

Cesarean birth is not associated with early childhood body mass index

L. G. Smithers, MPH PhD¹, B. W. Mol, MD PhD^{2,3}, L. Jamieson, BDS PhD⁴ and J. W. Lynch, MPH PhD^{1,5}

¹School of Public Health, University of Adelaide, Adelaide, Australia; ²The Robinson Institute, School of Paediatrics and Reproductive Health, University of Adelaide, Adelaide, Australia; ³The South Australian Health and Medical Research Institute, Adelaide, Australia; ⁴Indigenous Oral Health Unit, University of Adelaide, Adelaide, Australia; ⁵School of Social and Community Medicine, University of Bristol, Bristol, England, UK

Address for correspondence: LG Smithers, MPH PhD, School of Public Health, Mail Drop DX 650 550, University of Adelaide, Adelaide, SA 5005, Australia.
E-mail: lisa.smithers@adelaide.edu.au

Received 17 November 2015; revised 15 June 2016; accepted 22 August 2016

Summary

Cesarean birth leads to a markedly different microbiome compared to vaginal birth, and the microbiome has been implicated in childhood obesity. Among mothers who had a previous cesarean, we compared anthropometry of 3- to 6-year-old children who were subsequently born by cesarean section versus vaginal birth. This large population-based study involved linking de-identified administrative perinatal and anthropometric data. Children's weight and height were collected at community-based clinics and converted to age- and sex-adjusted z-scores of height-for-age (HFAz), weight-for-age (WFAz) and BMI-for-age (BMIz). The average treatment effect (ATE) of cesarean versus vaginal birth was calculated from augmented inverse probability weighted analyses accounting for a wide range of confounding variables. There was little evidence of an effect of cesarean birth on HFAz (ATE = 0.26 95%CI -0.35, 0.87, $n = 3993$), WFAz (ATE = 0.35, 95%CI -0.19, 0.89, $n = 4817$) or BMIz (ATE = 0.11, 95%CI -0.25, 0.46, $n = 3909$). Cesarean section was not associated with anthropometry among children aged 3–6 years.

Keywords: Anthropometry, body mass index, cesarean section, vaginal birth.

Abbreviations: HFAz, height for age z-score; WFAz, weight for age z-score; BMIz, body mass index for age z-score; ATE, average treatment effect; CI, confidence interval; BMI, body mass index; SA, South Australia; aipw, augmented inverse probability of treatment weighting

What is already known about this subject?

- Cesarean section has been linked to higher BMI of offspring
- The microbiome has been implicated in the link between cesarean birth and childhood obesity

What this study adds?

- Among mothers whose previous child was born by cesarean, current cesarean compared to vaginal birth was not associated with BMI in their child at age 3–6 years

The early life environment is thought to influence the development of obesity, with recent attention focusing on the microbiome. Inoculation of the newborn gut by vaginal and gastrointestinal microorganisms occurs during vaginal but not cesarean births, offering a potential mechanism linking cesareans with obesity (1).

A recent systematic review suggested that cesarean was associated with 0.44 higher BMI (95% CI 0.17, 0.72) but was unadjusted for confounding (2). Addressing confounding is crucial because indications for cesarean are associated with childhood obesity, e.g. larger fetal size leads to cesarean birth and to higher childhood BMI. Usually cesareans are conducted for medical reasons; however, women who previously had a cesarean are unique, as they may opt for an 'elective' cesarean or a vaginal birth for subsequent children. Comparing cesarean with vaginal births among these women may reduce confounding by indication. In a large population-based study, we examined anthropometry of children whose mothers previously had a cesarean and subsequently elected for either vaginal or elective cesarean birth.

This study involves linking government administrative datasets. Approval was granted by South Australian

(SA) Department for Health and Ageing (DHA, HREC/15/SAH/61) and University of Adelaide (H-185-2011) ethics committees.

Exposure

Birth information was obtained from the Perinatal Statistics Collection and included all births in SA, 1999–2005. Information is collected by midwives and reported to the SA DHA. Women with vertex presentation, who previously had a cesarean and then had an elective cesarean or a spontaneous vaginal birth were eligible. All other births, including women who intended vaginal delivery but then needed emergency Cesarean section, were excluded. Exposures were chosen to reduce confounding by indication.

