Relationship between Obstetric Mode of Delivery and Risk of Overweight/Obesity in 1- to 4-Year-Old Children

Peiying Huang^{a, b} Xiulin Shi^{a, b} Fangsen Xiao^{a, b} Liying Wang^{a, b} Wei Liu^{a, b}
Jinyang Zeng^{a, b} Mingzhu Lin^{a, b} Xuejun Li^{a, b}

^aDepartment of Endocrinology and Diabetes, The First Affiliated Hospital of Xiamen University, Xiamen, PR China;

^bXiamen Diabetes Institute, Xiamen, PR China

Keywords

Childhood obesity · Mode of delivery · Z-score

Abstract

Introduction: Childhood obesity is an important public health problem, which may lead to increased risk of obesity in adulthood. The relationship between the incidence of obesity and the mode of delivery is not clear. Cesarean section (CS) may be one of the risk factors of obesity in children. We investigated the relationship between the mode of delivery of pregnant women and the risk of overweight/obesity in children of all ages from 1 to 4 years. **Methods:** Registered in the maternal and child registration system of Xiamen city, newborns born between January 2011 and December 2012 were followed up to 4 years old. **Results:** 9,964 cases were included in the study, of which 3,462 cases (34.7%) were cesarean deliveries. From 1 to 4 years of age, BMI Z-scores and the risk for overweight/obesity of children delivered by CS were higher than by the vagina. Longitudinal analysis of anthropometric outcomes assessed during study visits in 1- to 4-year-old offspring exposed to CS showed that after adjustment for kinds of effect factors, the changes in BMI Z-scores were 0.04 (95% CI: 0.01–0.09, $p = 0.003$), significantly higher than vaginal delivery, and the risk incidence of overweight/obesity by increased 8% in CS offspring; OR = 1.08 (1.01–1.21,

$p < 0.05$). **Conclusion:** The mode of cesarean delivery is related to the risk of overweight and obesity in children aged 1–4 years. When pregnant women choose cesarean delivery without medical indications, they should be concerned that their offspring may have a higher risk of obesity.

© 2022 The Author(s).

Published by S. Karger AG, Basel

Introduction

Obesity prevalence has substantially increased in China over the past decade, and the overall prevalence of general obesity in Chinese adults was 14.0% in 2013–2014 [1]. Childhood obesity is an important public health problem, and it increases the risk of obesity in adulthood [2] and leads to multiple serious obesity-related comorbidities [3]. The overweight prevalence was 8.4% and obesity was seen in 4.2% of children under 7 years of age in 9 cities of China in 2016 [4]. The rapidly increasing trend of childhood obesity has not been controlled, so the prevention of obesity in childhood is essential.

A complex lot of factors lead to childhood obesity, and risks of childhood obesity have been shown to be associ-

Peiying Huang and Xiulin Shi contributed equally to this work.

ated with perinatal factors [5], birth size [6], parental feeding style, antibiotic use [7], environmental chemicals, microbiota [8], and adverse life experiences [9]. Mode of delivery is one of the perinatal factors. Cesarean section (CS) of delivery is a key requisite to improve maternal and perinatal outcomes [10], the proportion of 10–15% of CS births is considered optimal [11], but both over- and underuse of cesarean sections can contribute to adverse outcomes [12]. The total CS rate in China is 46.5% 2007–2008, which is more than three times higher than the world warning line [13]. CS may be consistently associated with an increased risk of children's obesity, but studies have been inconclusive. The relationship between CS delivery and offspring being overweight or obese has been explored by several systematic reviews and meta-analyses, but these have been limited by small sample sizes [14, 15]. Many studies showed that at 5 years or older, the association between CS and the risk of overweight or obesity was not statistically significant [16, 17]. In China, a large-scale study reported that CS may be a risk factor for children's obesity [18], but it was a research on questionnaire, and others were cross-sectional studies [19]. This study aimed to investigate the relationship between CS delivery and overweight/obesity risk of children before 4 years, using a well-prospective longitudinal birth cohort with detailed clinical phenotyping of both mothers and their children.

