinatal complications and mortality.

Contributors

L. F. P. Cavalcante contributed to the data analysis and writing. C. A. Carvalho, L. L. Padilha, and A. A. M. Silva contributed to the data analysis and review. P. C. A. F. Viola and V. M. F. Simões contributed to the review. All the authors approved the final version of the manuscript.

Additional informations

ORCID: Lilian Fernanda Pereira Cavalcante (0000-0002-5578-221X); Carolina Abreu de Carvalho (0000-0001-7900-4642); Luana Lopes Padilha (0000-0002-7162-2726); Poliana Cristina de Almeida Fonseca Viola (0000-0002-8875-5154); Antônio Augusto Moura da Silva (0000-0003-4968-5138); Vanda Maria Ferreira Simões (0000-0001-8351-1348).

Conflicts of interest

The authors declare no conflict of interest.

Acknowledgments

To the Maranhão State Research Foundation (FAPEMA) and the Brazilian National Research Council (CNPq).

References

1. Nauta AJ, Amor KB, Knol J, Garssen J, van der Beek EM. Relevance of pre- and postnatal nutrition to development and interplay between the microbiota and metabolic and immune systems. Am J Clin Nutr 2013; 98:586S-93S.
2. Lucas C, Charlton KE, Yeatman H. Nutrition advice during pregnancy: do women receive it and can health professionals provide it? Matern Child Health J 2014; 18:2465-78.
3. Amarasekara R, Jayasekara RW, Senanayake H, Dissanayake VH. Microbiome of the placenta in pre-eclampsia supports the role of bacteria in the multifactorial cause of pre-eclampsia. J Obstet Gynaecol Res 2015; 41:662-9.
4. De Onis M, Blössner M, Borghi E. Global prevalence and trends of overweight and obesity among preschool children. Am J Clin Nutr 2010; 92:1257-64.
5. Owen CG, Martin RM, Whincup PH, Smith GD, Cook DG. Effect of infant feeding on the risk of obesity across the life course: a quantitative review of published evidence. Pediatrics 2005; 115:1367-77.
6. Haemer MA, Huang TT, Daniels SR. The effect of neurohormonal factors, epigenetic factors, and gut microbiota on risk of obesity. Prev Chronic Dis 2009; 6:A96.
7. Goldani HA, Bettiol H, Barbieri MA, Silva AA, Agranonik M, Morais MB, et al. Cesarean delivery is associated with an increased risk of obesity in adulthood in a Brazilian birth cohort study. Am J Clin Nutr 2011; 93:1344-7.
8. Huh SY, Rifas-Shiman SL, Zera CA, Edwards JWR, Oken E, Weiss ST, et al. Delivery by caesarean section and risk of obesity in preschool age children: a prospective cohort study. Arch Dis Child 2012; 97:610-6.
9. Mesquita DN, Barbieri MA, Goldani HA, Cardoso VC, Goldani MZ, Kac G, et al. Cesarean section is associated with increased peripheral and central adiposity in young adulthood: cohort study. PLoS One 2003; 8:e66827.
10. Hamilton BE, Martin JA, Ventura SJ. Births: preliminary data for 2008. Natl Vital Stat Rep 2010; 59:1-19.
11. NHS Institute for Innovation and Improvement. Focus on: caesarean section. London: National Health Service; 2011.
12. Departamento de Informática do SUS. Estatísticas vitais. http://www2.datasus.gov.br/DATASUS/index.php?area=0205 (accessed on 05/Aug/2020).
13. Moore B. Appropriate technology for birth. Lancet 1985; 326:787.
14. Betran AP, Torloni MR, Zhang J, Ye J, Mikolajczyk R, Deneux-Tharaux C, et al. What is the optimal rate of caesarean section at population level? A systematic review of ecologic studies. Reprod Health 2015; 12:57.
15. Molina G, Weiser TG, Lipsitz SR, Esquivel MM, Uribe-Leitz T, Azad T. Relationship between cesarean delivery rate and maternal and neonatal mortality. JAMA 2015; 314:2263-70.

