Cesarean Section Is Associated with Increased Peripheral and Central Adiposity in Young Adulthood: Cohort Study

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Abstract

**Background:** Cesarean section (CS) has been associated with obesity, measured by body mass index (BMI), in some studies. It has been hypothesized that this association, if causal, might be explained by changes in gut microbiota. However, little is known about whether CS is also associated with increased adiposity as measured by indicators other than BMI. Objective: To assess the association between CS and indicators of peripheral and central adiposity in young adults.

**Methods:** The study was conducted on 2,063 young adults aged 23 to 25 years from the 1978/79 Ribeirão Preto birth cohort, São Paulo, Brazil. CS was the independent variable. The anthropometric indicators of adiposity were: waist circumference (WC), waist-height ratio (WHtR), waist-hip ratio (WHR), tricipital skinfold (TSF), and subscapular skinfold (SSF). The association between CS and indicators of adiposity was investigated using a Poisson model, with robust adjustment of variance and calculation of incidence rate ratio (IRR) with 95% confidence interval (95%CI), and adjustment for birth variables.

**Results:** Follow-up rate was 31.8%. The CS rate was 32%. Prevalences of increased WC, WHtR, WHR were 32.1%, 33.0% and 15.2%, respectively. After adjustment for birth variables, CS was associated with increased risk of adiposity when compared to vaginal delivery: 1.22 (95%CI 1.07; 1.39) for WC, 1.25 (95%CI 1.10; 1.42) for WHtR, 1.45 (95%CI 1.18; 1.79) for WHR, 1.36 (95%CI 1.04; 1.78) for TSF, and 1.43 (95%CI 1.08; 1.91) for SSF.

**Conclusion:** Subjects born by CS had a higher risk for increased peripheral and central adiposity during young adult age compared to those born by vaginal delivery. The association of CS with adiposity was consistently observed for all indicators and was robust after adjustment for a variety of early life confounders.

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Introduction

Over the last years, the prevalence of overweight and obesity has increased in the world population [1,2]. A systematic analysis of the worldwide trends in body mass index (BMI) for adults 20 years old and older in 199 countries and territories between 1980 and 2008 showed that, despite a substantial variation in BMI between nations, mean BMI has increased on average 0.4 kg/m² per decade for men and 0.5 kg/m² per decade for women over the period [3].

This increase is also observed in the excessive accumulation of subcutaneous and visceral fat, which greatly contributes to metabolic complications and to adverse effects on health [4]. The accumulation of visceral or central fat has been shown to be a better predictor of adult morbidity than obesity alone measured by BMI, justifying the use of indicators related to visceral fats such as waist circumference (WC) and waist/height ratio (WHtR) [5].

Recent studies have shown that cesarean section (CS) is associated with a greater BMI both in children and adults [6,7,8,9,10]. A recent systematic review and meta-analysis including two case-control and seven cohort studies indicates that CS represents 33% higher risk of overweight and obesity for the offspring and 50% for adults 19 years old or older when compared to vaginal deliveries [11]. Gut microbiota seems to be an important factor connecting genes, environment, and the immune system [12]. Type of delivery seems to play a role in the composition of the intestinal microbiota in early infancy and this may be an environmental factor that modulates obesity and other metabolic diseases [13]. The mechanism by which CS may contribute to a greater risk of obesity appears to be based on changes in gut microbiota due to lack of contact of the baby with the maternal vaginal flora [14]. During vaginal delivery the baby is exposed to a wide variety of microorganisms, a fact that does not occur during CS [15,16]. It has been hypothesized that this may lead to obesity in later life, probably due to increased absorption of
fat and possibly by induction of low-grade inflammation [17,18,19].

To our knowledge, only one study [10], conducted on children, used measurements of adiposity other than the BMI, i.e., tricipital and subscapular skinfolds, to explore the association between CS and adiposity in early life. It was observed that babies born by CS had a 0.94 mm (95% CI 0.36 to 1.51) increment in the sum of skinfolds; however, CS was not associated with the subcapular/triceps skinfold ratio ($b_0 = 0.18$, 95% CI $-2.30$ to $1.94$), a measure of central adiposity, when compared to those delivered vaginally.

A previous study on a cohort of young Brazilian adults showed an association between CS and total obesity measured by BMI [7]. To date, little is known about whether CS is also associated with increased central adiposity. Thus, the objective of the present study was to investigate in this same cohort whether babies born by CS have a higher risk for increased peripheral and central adiposity measured on the basis of indicators other than BMI.