Materials and Methods

We aimed to assess the association of obstetric mode of delivery and other maternal factors with BMI and the risk for overweight/obesity in offspring from infant to 4 years. This linked database cohort study used the Medical Birth Registry of Xiamen (MBRX), China. This study was approved by the Ethics Committee of the First Affiliated Hospital of Xiamen University (KYH2018-007) and carried out in accordance with the rules of the Declaration of Helsinki of 1975, revised in 2013. The MBRX was based on a compulsory notification of all live and stillbirths from 12 weeks' gestation, containing general information (age, education, weight in 12 weeks before pregnancy, date of the first visit, number of pregnancy/infants, and last menstrual period), medical history, clinical measurements (height, weight, blood pressure, fasting glucose, gestational weight gain, and gestational diabetes screening test), complications during pregnancy, and pregnancy outcomes.

All women in Xiamen are registered at their community health centers when they get pregnant and then referred to a secondary hospital or a tertiary hospital for healthcare from the 32nd gestational week till delivery in MBRX. Their children underwent health examinations at birth (<3 days after birth) and then annual examinations until 6 years of age, including information of newborns to preschool (date of birth, sex, gestational week of birth, weight, Apgar score, name of the child and his/her parents, family history of diseases, feeding modalities [exclusive breastfeeding, mixed breast and formula feeding, and exclusive formula feeding] during

the first 6 months, date of examination, weight, height, number of teeth, and blood pressure). Every woman and child were linked by individual record linkages to the Xiamen citizen health information system using the person-unique identification number assigned to each Xiamen citizen. Every child was also linked to his/her biological mother's maternal identification number.

Between January 2011 and December 2012, we performed a population-based cohort study, obtaining mother-child's information from MBRX. Large for gestational age (LGA) was defined as birth weight ≥ 90 th percentile and small for gestational age (SGA) was defined as birth weight ≤ 10 th percentile. All children underwent health examinations at birth (<3 days after birth), and annual examinations were performed. The data were available for 4 years. We measured each child's height as length before age 2 and as standing height to the nearest 0.1 cm after age 2 and measured a wall-mounted stadiometer. We measured body weight in kilograms using regularly calibrated electronic scales. BMI Z-score for age was used to describe the change in the offspring's BMI. We calculated sex-adjusted and age-adjusted Z-score of childhood BMI using Chinese reference growth charts. Childhood overweight was defined as a BMI at or above the 85th percentile and below the 95th percentile, and obesity was defined as a BMI at or above the 95th percentile [20]. Birth weight was transformed into a Z-score [21].

Statistical Methods

To assess our hypothesis that CS was associated with higher risk for offspring's BMI gain and overweight/obesity, we performed several analyses. Data were reported using frequencies and counts for categorical variables and means and standard deviations for continuous variables. We used linear and logistic regression models to assess the differences in offspring's anthropometric outcome (BMI Z-score and overweight/obese) in yearly time intervals between offspring exposed and not to CS. Multiple linear regression was used for continuous outcomes, and results are reported as regression coefficients (β estimates) with 95% CI. First, in the cross-sectional analyses, the difference in offspring's anthropometric outcomes (BMI Z-score and overweight/obesity) in yearly time intervals between offspring exposed to CS and offspring unexposed to CS was assessed using linear and logistic regression models. Second, longitudinal analyses between exposed to CS and anthropometric outcomes measured from 1 to 4 years of age were performed through mixed-effects regression models with random intercepts for each subject to account for the correlation between repeated observations within subjects. Three multivariable-adjusted models were included in these analyses: model 1 was adjusted for sex, maternal age, education, fetus time, parity, GDM, infant feeding, and maternal gestational weight gain; model 2 was further adjusted for maternal pre-pregnancy BMI; model 3 was additionally adjusted for birth weight Z-scores. Significance tests were two tailed, and a p value <0.05 was considered statistically significant. The data analysis was generated using SAS version 9.4 for the Windows x64-based system.

Results

We excluded mother-child pairs with missing mother's weight or height data ($n = 469$) and missing children's birth weight data ($n = 513$); a total of 10,150 mother-child