Outcome

Anthropometrical data (2003–2012) was provided by the Women's and Children's Hospital Network, SA DHA, from community-based well-child health checks. Children aged 3–6 years were included because this age group represents peak attendance for a preschool health check. Height (shoes removed) and weight (light clothing) were collected by nurses. Children's BMI was converted to age- and sex-specific BMI z-scores (BMIz) using the World Health Organization's Child Growth Standards (3,4). Height-for-age z-scores (HFAz) and weight-for-age z-scores (WFAz) were also calculated. Z-scores were generated by the *zanthro* programme in STATA (13.0, TX, USA).

Confounding

The following potential confounders were identified *a priori*: maternal age (years), antenatal care (hospital, obstetrician, general practitioner, other), antenatal visits (≤ 7 , 8–12, ≥ 13), medical conditions during pregnancy (asthma as a marker of chronic disease, diabetes, hypertension), smoking in pregnancy (yes/no), gestational age, birthweight for gestational age z-scores (5), mother had a partner (yes/no), maternal ethnicity (Caucasian, Aboriginal or Torres Strait Islander, Asian, Other), maternal occupation (6), neighbourhood-level indicators of socioeconomic disadvantage (7) and remote residence (8).

Statistical analyses

The distribution of confounders across the exposure groups were compared by *t*-tests and χ^2 tests. Associations were analysed using augmented inverse probability of treatment weighting (aipw) (9,10). This method generates the probability of having a

cesarean given an individual's confounders and weights a regression by this probability to calculate the average treatment effect (ATE). Weighting helps to better balance confounders. The ATE can be interpreted as the average effect for the population of cesarean compared to vaginal birth on anthropometry. Sensitivity analyses excluding women with diabetes or hypertension were undertaken because of associations with planned cesareans and childhood anthropometry.

Of 16375 women who previously had a cesarean, 61% birthed by elective cesarean (9925/16375) and 11% had spontaneous vaginal birth (1842/16375). The remaining 28% had emergency cesarean or instrument-assisted deliveries (4608/16375) and were excluded. Successful linkage to anthropometrical data included 4099 children (3909 with BMIz measurements, 4817 WFAz and 3993 HFAz).

Sample characteristics (Table 1) show that although the exposure groups intended to minimize confounding by indication, imbalances remained. For example, women who had cesarean births were older and had higher proportions of diabetes and antenatal care by an obstetrician than those who had vaginal births.

In unadjusted analyses, HFAz was similar but BMIz and WFAz were higher among children born by cesarean compared to vaginal births (Table 2). The *apiw* analysis suggested no differences in BMIz, WFAz and HFAz according to mode of delivery. Sensitivity analyses excluding women with diabetes and hypertension were consistent with these main findings (BMIz ATE=0.05, 95%CI –0.46, 0.54, $p=0.856$, $n=3180$; WFAz ATE=0.48, 95%CI –0.32, 1.29, $p=0.240$, $n=3909$; HFAz ATE=0.38 95%CI –0.38, 1.15, $p=0.329$, $n=3251$).

In our analyses, we found little evidence of an association between cesarean birth and the BMI of 3 to 6-year-old children. Previously, cesarean birth has been associated with 18% higher odds of obesity (95%CI 1.09, 1.27) (11), although there is evidence of publication bias (11). Other large population-based studies have reported null (12) and positive (13) associations between non-medically indicated cesareans and adiposity. It is difficult to judge whether differing analytical approaches, samples or definitions of cesareans (e.g. non-medically indicated nullipara, low-risk multiparous) have contributed to the mixed findings. Whether an association is manifested at younger or older ages is conflicting (14,15), and our dataset has too few children at older ages to examine this issue.