### Methods

This was a prospective cohort study including live-born neonates in the city of Ribeirão Preto/São Paulo, from June 1978 to May 1979 [20]. During this period, 9,067 live newborns born in the eight Ribeirão Preto hospitals (98% of the total number of live newborns during the period) participated in the study. There were 3.5% losses due to refusal or early discharge from hospital. Babies whose mothers did not reside in the city and were not from Ribeirão Preto at the time of delivery were excluded, with 6,973 live newborns remaining, 6,827 of them singletons and 146 twin deliveries.

The cohort was re-evaluated between April 2002 and May 2004 when the individuals had completed 23–25 years of age. Of these, 246 died during the first year of life [21] and 97 died by 20 years of age, for a total of 343 deaths [22], leaving 6,484 eligible subjects. Contact was sought with one in each three individuals based on the geo-economic characterization of the city, divided into four

### Table 1. Comparison of birth characteristics of those followed-up with those not followed-up in early adulthood.

| Variables                              | Not followed-up (n = 4,421)* | Followed-up (n = 2,063)* | P-value** |
|----------------------------------------|------------------------------|--------------------------|-----------|
|                                        | n   | %       | n   | %       |           |
| Type of delivery                       |     |         |     |         | 0.055     |
| Vaginal                                | 3,108 | 68.9 | 1,402 | 31.1 |           |
| Cesarean                               | 1,312 | 66.5 | 661 | 33.5 |           |
| Maternal schooling (years)             |     |         |     |         | <0.001    |
| ≥12                                    | 440 | 67.2 | 215 | 32.8 |           |
| 9–11                                   | 542 | 62.1 | 331 | 37.9 |           |
| 5–8                                    | 1,053 | 65.4 | 557 | 34.6 |           |
| 0–4                                    | 2,266 | 71.1 | 920 | 28.9 |           |
| Sex                                    |     |         |     |         | 0.004     |
| Female                                 | 2,117 | 66.5 | 1068 | 33.5 |           |
| Male                                   | 2,304 | 69.8 | 995 | 30.2 |           |
| Birth weight (grams)                   |     |         |     |         | 0.618     |
| <2500                                  | 252 | 66.3 | 128 | 33.7 |           |
| 2500 |–|3000 | 935 | 69.3 | 414 | 30.7 |           |
| 3000 |–|3500 | 1,796 | 67.9 | 848 | 32.1 |           |
| 3500 |–|4000 | 1,149 | 68.7 | 524 | 31.3 |           |
| ≥4000                                  | 289 | 66.0 | 149 | 34.0 |           |
| Maternal smoking during pregnancy (cigarettes/day) |     |         |     |         | <0.001    |
| Non-smoker                             | 3,004 | 66.6 | 1509 | 33.4 |           |
| 1–10                                   | 730 | 69.7 | 318 | 30.3 |           |
| >10                                    | 538 | 75.7 | 173 | 24.3 |           |
| Parity                                 |     |         |     |         | <0.001    |
| 1                                      | 1,525 | 66.4 | 771 | 33.6 |           |
| 2–4                                    | 2,247 | 67.5 | 1083 | 32.5 |           |
| ≥5                                     | 511 | 75.2 | 169 | 24.8 |           |
| Maternal age (years)                   |     |         |     |         | 0.065     |
| <20                                    | 635 | 71.4 | 254 | 28.6 |           |
| 20–34                                  | 3,372 | 67.5 | 1626 | 32.5 |           |
| ≥35                                    | 366 | 68.2 | 171 | 31.8 |           |

*Totals may not add up to 6,484 because of missing values.

**P-value refers to the chi-squared test.

1978/89 Ribeirão Preto birth cohort, 2002/2004.

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regions, according to family head income. Based on the records of the Unified Health System and of private health plans and on the contacts made in the 2nd and 3rd phase of the study, it was possible to locate 5,665 individuals. The losses due to refusal to participate in the study (209 cases), to death after 20 years of age (34 cases), imprisonment (31 cases) and failure to attend the interview (431 cases) corresponded to a total of 705 individuals. Losses were replaced using the same sampling frame, resulting in 2,063 young adults aged 23 to 25 years, corresponding to 31.8% of the 6,484 subjects, participating in the 4th phase of the study of the Ribeirão Preto cohort [23].

The final sample consisted of 2,063 participants. This sample size permitted us to detect a 6% difference in the increased prevalence of adiposity between GS and vaginal delivery, assuming a prevalence of about 30%, with an 80% power and a 5% probability of type I error. For prevalence around 10% this same sample size permits the detection of 4% differences with the same power and the same probability of type I error. Details of the methodology have been previously published [23,24].

The mothers were interviewed soon after delivery using a questionnaire with socioeconomic and demographic information. The newborns were weighed by trained personnel, using standardized techniques [25]. Gestational age was calculated on the basis of the mother’s information about the last normal menstrual period.