16. Barros FC, Matijasevich A, Maranhão AGK, Escalante JJ, Rabello Neto DL, Fernandes RM, et al. Cesarean sections in Brazil: will they ever stop increasing? Rev Panam Salud Pública 2015; 38:217-25.
17. Carniel EF, Zanolli ML, Morcillo AM. Fatores de risco para indicação do parto cesáreo em Campinas (SP). Rev Bras Ginecol Obstet 2007; 29:34-40.
18. Hyde MJ, Mostyn A, Modi N, Kemp PR. The health implications of birth by caesarean section. Biol Rev Camb Philos Soc 2012; 87:229-43.
19. Kiriakopoulos N, Grigoriadis S, Maziotis E, Philippou A, Rapani A, Giannelou P, et al. Investigating stress response during vaginal delivery and elective cesarean section through assessment of levels of cortisol, interleukin 6 (IL-6), growth hormone (GH) and insulin-like growth factor 1 (IGF-1). J Clin Med 2019; 8:1112.
20. Masukume G, Khashan AS, Morton SM, Baker PN, Kenny LC, McCarthy FP. Caesarean section delivery and childhood obesity in a British longitudinal cohort study. PLoS One 2019; 14:e0223856.
21. Turnbaugh PJ, Ley RE, Mahowald MA, Magrini V, Mardis ER, Gordon JI. An obesity-associated gut microbiome with increased capacity for energy harvest. Nature 2006; 444:1027.
22. Jumpertz R, Le DS, Turnbaugh PJ, Trinidad C, Bogardus C, Gordon JI, et al. Energy-balance studies reveal associations between gut microbes, caloric load, and nutrient absorption in humans. Am J Clin Nutr 2011; 94:58-65.
23. Tun HM, Bridgman SL, Chari R, Field CJ, Guttman DS, Becker AB, et al. Roles of birth mode and infant gut microbiota in intergenerational transmission of overweight and obesity from mother to offspring. JAMA Pediatr 2018; 172:368-77.
24. Sutharsan R, Mannan M, Doi SA, Mamun AA. Caesarean delivery and the risk of offspring overweight and obesity over the life course: a systematic review and bias-adjusted meta-analysis. Clin Obes 2015; 5:293-301.
25. Zhou Y, Zhang Y, Sun Y, Zhang D. Association of cesarean birth with body mass index trajectories in adolescence. Int J Environ Res Public Health 2020; 17:2003.
26. Sogunle E, Masukume G, Nelson G. The association between caesarean section delivery and later life obesity in 21-24 year olds in an Urban South African birth cohort. PLoS One 2019; 14:e0221379.
27. Silva AAM, Batista RFL, Simões VMF, Thomaz EBAF, Ribeiro CCC, Lamy-Filho F, et al. Changes in perinatal health in two birth cohorts (1997/1998 and 2010) in São Luís, Maranhão State, Brazil. Cad Saúde Pública 2015; 31:1437-50.
28. World Health Organization. Physical status: the use and interpretation of anthropometry. Geneva: World Health Organization; 1995. (WHO Technical Report Series, 854).
29. Associação Brasileira de Empresas de Pesquisas. Critério de Classificação Econômica Brasil. https://www.abep.org/criterio-brasil (accessed on Mar/2022).
30. Institute of Medicine. Nutrition during pregnancy. Washington DC: Committee on Nutritional Status and Weight Gain during Pregnancy, Institute of Medicine; 1992.
31. Villar J, Ismail LC, Victora CG, Ohuma EO, Bertino E, Altman DG, et al. International standards for newborn weight, length, and head circumference by gestational age and sex: the Newborn Cross-Sectional Study of the INTERGROWTH-21st Project. Lancet 2014; 384:857-68.
32. World Health Organization. WHO child growth standards: head circumference-for-age, arm circumference-for-age, triceps skinfold-for-age and subscapular skinfold-for-age: methods and development. Geneva: World Health Organization; 2007.
33. Pearl J. Causality. 2nd Ed. New York: Cambridge University Press; 2009.
34. Hernán MA, Robins JM. Causal inference. Boca Raton: CRC Press; 2010.
35. Nyholm M, Gullberg B, Merlo J, Lundqvist-Persson C, Råstam L, Lindblad U. The validity of obesity based on self-reported weight and height: implications for population studies. Obesity (Silver Spring) 2007; 15:197-208.
36. Craig BM, Adams AK. Accuracy of body mass index categories based on self-reported height and weight among women in the United States. Matern Child Health J 2009; 13:489-96.
37. Steur M, Smit HA, Schipper CMA, Scholtens S, Kerkhof M, Jongste JC, et al. Predicting the risk of newborn children to become overweight later in childhood: the PIAMA birth cohort study. Int J Pediatr Obes 2011; 6:e170-8.
38. Béhague DP, Victora CG, Barros FC. Consumer demand for caesarean sections in Brazil: informed decision making, patient choice, or social inequality? A population based birth cohort study linking ethnographic and epidemiological methods. BMJ 2002; 324:942.
39. Moraes MS, Goldenberg P. Cesáreas: um perfil epidêmico. Cad Saúde Pública 2001; 17:509-19.
40. Gomes UA, Silva AAM, Bettiol H, Barbieri MA. Risk factors for the increasing caesarean section rate in Southeast Brazil: a comparison of two birth cohorts, 1978-1979 and 1994. Int J Epidemiol 1999; 28:687-94.
41. Goldani MZ, Barbieri MA, Silva AAM, Gutierrez MRP, Bettiol H, Goldani HAS. Cesarean section and increased body mass index in school children: two cohort studies from distinct socioeconomic background areas in Brazil. Nutr J 2013; 12:104.
42. Blustein J, Attina T, Liu M, Ryan AM, Cox LM, Blaser MJ, et al. Association of caesarean delivery with child adiposity from age 6 weeks to 15 years. Int J Obes (Lond) 2013; 37:900-6.