Table 1. Characteristics of mother-child pairs according to the mode of delivery

Variable	Available, <i>n</i>	Unexposed to cesarean (<i>n</i> = 6,502)	Exposed to cesarean (<i>n</i> = 3,462)	<i>p</i> value
Maternal characteristics				
Maternal age before pregnancy, mean (SD), years	9,964	27.2 (3.9)	28.7 (3.7)	<0.0001
Gestational age at delivery, mean (SD), weeks	9,964	38.9 (1.4)	38.7 (6.5)	0.062
Pre-pregnancy BMI, mean (SD), kg/m ²	9,964	20.6 (2.6)	21.4 (3.1)	<0.0001
Pre-pregnancy BMI category, <i>n</i> (%)				
<18.5	9,964	1,456 (21.4)	507 (14.2)	
18.5–23.9		4,637 (68.3)	2,439 (68.1)	<0.001
24.0–27.9		606 (8.9)	524 (14.6)	
≥28.0		88 (1.3)	110 (3.1)	
Gestational weight gain, mean (SD), kg	6,546	13.1 (4.1)	13.2 (4.4)	0.107
Education, <i>n</i> (%)				
≤9 years	8,580	1,153 (20.6)	634 (21.3)	0.485
>9 years		4,443 (79.4)	2,350 (78.8)	
Mean systolic pressure, mean (SD), mm Hg	8,779	106.1 (10.9)	106.1 (11.1)	0.979
Mean diastolic pressure, mean (SD), mm Hg	8,779	65.6 (7.8)	66.1 (8.2)	0.240
Fasting plasma glucose level, mean (SD), mmol/L	9,964	4.4 (0.4)	4.5 (0.4)	<0.0001
1-h plasma glucose level, mean (SD), mmol/L	9,964	7.9 (1.6)	8.2 (1.6)	<0.0001
2-h plasma glucose level, mean (SD), mmol/L	9,964	6.7 (1.3)	6.9 (1.3)	<0.0001
Child characteristics				
Boy, %	9,964	3,474 (53.4)	2,007 (58.0)	<0.0001
Birth weight Z-scores	9,964	−0.03 (0.8)	0.04 (1.0)	0.0002
Birth weight: LGA	9,964	902 (13.9)	779 (22.5)	<0.0001
Birth weight: appropriate for gestational age	9,964	5,157 (79.3)	2,289 (66.1)	<0.0001
Birth weight: SGA	9,964	233 (3.6)	181 (5.2)	<0.0001
BMI Z-scores for age, mean (SD)				
At 1 year	9,964	0.08 (0.910)	0.18 (0.91)	<0.0001
At 2 years	9,684	0.04 (0.88)	0.13 (0.91)	<0.0001
At 3 years	9,613	−0.17 (0.92)	−0.04 (0.96)	<0.0001
At 4 years	9,498	−0.14 (0.93)	−0.03 (0.98)	<0.001
Overweight/obesity for age, <i>n</i> (%)				
At 1 year	9,964	897 (13.8)	569 (16.4)	0.0004
At 2 years	9,684	795 (12.6)	501 (15.0)	0.001
At 3 years	9,613	594 (9.5)	429 (12.8)	<0.0001
At 4 years	9,498	626 (10.0)	411 (12.6)	0.0001
Mode of infant feeding within the first 6 months, <i>n</i> (%)				
Exclusive formula feeding	9,704	1,159 (18.3)	731 (21.7)	
Exclusive breastfeeding		616 (9.7)	285 (8.5)	0.0001
Mixed breast and formula		4,559 (72.0)	2,354 (70.0)	

pairs met the inclusion criteria and were included in the study cohort. 9,964 neonates completed the follow-up, 34.7% were by CS, and 65.3% were by vaginal delivery. The characteristics of the mothers and their children are summarized in Table 1. Mothers exposed to cesarean are older, but there were no differences in their gestational age at delivery between the 2 groups. Mean maternal pre-pregnancy BMI was significantly higher in the group exposed to cesarean. Gestational weight gain, maternal education, mean systolic pressure, and mean diastolic pressure were not statistically significant in the 2 groups.

Blood glucose of the group exposed to cesarean in pregnancy according to 75-g OGTT was higher. Child characteristics: group exposed to cesarean had a significantly higher birth weight Z-score. The incidence of LGA and SGA in birth weight was both significantly higher in the group exposed to cesarean. Absolute changes in BMI Z-score for children with CS remained higher at age 1–4 years subsequently than by vaginal delivery. Even if multiple logistic stepwise regression models adjusted as model 1, model 2, and model 3 were used, from 1 to 4 years of age, the absolute changes in BMI Z-scores for children by

Table 2. Analysis of anthropometric outcomes of offspring according to the mode of delivery in different ages