The young adults were interviewed in order to obtain socioeconomic, demographic and life habit information. The following anthropometric measurements were obtained: weight, height, waist and hip circumference, and tricipital and subscapular skinfolds using standardized techniques applied by trained personnel. All measurements were obtained with the subjects wearing light clothing and no shoes.

WC was measured at the midpoint between the last rib and the upper margin of the iliac crest using an inextensible metric tape [26] and classified as increased when its value was ≥90 cm for men and ≥80 cm for women, as proposed by the International Diabetes Federation [27].

Height was measured with the individual standing up and barefoot, using a wood stadiometer with a wood support and an inextensible ruler. The subject stood up erect, with arms along the body and head on the Frankfurt plane [25].

WHiR was calculated as waist circumference in cm divided by height in cm and was defined as increased for men and women when its value was >0.5 [28].

Hip circumference was measured at the point of greater circumference on the gluteal region using an inextensible tape [25]. The waist-hip ratio (WHR) was calculated by dividing waist circumference in cm by the hip circumference in cm, and was considered to be increased when its value was ≥0.90 for men and ≥0.85 for women [29].

The tricipital skinfold (TSF) was measured in the posterior midpoint of the arm between the acromion and olecranon and the subscapular skinfold (SSF) was measured 2 cm below the margin of the lower angle of the scapula [25] using a caliper (Holtain Ltd., Crynchy, U.K.) with a limit measurement of 40 mm. Values above the 90th percentile obtained for the study population were considered to be increased.

The birth variables selected were birth weight (<2500 g, 2500–3000 g, 3000–3500 g, 3500–4000 g and ≥4000 g), type of delivery (vaginal and cesarean), newborn’s sex, maternal schooling in years of study (0–4, 5–8, 9–11 and ≥12), maternal smoking during pregnancy as number of cigarettes smoked per day (non-smoker, 1–10, >10), parity (1, 2–4, >4), maternal age (<20, 20–34 and ≥35 years) and gestational age as a continuous variable.

The association of type of delivery with increased WC, WHiR, WHR, TSF and SSF was estimated by Poisson regression with robust adjustment of variance, with the calculation of the incidence rate ratio (IRR) and its respective 95% confidence interval [95% CI] [30,31], and with the level of significance set at 0.05. The independent variables listed above were first submitted to non-adjusted analysis for each response variable; next, adjusted analyses were carried out, with the type of delivery being the explanatory variable and the remaining variables being possible confounders. Since there was selective attrition according to some birth variables, probabilities of selection for each individual were calculated in a logistic regression model. In this model those followed-up were coded 1 and those not followed up were coded 0. Maternal schooling, sex, maternal smoking during pregnancy and parity were predictors of the probability of participation in the follow-up. To verify if these different probabilities of selection would have biased the estimates, models using inverse-probability weighting were then fitted and compared with estimates derived from models without weighting [32].

Four models were fitted for each response variable. The first was the unadjusted model. The second was the unadjusted model using inverse-probability weighting. The third model was adjusted for birth variables (newborn’s weight and sex, maternal schooling, maternal smoking during pregnancy, parity, maternal age and gestational age), and the last model was adjusted for birth variables using inverse-probability weighting. No significant interactions were detected between sex and the remaining adjustment

| Table 2. Distribution of the indicators of increased adiposity of young adults |
|-------------------------------------------------|-----|-----|
| Anthropometric indicators | N | % |
| Waist circumference (WC) | | |
| Increased* | 662 | 32.1 |
| Not increased | 1,399 | 67.8 |
| Not known | 2 | 0.1 |
| Waist-height ratio (WHtR) | | |
| Increased** | 681 | 33.0 |
| Not increased | 1,375 | 66.6 |
| Not known | 7 | 0.4 |
| Waist-hip ratio (WHR) | | |
| Increased*** | 314 | 15.2 |
| Not increased | 1,746 | 84.6 |
| Not known | 3 | 0.2 |
| Tricipital skinfold (TSF) | | |
| Increased**** | 207 | 10.0 |
| Not increased | 1,855 | 89.9 |
| Not known | 1 | 0.1 |
| Subcapular skinfold (SSF) | | |
| Increased***** | 194 | 9.4 |
| Not increased | 1,865 | 90.4 |
| Not known | 4 | 0.2 |
| Total | 2,063 | 100.0 |

*Increased WC: ≥90 cm for men and ≥80 cm for women.
**Increased WHR: >0.5.
***Increased WHR: ≥0.90 for men and ≥0.85 for women.
****Increased TSF and SSF: >90th percentile of the study population.
Ribeirão Preto, 2002/04.
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variables. All analyses were carried out using Stata, version 12. Model fit was evaluated by the goodness of fit chi-squared test.