43. Darmasseelane K, Hyde MJ, Santhakumaran S, Gale C, Modi N. Mode of delivery and offspring body mass index, overweight and obesity in adult life: a systematic review and meta-analysis. PLoS One 2014; 9:e87896.
44. Barros FC, Matijasevich A, Hallal PC, Horta BL, Barros AJ, Menezes AB, et al. Cesarean section and risk of obesity in childhood, adolescence, and early adulthood: evidence from 3 Brazilian birth cohorts. Am J Clin Nutr 2012; 95:465-70.
45. Rooney BL, Mathiason MA, Schauberger CW. Predictors of obesity in childhood, adolescence, and adulthood in a birth cohort. Matern Child Health J 2011; 15:1166-75.
46. Ajslev TA, Andersen CS, Gamborg M, Sørensen TIA, Jess T. Childhood overweight after establishment of the gut microbiota: the role of delivery mode, pre-pregnancy weight and early administration of antibiotics. Int J Obes (Lond) 2011; 35:522-9.
47. Rifas-Shiman SL, Gillman MW, Hawkins SS, Oken E, Taveras EM, Kleinman KP. Association of cesarean delivery with body mass index z score at age 5 years. JAMA Pediatr 2018; 172:777-9.
48. Ahlqvist VH, Persson M, Magnusson C, Berglind D. Elective and nonelective cesarean section and obesity among young adult male offspring: a Swedish population-based cohort study. PLoS Med 2019; 16:e1002996.
49. Masukume G, O'Neill SM, Baker PN, Kenny LC, Morton SM, Khashan AS. The impact of caesarean section on the risk of childhood overweight and obesity: new evidence from a contemporary cohort study. Sci Rep 2018; 8:15113.
50. Masukume G, McCarthy FP, Baker PN, Kenny LC, Morton SM, Murray DM, et al. Association between caesarean section delivery and obesity in childhood: a longitudinal cohort study in Ireland. BMJ Open 2019; 9:e025051.
51. Textor J, Hardt J, Knüppel S. DAGitty: a graphical tool for analyzing causal diagrams. Epidemiology 2001; 22:745.
52. Penders J, Thijs C, Vink C, Stelma FF, Snijders B, Kummeling, et al. Factors influencing the composition of the intestinal microbiota in early infancy. Pediatrics 2006; 118:511-21.
53. Bäckhed F, Manchester JK, Semenkovich CF, Gordon JI. Mechanisms underlying the resistance to diet-induced obesity in germ-free mice. Proc Natl Acad Sci U S A 2007; 104:979-84.
54. Suez J, Korem T, Zeevi D, Zilberman-Schapira G, Thaiss CA, Maza O, et al. Artificial sweeteners induce glucose intolerance by altering the gut microbiota. Nature 2014; 514:181-6.
55. Wilson AS, Koller KR, Ramaboli MC, Nesengani LT, Ocvirk S, Chen C, et al. Diet and the human gut microbiome: an international review. Dig Dis Sci 2020; 65:723-40.
56. Raspini B, Porri D, Giuseppe R, Chieppa M, Liso M, Cerbo RM, et al. Prenatal and postnatal determinants in shaping offspring's microbiome in the first 1000 days: study protocol and preliminary results at one month of life. Ital J Pediatr 2020; 46:45.
57. Höfelmann DA. Tendência temporal de partos cesáreos no Brasil e suas regiões: 1994 a 2009. Epidemiol Serv Saúde 2012; 21:561-8.