Outcome	Model 1		Model 2		Model 3	
	estimate (95% CI)	<i>p</i> value	estimate (95% CI)	<i>p</i> value	estimate (95% CI)	<i>p</i> value
Age: 1 year						
BMI Z-score ^a	0.07 (0.03–0.12)	0.0016	0.06 (0.01–0.11)	0.0110	0.06 (0.01–0.10)	0.0176
Overweight/obesity ^b	1.18 (1.02–1.36)	0.0266	1.15 (0.99–1.33)	0.0597	1.08 (0.94–1.25)	0.2894
Age: 2 years						
BMI Z-score	0.07 (0.02–0.11)	0.0005	0.05 (0.01–0.09)	0.0405	0.04 (0.01–0.09)	0.0493
Overweight/obesity	1.19 (1.02–1.38)	0.0229	1.14 (0.98–1.32)	0.0954	1.11 (0.95–1.29)	0.1914
Age: 3 years						
BMI Z-score	0.11 (0.06–0.16)	<0.0001	0.08 (0.03–0.12)	0.0022	0.07 (0.02–0.12)	0.0037
Overweight/obesity	1.39 (1.18–1.64)	<0.0001	1.31 (1.11–1.55)	0.0014	1.26 (1.07–1.49)	0.0069
Age: 4 years						
BMI Z-score	0.10 (0.05–0.15)	0.0002	0.06 (0.01–0.11)	0.0210	0.05 (0.01–0.10)	0.0329
Overweight/obesity	1.23 (1.04–1.46)	0.0147	1.13 (0.96–1.34)	0.1106	1.08 (0.91–1.28)	0.2199

Model 1: adjusted for sex, maternal age, education, fetus times, parity, GDM, infant feeding, and maternal gestational weight gain; model 2: adjusted for covariates in model 1 + maternal pre-pregnancy body mass index; model 3: adjusted for covariates in model 2+ birth weight Z-scores. Reference: unexposed to cesarean. ^a Absolute change in BMI Z-score. ^b OR change in overweight/obesity.

Table 3. Longitudinal analysis of anthropometric outcomes assessed during study visits in 1- to 4-year-old offspring exposed to cesarean

Outcome	BMI Z-score		Overweight/obesity	
	absolute change in Z-score estimate (95% CI)	<i>p</i> value	OR (95% CI)	<i>p</i> value
Model 1	0.09 (0.05–0.14)	<0.0001	1.24 (1.10–1.41)	0.0005
Model 2	0.06 (0.01–0.10)	0.0082	1.17 (1.03–1.30)	0.0138
Model 3	0.04 (0.01–0.09)	0.0380	1.08 (1.01–1.21)	0.0461

Model 1: adjusted for sex, maternal age, education, fetus times, parity, GDM, infant feeding, and maternal gestational weight gain; model 2: adjusted for covariates in model 1 + maternal pre-pregnancy body mass index; model 3: adjusted for covariates in model 2+ birth weight Z-scores. Reference: unexposed to cesarean.

CS were always significantly higher than by vaginal delivery. Comparison of children's OR changes in overweight/obesity age groups according to the mode of delivery, in model 1, from 1 to 4 years, showed that the CS group was significantly higher. However, after adjustment for maternal pre-pregnancy BMI (model 2), these associations attenuated toward the null at age 1, 2, and 4 years: OR = 1.08 [95% CI: 0.94–1.25] at age 1 year, OR = 1.11 [95% CI: 0.95–1.29] at age 2 years, and OR = 1.08 [95% CI: 0.91–1.28] at age 4 years, but overweight/obese children by CS were significantly higher in model 2 or model 3 at age 3 years (Table 2). Longitudinal analysis of anthropometric outcomes assessed during study visits in 1- to 4-year-old offspring exposed to cesarean, further stratified by all above factors that could affect the effects, absolute change

in Z-score continued statistical differences with age (Table 3), shown in Figure 1, and cesarean birth had higher risk in offspring from 1 to 4 years exposed to overweight/obesity, OR = 1.08 (1.01–1.21, *p* = 0.0461).

Discussion

CS has played an important role in the treatment of dystocia and pregnancy complications and in reducing maternal mortality. However, in the past 20 years, the CS rate in many countries has been rising. In our study, 34.7% of the CS rate was in Xiamen from January 2011 to December 2012. We investigated the association between CS birth and the risk of overweight/obesity in infants to

Fig. 1. Mixed model for BMI Z-score of offspring delivered via vaginal birth or cesarean birth.