The study was approved by the Research Ethics Committee of the University Hospital, Faculty of Medicine of Ribeirão Preto, University of São Paulo (protocol HCRP n. 7606/99). All subjects gave written informed consent to participate in the study.

Results

There was selective attrition. Males and individuals whose mothers were smokers, had ≥5 deliveries or had low schooling at the time of their birth were less likely to be interviewed (Table 1). The prevalence of increased WC, WHtR, WHR were 32.1%, 33.0% and 15.2%, respectively for the 2,063 young adults evaluated (Table 2).

CS was more common among women with schooling ≥12 (45.1%) when compared with those with 0–4 years (26.8%, p-value < 0.0001) or mothers with ≥35 years of age (43.5%) when compared with those, 20 (18.4%, p-value < 0.0001), and those with birth weight ≥4000 (41.6%) when compared with those <2500 grams (32.2%, p-value = 0.002) (Table 3).

CS rate was 32%. Subjects born by CS had greater proportions of increased indicators of adiposity than subjects born by vaginal delivery (p<0.05). Individuals born from mothers with lower schooling levels (0–4 and 5–8 years) also had increased adiposity, except when measured by WHR, men had higher proportions of increased WC, WHtR and WHR, whilst the female gender was associated to increased skinfolds; birth weight ≥4000 g was associated with increased WC but not with other adiposity measures. Multi-parity (≥5) was associated with increased TSF, whilst maternal smoking during pregnancy and maternal age were not associated with increased adiposity (Table 4).

Subjects born by CS had a higher risk for increased adiposity, which persisted even after adjustment for birth variables, with small and non-significant changes. In the adjusted model, babies born by cesarean delivery had an increased risk of 22% for WC, of 25% for WHtR, of 45% for WHR, and of 36% for SSF, and also an increased risk of 43% for peripheral obesity measured by TSF. Models using inverse-probability weighting did not change the estimates appreciably (Table 5). All Poisson models fitted the data well (goodness of fit chi-squared tests were non-significant).

Discussion

The main finding of this study was those individuals born by CS have a higher risk for increased adiposity in adulthood. To our

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### Table 3. Type of delivery according to birth variables, 1978/79 Ribeirão Preto birth cohort.

| Variables                           | Vaginal (n = 1,402)* | Cesarean (n = 661)* | P-value** |
|-------------------------------------|----------------------|---------------------|-----------|
|                                     | n               | %      | n               | %      |          |
| Maternal schooling (years)          |                    |        |                |        | <0.001   |
| ≥12                                 | 118              | 54.9   | 97              | 45.1   |          |
| 9–11                                | 207              | 62.5   | 124             | 37.5   |          |
| 5–8                                 | 373              | 67.0   | 184             | 33.0   |          |
| 0–4                                 | 673              | 73.2   | 247             | 26.8   |          |
| Sex                                 |                    |        |                |        | 0.985    |
| Male                                | 676              | 67.9   | 319             | 32.1   |          |
| Female                              | 726              | 68.0   | 342             | 32.0   |          |
| Birth weight (grams)                |                    |        |                |        | 0.002    |
| <2500                               | 88               | 68.8   | 40              | 32.2   |          |
| 2500–3000                           | 310              | 74.9   | 104             | 25.1   |          |
| 3000–3500                           | 571              | 67.3   | 277             | 32.7   |          |
| 3500–4000                           | 346              | 66.0   | 178             | 34.0   |          |
| ≥4000                               | 87               | 58.4   | 62              | 41.6   |          |
| Maternal smoking during pregnancy (cigarettes/day) |        |        |                |        | 0.762    |
| Non-smoker                          | 1,018            | 67.5   | 491             | 32.5   |          |
| 1–10                                | 220              | 69.2   | 98              | 30.8   |          |
| >10                                 | 120              | 69.4   | 53              | 30.6   |          |
| Parity                              |                    |        |                |        | 0.300    |
| 1                                   | 511              | 66.3   | 260             | 33.7   |          |
| 2–4                                 | 739              | 68.2   | 344             | 31.8   |          |
| ≥5                                  | 122              | 72.2   | 47              | 27.8   |          |
| Maternal age (years)                |                    |        |                |        | <0.001   |
| <20                                 | 124              | 81.6   | 28              | 18.4   |          |
| 20–34                               | 1,169            | 67.9   | 553             | 32.1   |          |
| ≥35                                 | 96               | 56.5   | 74              | 43.5   |          |

*Totals may not add up to 2063 because of missing values.