Resumo

A obesidade é considerada um problema de saúde pública global. Alguns estudos têm mostrado associação entre índice de massa corporal (IMC) elevado e aumento da obesidade em todas as fases da vida. Entretanto, essa mesma associação tem sido contestada por outros estudos. O objetivo foi de avaliar o efeito causal do parto cesáreo sobre o IMC das crianças entre 1 e 3 anos de idade. O estudo de coorte analisou 2.181 crianças de 1 a 3 anos de idade, nascidas em 2010, com dados obtidos da Coorte de Nascimentos BRISA em São Luís, Maranhão, Brasil. Foram avaliados dados sociodemográficos, características maternas, tipo de parto, morbidades, medidas antropométricas e IMC. Foram usados modelos estruturais marginais com abordagem contrafactual para verificar o efeito causal do tipo de parto sobre a obesidade, ponderado pela probabilidade inversa de seleção e exposição. Entre as 2.181 crianças avaliadas 52% eram do sexo feminino, 50,6% nascidas de parto cesáreo, 5,9% grandes para a idade gestacional e 10,7% com excesso de peso. Não foi observado efeito causal da cesariana sobre o IMC da criança (coeficiente = -0,004; IC95%: -0,136; 0,127; p = 0,948). O parto cesáreo não teve efeito causal sobre o IMC de crianças entre 1 e 3 anos de idade.

Cesárea; Obesidade Infantil; Índice de Massa Corporal

Resumen

La obesidad está considerada un problema global de salud pública. El parto por cesárea ha sido asociado con un alto índice de masa corporal (IMC) y mayor obesidad en todos los estadios de la vida. Esta asociación, sin embargo, ha sido recusada en algunos estudios. El objetivo fue evaluar el efecto causal del parto por cesárea en el IMC de niños con edades de 1 a 3 años. Esta es una cohorte de estudio de 2.181 niños con edades de 1 a 3 años, nacidos en 2010, obtenidos de la Cohorte de Nacimientos BRISA, en São Luís, estado de Maranhão, Brasil. Se evaluaron las variables sociodemográficas, características maternales, tipo de parto, morbilidad, medidas antropométricas, e IMC. Se usaron modelos marginales estructurales con un enfoque contrafactual para comprobar el efecto causal del tipo de parto en la obesidad, ponderado por la probabilidad inversa de selección y exposición. Aparte de los 2.181 niños evaluados (52% mujeres), 50,6% nacieron por parto por cesárea, 5,9% de los niños recién nacidos fueron grandes para la edad gestacional, y 10,7% de ellos tenían exceso de peso. No se observó un efecto causal del parto por cesárea en el índice de masa corporal (coeficiente = -0,004; IC95%: -0,136; 0,127; p = 0,948). El parto por cesárea no tuvo un efecto a causal en el IMC de niños con edades entre 1 a 3 años.

Cesárea; Obesidad Pediátrica; Índice de Masa Corporal

Submitted on 10/Dec/2020
Final version resubmitted on 22/Sep/2021
Approved on 01/Oct/2021