4-year-old preschool-age children. BMI Z-scores of 1- to 4-year-old children exposed to cesarean were continuous, significantly higher than unexposed to cesarean, and cesarean delivery increases the risk of overweight/obesity in offspring by 19%. Many small case-control studies reported higher odds of obesity associated with cesarean delivery [14, 22], but our research has the larger population than before. Strengths of our study include a well-characterized cohort with adequate control for a large set of potential confounding variables such as maternal age, fetus time, GDM, infant feeding, maternal gestational weight gain, maternal pre-pregnancy BMI, and birth weight to examine the relationship between cesarean delivery and overweight/obesity. Some studies have reported that pre-pregnancy BMI is significantly associated with offspring obesity [23, 24], GDM is a risk factor for 1-year-old obesity [25], and a high gestational weight gain was associated with infant overweight risk at 1 year [26, 27]. Analyzed data individually at 1-year follow-up, adjusted for GDM and maternal gestational weight gain, the group exposed to cesarean still increased the risk of occurrence of overweight/obesity, but adjusted for maternal pre-pregnancy BMI and birth weight Z-scores, CS is not an independent risk factor for overweight/obesity at 1- and 2-year-old. In other words, maternal pre-pregnancy

BMI and birth weight Z-scores may be more important factors than mode of delivery at 1- and 2-year-old. However, CS is still an independent risk factor for overweight/obesity at 3 years old even if adjusted for maternal pre-pregnancy BMI and birth weight Z-scores. Few articles reported maternal pre-pregnancy obesity, gestational weight gain, and GDM individually and jointly predicted obesity at age 4 years in offspring. In our study, CS is an independent risk factor adjusted for GDM at age 4 years, but adjusted for maternal pre-pregnancy BMI and birth weight Z-scores, CS or not became no statistical difference. It seems that influence of CS birth on the risk of overweight/obesity was declining follow with children grow older, because of the increasing influence of other risk factors for obesity like physical inactivity, family dietary habits, watching television (the use of other electronic devices) probably [28], but CS birth still an independent risk factor whether offspring overweight/obesity or absolute change in BMI Z score in general on the whole from 1 to 4 years children.

Birth by CS is associated with an increased risk of preschool-age child overweight and obesity; possible mechanisms underlying this association are differences in the infant gut microbiome resulting from differences in exposure to maternal vaginal secretions. Infants born by CS,

in particular elective CS before labor begins, largely circumvent their mother's vaginal and fecal microbiota during birth; therefore, they have been hypothesized to acquire an atypical intestinal microbiota, but infants were scoured by their mother's vaginal microflora during vaginal birth. Several studies have demonstrated a lower microbial community diversity over the first 6–12 months in infants born via CS, due in part to a consistently lower detection and/or abundance of *Bacteroides* species [29, 30]. Data in mice and humans have shown that obese individuals display a relative abundance of Firmicutes and a lower proportion of Bacteroidetes than lean individuals [31, 32].

We analyzed the causes of pregnant women choosing CS in the current period. Except for clinical CS indications, the most common reasons were pain-related fear of vaginal birth and fear of perineal cut or tearing of the perineum, considering the risks of vaginal delivery for the baby (feel that CS is “safe and fast,” avoiding “any risk” to their baby). Other reasons for selecting CS were regarding cultural and societal beliefs that choosing an auspicious date for birth can bring good luck, and the convenience of planning the birth.

High CS rate is gradually improving now; fortunately, the nationwide CS rate was 36.7% in China in 2018 [33], a significant decline compared with 2007–2008. Something had to be done against the still uncomfortably high CS rate. Mothers who choose CS should know the potential health risks to her baby, achieving a healthy pre-pregnancy weight and gaining an appropriate amount of weight during pregnancy to reduce CS, thus carrying out a more painless delivery; vaginal birth after CS is recommended as a safe option for most women following previous CS. At the provincial and national level, education for health professionals is given, setting a targeted CS rate at the health facility level.

Our study had several limitations; to calculate maternal BMI, we relied on self-reported maternal pre-pregnancy weight. Smoking, folic acid use during pregnancy, emergency CS, or elective CS did not get further classification due to the flaws in the registration system. Prenatal antibiotics exposure might impact offspring's BMI, but we did not have details of the time of antimicrobial use and how long was the antibiotics given since we used healthcare records as a main source of data. No further analysis was made on above relationship. Future studies also need to explore the underlying mechanism of CS-obesity association.