**P-value refers to the chi-squared test.

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knowledge, this is the first population-based study to show that individuals born by CS had a higher risk for increased central and peripheral adiposity in young adulthood than those born by vaginal delivery. This finding is in accordance with a previous study demonstrating that young adults born by CS had an increased risk of obesity assessed by BMI [7]. Other studies have shown the association between CS and obesity assessed by BMI [6,7,8,9,10]; however, this is the first

| Birth variables | Total | Waist Circumference (WC)* | Waist-Height Ratio (WHtR)* | Waist-Hip Ratio (WHR)* | Tricipital Skinfold (TSF)** | Subscapular Skinfold (SSF)** |
|-----------------|--|--------------------------|---------------------------|------------------------|-----------------------------|-------------------------------|
| Type of delivery | - | - | - | - | - | - |
| Vaginal | 1,402 (68.0) | 419 (29.9) | 434 (31.0) | 190 (13.6) | 127 (9.1) | 118 (8.4) |
| Cesarean | 661 (32.0) | 243 (36.8) | 247 (37.6) | 124 (18.8) | 80 (12.1) | 76 (11.5) |
| P-value | 0.002 | 0.003 | 0.002 | 0.032 | 0.025 |
| Maternal schooling (years) | - | - | - | - | - | - |
| ≥12 | 215 (10.6) | 55 (25.6) | 51 (23.7) | 26 (12.1) | 12 (5.6) | 13 (6.0) |
| 9–11 | 331 (16.0) | 99 (29.9) | 105 (31.7) | 46 (13.9) | 26 (7.8) | 23 (7.0) |
| 5–8 | 557 (27.0) | 201 (36.1) | 195 (35.1) | 93 (16.7) | 78 (14.0) | 65 (11.7) |
| 0–4 | 920 (44.6) | 296 (32.2) | 318 (34.7) | 144 (15.7) | 89 (9.7) | 88 (9.6) |
| Not known | 40 (2.0) | - | - | - | - | - |
| P-value | 0.028 | 0.012 | 0.363 | 0.001 | 0.034 |
| Sex | - | - | - | - | - | - |
| Male | 995 (48.2) | 360 (36.2) | 407 (41.0) | 215 (21.6) | 37 (3.7) | 76 (7.7) |
| Female | 1,068 (51.8) | 302 (28.3) | 274 (25.7) | 99 (9.3) | 170 (15.9) | 118 (11.2) |
| P-value | <0.001 | <0.001 | <0.001 | <0.001 | 0.008 |
| Birth weight | - | - | - | - | - | - |
| <2500 | 128 (6.2) | 40 (31.2) | 46 (35.9) | 16 (12.5) | 15 (11.7) | 12 (9.4) |
| 2500–3000 | 414 (20.1) | 114 (27.6) | 121 (29.4) | 55 (13.3) | 38 (9.2) | 35 (8.5) |
| 3000–3500 | 848 (41.1) | 264 (31.1) | 275 (32.5) | 129 (15.2) | 92 (10.8) | 83 (9.8) |
| 3500–4000 | 524 (25.4) | 181 (34.5) | 177 (33.8) | 90 (17.2) | 48 (9.2) | 48 (9.2) |
| ≥4000 | 149 (7.2) | 63 (42.6) | 62 (41.9) | 24 (16.2) | 14 (9.5) | 16 (10.8) |
| P-value | 0.011 | 0.079 | 0.470 | 0.762 | 0.918 |
| Parity | - | - | - | - | - | - |
| 2–4 | 1,083 (52.5) | 339 (31.3) | 353 (32.7) | 159 (14.7) | 94 (8.7) | 94 (8.7) |
| 1 | 771 (37.4) | 255 (33.1) | 253 (32.9) | 118 (15.3) | 89 (11.5) | 78 (10.1) |
| ≥5 | 169 (8.2) | 58 (34.3) | 63 (37.3) | 33 (19.5) | 23 (13.6) | 18 (10.6) |
| Not known | 40 (1.9) | - | - | - | - | - |
| P-value | 0.062 | 0.497 | 0.271 | 0.041 | 0.487 |
| Maternal age (years) | - | - | - | - | - | - |
| <20 | 152 (7.4) | 50 (32.9) | 57 (37.5) | 26 (17.1) | 23 (15.1) | 17 (11.3) |
| 20–34 | 1722 (83.5) | 545 (31.7) | 558 (32.4) | 252 (14.6) | 161 (9.4) | 154 (8.9) |
| ≥35 | 170 (8.2) | 61 (35.9) | 63 (37.1) | 32 (18.8) | 20 (11.8) | 19 (11.2) |
| Not known | 19 (0.9) | - | - | - | - | - |
| P-value | 0.517 | 0.234 | 0.274 | 0.054 | 0.427 |