We attempted to reduce confounding by accounting for many variables associated with both cesarean and obesity. This was important because baseline

Table 1 Characteristics of the study sample according to vaginal birth or elective cesarean among women who had a cesarean section in a previous pregnancy and children who have one or more of the anthropometric outcomes measured

	Vaginal birth <i>n</i> = 792	Elective cesarean <i>n</i> = 4099	Mean difference (95% CI)	<i>P</i> value*
	Mean ± SD or <i>n</i> (%)	Mean ± SD or <i>n</i> (%)		
Mothers age (y)	30.4 ± 4.8	31.8 ± 4.7	-1.4 (-1.7, -1.0)	<0.001
Type of antenatal care [†]			—	<0.001
-Hospital-based	374 (47%)	1380 (34%)		
-Obstetrician	238 (30%)	1905 (47%)		
-GP	156 (20%)	800 (20%)		
-Other (e.g. midwife, none, home birth, shared care)	24 (3%)	14 (<1%)		
Antenatal visits			—	0.066
-≤7	84 (11%)	332 (8%)		
-8–12	574 (72%)	3071 (75%)		
-≥13	134 (17%)	696 (17%)		
Maternal asthma	44 (6%)	270 (7%)	—	0.278
Diabetes in pregnancy	27 (3%)	283 (7%)	—	<0.001
High BP in pregnancy	53 (7%)	309 (8%)	—	0.627
Smoked, second half pregnancy	144 (18%)	610 (15%)	—	0.019
Mothers ethnicity			—	0.104
-Caucasian	745 (94%)	3888 (95%)		
-ATSI and other	16 (2%)	109 (3%)		
-Asian	31 (4%)	102 (2%)		
IRSD	972 ± 72	979 ± 71	-8 (-13, -2)	0.006
ARIA [†]			—	0.179
-City	542 (68%)	2650 (65%)		
-Inner regional	90 (11%)	517 (13%)		
-Outer regional	131 (17%)	720 (18%)		
-Remote + very remote	29 (4%)	212 (5%)		
Mother had partner	728 (92%)	3826 (93%)	—	0.148
Maternal occupation ^{†^}			—	
-Managers	38 (5%)	307 (8%)		0.003
-Professionals	68 (9%)	426 (10%)		
-Para professionals	52 (7%)	253 (6%)		
-Tradespersons	25 (3%)	140 (3%)		
-Clerks and Salespersons	208 (26%)	1057 (26%)		
-Machine/labourers [†]	37 (5%)	151 (4%)		
-Home duties	317 (40%)	1634 (40%)		
-Students, pensioners, other and unemployed [†]	47 (6%)	131 (3%)		
Infant characteristics				
GA at birth (week)	39.0 ± 1.9	38.5 ± 1.0	0.5 (0.4, 0.6)	<0.001
BWGA z-score	-0.06 ± 1.0	0.24 ± 1.02	-0.30 (-0.38, -0.23)	<0.001
Male	367 (46%)	2150 (52%)	—	0.002

Abbreviations: ARIA, Australian remoteness Index; ATSI, identifies as Aboriginal and/or Torres Strait Islander; BWGAz, birth weight for gestational age z-scores; GA, gestational age at birth; IRSD, index of relative disadvantage. **P*-values compared the distribution of potential confounders according to cesarean versus vaginal birth and were obtained from a *t*-test for continuous variables or a χ^2 test for categorical variables. [†]Categories were collapsed to protect against small numbers. [^]Categorized according to the Australia and New Zealand Classification of Occupations.

Table 2 Associations between elective cesarean compared to vaginal birth on z-scores of weight-for-age (WFAz), height-for-age (HFAz) and BMI for age (BMIZ)

	N cesarean/total (%)	Unadjusted		aipw analysis	
		Mean difference (95% CI)	P [*]	Average treatment effect (95% CI)	p
BMIZ	3330/3909 (85%)	-0.23 (-0.32, 0.14)	<0.001	0.12 (-0.23, 0.46)	0.518
WFAz	4037/4817 (84%)	-0.18 (-0.26, -0.11)	<0.001	0.37 (-0.20, 0.93)	0.203
HFAz	3401/3993 (85%)	-0.06 (-0.14, 0.03)	0.208	0.27 (-0.35, 0.89)	0.399

characteristics demonstrated imbalances. A potential limitation is that confounding by women with high risk pregnancies (e.g. type 1 diabetes) may remain, as these women often plan cesarean births and their children may be at higher risks of obesity. However, excluding women with diabetes or hypertension supported the main analyses. Another limitation is we were unable to adjust for other known confounders including maternal pre-pregnancy BMI (16), pregnancy weight gain or physical activity, as these data were not available. We hypothesize that adjustment for these confounders is likely to attenuate the association between cesarean and BMI even further.