Conclusion

Absolute change in BMI Z-score significantly increased in 1- to 4-year-old preschool-age children by CS in China; birth by CS was an increased risk of independent risk factor for overweight/obesity before 4 years old. Our findings may contribute to the development of public health. Pregnant women choose CS in the absence of a medical indication and should be aware that their children may have a higher risk of obesity.

Acknowledgments

We would like to thank all doctors, nurses, technicians, and patients involved in their dedication to the study.

Statement of Ethics

This study was carried out in accordance with the rules of the Declaration of Helsinki of 1975, revised in 2013. The study was approved by the Ethics Committee of the First Affiliated Hospital of Xiamen University (KYH2018-007), and written informed consent was obtained from every participant.

Conflict of Interest Statement

The authors declare no conflict of interest.

Funding Sources

The authors have not declared a specific grant for this research from any funding agency in the public, commercial, or not-for-profit sectors.

Author Contributions

P.H., M.L., and X.L. designed the study. X.S. and F.X. designed the clinical questionnaire. L.W., W.L., J.Z., and M.L. collated the data. P.H. performed statistical data analyses. X.L., M.L., and P.H. contributed to drafting the manuscript. P.H. and X.L. contributed equally to this work. All authors read and approved the final manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

References

- Zhang X, Zhang M, Zhao Z, Huang Z, Wang L. Geographic variation in prevalence of adult obesity in china: results from the 2013–2014 national chronic disease and risk factor surveillance. *Ann Intern Med*. 2019 Oct 29; 172(4):291–3.
- Whitaker RC, Wright JA, Pepe MS, Seidel KD, Dietz WH. Predicting obesity in young adulthood from childhood and parental obesity. *N Engl J Med*. 1997 Sep 25;337(13):869.
- Dietz WH, Robinson TN. Clinical practice: overweight children and adolescents. *N Engl J Med*. 2005;352(20):2100–9.
- Capital Institute of Pediatrics; Coordinating Study Group of Nine Cities on the Physical Growth and Development of Children. A national epidemiological survey on obesity of children under seven years of age in nine cities of China in 2016. *Zhonghua Er Ke Za Zhi*. 2018 Oct;56(10):745–52.
- Lau EY, Liu J, Archer E, McDonald SM, Liu J. Maternal weight gain in pregnancy and risk of obesity among offspring: a systematic review. *J Obes*. 2014;2014:524939.
- Yu ZB, Han SP, Zhu GZ, Zhu C, Wang XJ, Cao XG, et al. Birth weight and subsequent risk of obesity: a systematic review and meta-analysis. *Obes Rev*. 2011;12(7):525–42.
- Schwartz BS, Pollak J, Bailey-Davis L, Hirsch AG, Cosgrove SE, Nau C, et al. Antibiotic use and childhood body mass index trajectory. *Int J Obes*. 2016;40(4):615–21.
- Chang L, Neu J. Early factors leading to later obesity: interactions of the microbiome, epigenome, and nutrition. *Curr Probl Pediatr Adolesc Health Care*. 2015;45(5):134–42.
- Fuemmeler BF, Dedert E, McClernon FJ, Beckham JC. Adverse childhood events are associated with obesity and disordered eating: results from a U.S. population-based survey of young adults. *J Trauma Stress*. 2009;22(4):329–33.
- WHO; UNFPA; UNICEF; Mailman School of Public Health. *Monitoring emergency obstetric care: a handbook*. Geneva: World Health Organization; 2009.
- Boerma T, Ronsmans C, Melesse DY, Barros AJD, Barros FC, Juan L, et al. Global epidemiology of use of and disparities in caesarean sections. *Lancet*. 2018 Oct 13;392(10155):1341–8.
- Esteves-Pereira AP, Deneux-Tharaux C, Nakamura-Pereira M, Saucedo M, Bouvier-Colle MH, Leal Mdo C. Caesarean delivery and postpartum maternal mortality: a population-based case control study in Brazil. *PLoS One*. 2016;11:e0153396.