*Increased WC: ≥90 cm for men and ≥80 cm for women; 
†Increased WHtR: ≥0.5; 
‡Increased WHR: ≥0.90 for men and ≥0.85 for women; 
§Increased TSF and SSF: >90th percentile of the study population, Ribeirão Preto, 2002/04. 
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study to show the association between CS and other adiposity indicators apart from BMI in young adulthood. Utz et al. (2008) [6] showed that adolescents aged 15 to 19 years born by CS had a 1.4 higher risk of overweight when compared to those born by vaginal delivery. Zhou et al. (2011) [9] found a 5.23 higher risk of obesity in children aged 3 to 6 years born by CS. Rooney et al. (2011) [8] found a 2.5 higher risk at 4–5 years and Huh et al. (2012) [11], considering such studies and others, taking into account adjustment for confounding. On the other side, the meta-analysis by Li et al. [42], in a study of three Brazilian cohorts evaluated at the ages of 4, 11, 15 and 23 years, observed an association between CS and indicators of adiposity in children and adults seems to be consistent both for central markers such as WC, WHtR, WHR and SSF, and for total (BMI) and peripheral (TSF) adiposity; in addition, this association was maintained when adjusted for confounders also considered to be risk factors for adiposity.

However, there are studies in the literature that did not detect an association between CS and obesity in childhood as Ajlslev et al. [33]. Barros et al. [34], in a study of three Brazilian cohorts evaluated at the ages of 4, 11, 15 and 23 years, observed an association only for boys at 4 years of age. Rooney et al. [8] observed this association in children but not in adolescents aged 9 to 14 years or in young adults aged 18 to 20 years after adjustment for confounding. On the other side, the meta-analysis by Li et al. [11], considering such studies and others, taking into account unadjusted and adjusted estimates of the association between CS and overweight and obesity in offspring, indicated CS as a moderate early risk factor for late weight excess (33%) especially in adolescents (24%) and adults (50%). The present study adds this possibility also for central and peripheral adiposity.

The rationale for the association between CS and later obesity is based on the role of gut microbiota. Upon vaginal delivery, the newborn has contact with bacteria from the birth canal first and the infant gut begins to be colonized by an array of bacteria. Infants born by CS lack this contact, which is crucial for the adequate development of the infant’s gut microbiota as it is known that its role is related to enhanced availability of nutrients through extraction of calories from luminal oligosaccharides and is also related to improved nutrient uptake by the modulation of absorptive capacity of the intestinal epithelium [35]. Gut microbiota may also promote weight gain and fat accumulation through a condition of low-grade inflammation [18,19].

Other possible explanation for the association between CS and increased adiposity in adulthood is that absence of the hormonal milieu of labor results in altered metabolic trajectory in the offspring [36].

In a previous analysis of the association between CS and obesity measured by BMI [7] it was stated that a limitation of this study is the lack of data regarding breastfeeding during infancy, as breastfeeding is an important source of bacteria for infant gut development and maturation [37]. CS is seen as a risk factor for early weaning [38,39,40], but at the time of the present study, type of delivery was found to have little effect on breastfeeding rates among 6-month-old infants in another Brazilian study [41]. If this were the case in Ribeirão Preto, then the estimates of the present study would have changed little had we included breastfeeding data. Breastfeeding rates are associated with socioeconomic status [42], and the effect of the latter variable on the estimates of adiposity according to type of delivery was controlled for in this study.

The other limitation is the lack of information regarding maternal BMI, which is known to be a risk factor for offspring obesity. This limitation is partially overcome by adjustment for maternal schooling at the time of delivery, because around the time of this study, in 1975, obesity rates in Brazilian women were higher among the wealthy social groups [43]. Alternatively, since CS rate was more incident among mothers of higher schooling, the association between CS and adiposity could be explained by maternal BMI and not by CS, because BMI is an unmeasured confounder. However, this explanation seems unlikely because it is not plausible that BMI could totally explain the association between CS and adiposity.

In a previous analysis it was shown that there was a lower participation of young adults from families with less qualified occupations, of mothers with low schooling levels and smokers during pregnancy [23]. This selective attrition may have biased the association between CS and adiposity. CS was less common in these less privileged population groups [44], maybe leading to a super-estimation of the association. However, adjustment for such variables did not change the associations; in fact, although significant, the differences at birth and in the follow-up were small [23]. Furthermore, CS rates were similar between individuals not included [29.7%] and those included in the analysis at adult age [32%], after exclusion of those who died up to 20 years