A critique of this work may be that it is not 'representative' of typical cesareans, but representativeness was not our goal. Our intent was to examine whether cesarean section causes obesity by attempting to address both confounding and confounding by indication with more rigorous epidemiological methods than past studies. There is no doubt that the gut microbiome of children differs between cesarean and vaginal births; however, this study casts doubt over cesarean-induced microbiome differences on anthropometry of young children.

Conflict of interest statement

Professor Mol is a consultant for ObsEva. Payments go his institute. The authors have no conflicts of interest to declare.

Acknowledgements

LGS, BWM and JL conceived the study. LGS analysed the data. All authors were involved in writing the paper and all approval the final submitted version.

We thank the Data Custodians and the South Australian government Department for Health and Ageing for providing de-identified datasets for analysis. Thanks to Dr Angela Gialamas and Mr Daniel Scalzi for assistance with management of the datasets.

Financial support for this study was supported by a Partnership grant (#1056888) from the National

Health and Medical Research Council of Australia (NHMRC). Professor Lynch is the recipient of an NHMRC Australia Fellowship (#70120). None of the funding bodies had any role in the study design, collection, analysis, interpretation of data, writing and decision to submit the article

References

1. Prince AL, Chu DM, Seferovic MD, Antony KM, Ma J, Aagaard KM. The perinatal microbiome and pregnancy: moving beyond the vaginal microbiome. *Cold Spring Harb Perspect Med* 2015; 5.
2. 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.
3. World Health Organization (WHO). *WHO Child Growth Standards: Length/Height-for-age, Weight-for-Age, Weight-for-Length, Weight-for-Height and Body Mass Index-for-Age: Methods and Development*. WHO: Geneva, 2006.
4. De Onis M. World Health Organization. In: *WHO Child Growth Standards: Length/Height-for-Age, Weight-for-Age, Weight-for-Length, Weight-for-Height and Body Mass Index-for-age: Methods and Development*. WHO: Geneva, 2006.
5. Dobbins TA, Sullivan EA, Roberts CL, Simpson JM. Australian national birthweight percentiles by sex and gestational age, 1998–2007. *Med J Aust* 2012; 197: 291–294.
6. Australian Bureau of Statistics. *Australian Standard Classification of Occupations (ASCO) Statistical Classification*. Commonwealth of Australia: Canberra, 1986.
7. Australian Bureau of Statistics. *Information Paper: An Introduction to Socio-Economic Indexes for Areas (SEIFA), 2006*. Commonwealth of Australia: Canberra, 2008.
8. Australian Institute of Health and Welfare. *Rural, Regional and Remote Health: A Guide to Remoteness Classifications*. Commonwealth of Australia: Canberra, 2004.
9. Funk MJ, Westreich D, Wiesen C, Sturmer T, Brookhart MA, Davidian M. Doubly robust estimation of causal effects. *Am J Epidemiol* 2011; 173: 761–767.
10. Glynn AN, Quinn KM. An introduction to the augmented inverse propensity weighted estimator. *Polit Anal* 2010; 18: 36–56.

11. Li HT, Zhou YB, Liu JM. The impact of cesarean section on offspring overweight and obesity: a systematic review and meta-analysis. *Int J Obes (Lond)* 2013; 37: 893–899.
12. Ajslev TA, Andersen CS, Gamborg M, Sorensen TI, 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: 522–529.
13. Li H, Ye R, Pei L, Ren A, Zheng X, Liu J. Caesarean delivery, caesarean delivery on maternal request and childhood overweight: a Chinese birth cohort study of 181 380 children. *Pediatr Obes* 2013; 9: 10–16.
14. Robson SJ, Vally H, Abdel-Latif ME, Yu M, Westrupp E. Childhood health and developmental outcomes after cesarean birth in an Australian cohort. *Pediatrics* 2015; 136: e1285–e1293.
15. Blustein J, Attina T, Liu M, et al. Association of caesarean delivery with child adiposity from age 6 weeks to 15 years. *Int J Obes (Lond)* 2013; 37: 900–906.
16. Diesel JC, Eckhardt CL, Day NL, Brooks MM, Arslanian SA, Bodnar LM. Is gestational weight gain associated with offspring obesity at 36 months? *Pediatr Obes* 2015; 10: 305–310.