- Lumbiganon P, Laopaiboon M, Gulmezoglu AM, Souza JP, Taneepanichskul S, Ruyan P, et al. Method of delivery and pregnancy outcomes in Asia: the WHO global survey on maternal and perinatal health 2007–08. *Lancet*. 2010;375:490–9.
- Huh SY, Rifas-Shiman SL, Zera CA, Edwards J, 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.
- Bouhanick B, Ehlinger V, Delpierre C, Chamontin B, Lang T, Kelly-Irving M. Mode of delivery at birth and the metabolic syndrome in midlife: the role of the birth environment in a prospective birth cohort study. *BMJ Open*. 2014;4:e005031.
- 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(3):e025051.
- Masukume G, Khashan AS, Morton SMB, Baker PN, Kenny LC, McCarthy FP. Caesarean section delivery and childhood obesity in a British longitudinal cohort study. *PLoS One*. 2019 Oct 30;14(10):e0223856.
- Capital Institute of Pediatrics. A national epidemiological survey on obesity of children under seven years of age in nine cities of China in 2016. *Zhonghua Er Ke Za Zhi*. 2018 Oct 25;56(10):745.
- Rutayisire E, Wu X, Huang K, Tao S, Chen Y, Tao F. Cesarean section may increase the risk of both overweight and obesity in preschool children. *BMC Pregnancy Childbirth*. 2016 Nov 3;16(1):338.
- Li Hui JC, Zong X, Zhang Y. Body mass index growth curves for chinese children and adolescent aged 0–18 years. *Chin J Pediatr*. 2009; 47:493–8.
- Yang J, Lernmark A, Uusitalo UM, Lynch KF, Veijola R, Winkler C, et al. Prevalence of obesity was related to HLA-DQ in 2–4-year-old children at genetic risk for type 1 diabetes. *Int J Obes*. 2014 Dec;38(12):1491–6.
- Zhou L, He G, Zhang J, Xie R, Walker M, Wen SW. Risk factors of obesity in preschool children in an urban area in China. *Eur J Pediatr*. 2011;170:1401–6.
- Aune D, Saugstad OD, Henriksen T, Tonstad S. Maternal body mass index and the risk of fetal death, stillbirth, and infant death: a systematic review and meta-analysis. *JAMA*. 2014;311(15):1536–46.
- Yu Z, Han S, Zhu J, Sun X, Ji C, Guo X. Pre-pregnancy body mass index in relation to infant birth weight and offspring overweight/obesity: a systematic review and meta-analysis. *PLoS One*. 2013;8(4):e61627.
- Sun J, Mei H, Xie S, Wu L, Wang Y, Mei W, et al. The interactive effect of pre-pregnancy overweight and obesity and hypertensive disorders of pregnancy on the weight status in infancy. *Sci Rep*. 2019 Nov 4;9(1):15960.
- Bridgman SL, Azad MB, Persaud RR, Chari RS, Becker AB, Sears MR, et al. Impact of maternal pre-pregnancy overweight on infant overweight at 1 year of age: associations and sex-specific differences. *Pediatr Obes*. 2018 10;13(10):579–89.
- Agbota G, Fievet N, Heude B, Accrombessi M, Ahouayito U, Yovo E, et al. Poor maternal anthropometric status before conception is associated with a deleterious infant growth during the first year of life: a longitudinal preconceptional cohort. *Pediatr Obes*. 2020 Jan; 15(1):e12573.
- Pei Z, Heinrich J, Fuertes E, Flexeder C, Hoffmann B, Lehmann I, et al. Cesarean delivery and risk of childhood obesity. *J Pediatr*. 2014; 164:1068–73.
- Bäckhed F, Roswall J, Peng Y, Feng Q, Jia H, Kovatcheva-Datchary P, et al. Dynamics and stabilization of the human gut microbiome during the first year of life. *Cell Host Microbe*. 2015;17(6):852.
- Yassour M, Vatanen T, Siljander H, Hamalainen AM, Harkonen T, Ryhanen SJ, et al. Natural history of the infant gut microbiome and impact of antibiotic treatment on bacterial strain diversity and stability. *Sci Transl Med*. 2016;8:343ra81.
- Ley RE, Turnbaugh PJ, Klein S, Gordon JI. Microbial ecology: human gut microbes associated with obesity. *Nature*. 2006;444:1022–3.
- 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;444:1027–31.
- National Health Commission of the People's Republic of China. *Report on the development of maternal and child health career in China (2019)*; 2019.