### Table 5. Association of type of delivery with indicators of increased adiposity in young adults.

| Indicators of increased adiposity | Waist Circumference (WC)* | Waist-Height Ratio (WHR) | Waist-Hip Ratio (WHR)* | Tricipital Skinfold (TSF) | Subscapular Skinfold (SSF) |
|----------------------------------|---------------------------|--------------------------|------------------------|--------------------------|--------------------------|
| Non-adjusted model              | 1.23 (1.08–1.40)          | 1.21 (1.07–1.37)         | 1.39 (1.13–1.71)       | 1.34 (1.03–1.74)         | 1.37 (1.04–1.80)         |
| Non-adjusted model using inverse-probability weighting | 1.21 (1.06–1.38)          | 1.20 (1.05–1.36)         | 1.40 (1.13–1.72)       | 1.36 (1.04–1.78)         | 1.41 (1.06–1.87)         |
| Model adjusted for birth variables” | 1.22 (1.07–1.39)          | 1.25 (1.10–1.42)         | 1.45 (1.18–1.79)       | 1.36 (1.04–1.78)         | 1.43 (1.08–1.91)         |
| Model adjusted for birth variables using inverse-probability weighting” | 1.20 (1.05–1.37)          | 1.22 (1.08–1.39)         | 1.42 (1.15-1.76)       | 1.38 (1.05–1.82)         | 1.44 (1.08–1.92)         |

*Increased WC: ≥90 cm for men and ≥80 cm for women;  
1RR = Incidence rate ratio; 95%CI = 95% Confidence interval.  
2Increased WHR: >0.5;  
3Increased WHtR: ≥0.90;  
4Increased TSF and SSF: ≥90th percentile of the study population;  
5Birth weight; type of delivery; sex; maternal schooling; maternal smoking during pregnancy; parity; maternal age and gestational age as a continuous variable.  
Ribeirão Preto, 2002/04.  
doi:10.1371/journal.pone.0066827.t005
of age [22]. We implemented the inverse-probability weighting technique that compensates for losses to follow-up. Results did not change appreciably. Thus, it suggests that selective attrition did not bias our conclusions. We also do not have information on CS indication. However, CS rates were higher among the better-off, who had more prenatal visits, who delivered in private hospitals and during week days [44]. These findings suggest that non-clinical factors were more important in the decision to carry out a CS than medical factors, as stated by others around the time of this study [45]. Since we do not have data on CS with and without labor, we were not able to test if the association between CS and increased adiposity in adulthood is driven by emergency or elective CS, or both.

The strengths of the present study are as follows: the narrow age group (from 23 to 25 years of age) is a particular strength because it eliminates the confounding effect of age and many other age-dependent covariates that may have affected the analysis. Confounding variables from birth were adjusted for, particularly those related to socioeconomic status. This adjustment may have possibly minimized the effect of unmeasured confounding factors such as early weaning and maternal obesity, both more prevalent among those born by vaginal delivery. The association of CS with adiposity was consistently observed for all indicators and was associated with breastfeeding in the first hour of life. Revised: [Epub ahead of print].

In conclusion, subjects born by CS had a higher risk for overweight and obesity among preschool children. Am J Epidemiol 95: 465–70.

29. World Health Organization (WHO) (2008) Waist Circumference and waist hip ratio. Report of a WHO Expert Consultation. Geneva; dezembro, 8–11.

31. Zou G (2004) A Modified Poisson Regression Approach to Prospective Studies with Binary Data. Am J Epidemiol 159(7):702–6.

32. Adlerberth I, Lindberg E, Aberg N, Hesselmar B, Saalman R, et al. (2006) Reduced enterobacterial and increased staphylococcal colonization of the infantile bowel: an effect of hygienic lifestyle? Pediatr Res 59: 96–101

33. Ajslev TA, Andersen CS, Gamborg M, Sorensen TL, Jess T (2011) Childhood overweight after establishment of the gut microbiota: the role of delivery mode, pre-pregnancy weight and early administration of antibiotics. Int J Obesity. 35: 522–9.

34. Barros FC, Matijasevic A, Hallal PC, Horta BL, Barros AJ, et al. (2012) Cesarean section and risk of obesity in childhood, adolescence, and early adulthood: evidence from 3 Brazilian birth cohorts. Am J Clin Nutr 95: 465–70.

35. Barros FC, Matijasevic A, Hallal PC, Horta BL, Barros AJ, et al. (2012) Cesarean delivery is associated with an increased risk of obesity in adulthood in a Brazilian birth cohort study. Am J Clin Nutr 95: 1344–7.

36. Hyde MJ, Mostyn A, Modi N, Kemp PR (2012) The health implications of birth weight and pre-pregnancy weight and early administration of antibiotics. Int J Obesity 35: 522–9.

37. Gueimonde M, Laitinen K, Salminen S, Isolauri E (2007) Breast milk: a source of bifidobacteria for infant gut development and maturation? Neonatology 92:64–6.

38. Vieira TO, Vieira GO, Giugliani ER, Mendes CM, Martins WC, et al. (2010) Determinants of breastfeeding initiation within the first hour of life in a Brazilian population: cross-sectional study. BMC Public Health 10:769.

39. Boccolini CS, de Carvalho ML, de Oliveira MI, Vasconcellos AG (2011) Factors associated with breastfeeding in the first hour of life. Rev Sauda Publica 45:69–78.

40. Barros FC, Matijasevic A, Hallal PC, Horta BL, Barros AJ, et al. (2012) Cesarean section and risk of obesity in childhood, adolescence, and early adulthood: evidence from 3 Brazilian birth cohorts. Am J Clin Nutr 95: 465–70.

41. Zou G (2004) A Modified Poisson Regression Approach to Prospective Studies with Binary Data. Am J Epidemiol 159(7):702–6.

42. Seiki T, Hori Y, Ohta T, Jernigan BL, Hardin JO (2006) Early enteric flora and the risk of childhood asthma. J Allergy Clin Immunol 117:148–54.

43. Seidell JC, Ohlsson A, Dallman MF, Sjöqvist F, Cederholm T (2000) Fat mass in infancy is related to normal and impaired glucose tolerance in adulthood. J Clin Endocrinol Metab 85: 4507–14.

44. Seidell JC, Ohlsson A, Dallman MF, Sjöqvist F, Cederholm T (2000) Fat mass in infancy is related to normal and impaired glucose tolerance in adulthood. J Clin Endocrinol Metab 85: 4507–14.

45. Seidell JC, Ohlsson A, Dallman MF, Sjöqvist F, Cederholm T (2000) Fat mass in infancy is related to normal and impaired glucose tolerance in adulthood. J Clin Endocrinol Metab 85: 4507–14.

46. Seidell JC, Ohlsson A, Dallman MF, Sjöqvist F, Cederholm T (2000) Fat mass in infancy is related to normal and impaired glucose tolerance in adulthood. J Clin Endocrinol Metab 85: 4507–14.

47. Seidell JC, Ohlsson A, Dallman MF, Sjöqvist F, Cederholm T (2000) Fat mass in infancy is related to normal and impaired glucose tolerance in adulthood. J Clin Endocrinol Metab 85: 4507–14.

48. Seidell JC, Ohlsson A, Dallman MF, Sjöqvist F, Cederholm T (2000) Fat mass in infancy is related to normal and impaired glucose tolerance in adulthood. J Clin Endocrinol Metab 85: 4507–14.

49. Seidell JC, Ohlsson A, Dallman MF, Sjöqvist F, Cederholm T (2000) Fat mass in infancy is related to normal and impaired glucose tolerance in adulthood. J Clin Endocrinol Metab 85: 4507–14.

50. Seidell JC, Ohlsson A, Dallman MF, Sjöqvist F, Cederholm T (2000) Fat mass in infancy is related to normal and impaired glucose tolerance in adulthood. J Clin Endocrinol Metab 85: 4507–14.

51. Seidell JC, Ohlsson A, Dallman MF, Sjöqvist F, Cederholm T (2000) Fat mass in infancy is related to normal and impaired glucose tolerance in adulthood. J Clin Endocrinol Metab 85: 4507–14.
40. Prior E, Santhakumaran S, Gale C, Philipps LH, Modi N, et al. (2012) Breastfeeding after cesarean delivery: a systematic review and meta-analysis of world literature. The American journal of clinical nutrition. [Meta-Analysis Review]. May; 95(5):1113–35.

41. Victora CG, Huttly SR, Barros FC, Vaughan JP. (1990) Caesarean section and duration of breast feeding among Brazilians. Arch Dis Child 65: 632–4.

42. Marques NM, Lira PL, Lima MC, da Silva NL, Filho MB, et al. (2001) Breastfeeding and early weaning practices in northeast Brazil: a longitudinal study. Pediatrics 108: E66.

43. Monteiro CA, Conde WL, Popkin BM. (2007) Income-specific trends in obesity in Brazil: 1975–2003. Am J Public Health 97:1808–12.

44. Gomes UA, Silva AA, Bettiol H, Barbieri MA. (1999) Risk factors for the increasing caesarean section rate in Southeast Brazil: a comparison of two birth cohorts, 1978–1979 and 1994. Int J Epidemiol 28: 687–94.

45. Janowitz B, Covington DL, Higgins JE, Moreno LF, Nakamura MS, et al. (1982) Cesarean delivery in selected Latin American hospitals. Public Health. Jul. 96(4):191–201.