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Does previous cesarean section influence neonatal birth weight? A path analysis in China

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ABSTRACT

Background: Since the One-child Policy was revised to a Two-child policy in 2013, the number of pregnancies with previous cesarean section suddenly increased in China. The aim of this study was to test if a previous cesarean section influenced the neonatal birth weight under Chinese background.
Methods: A retrospective study was conducted. Path analysis was used to test the hypothesized model for the association among previous cesarean section, placenta previa, gestational age and neonatal birth weight. Comparative fit index, the root-mean-square error of approximation and weighted root-mean-square residual were used to evaluate the model fit.
Results: 3466 electronic records for second pregnancies met the criteria; a modified model was established (the root-mean-square error of approximation = 0.049, comparative fit index = 0.992, weighted root-mean-square residual = 0.960). The effects of previous cesarean section on neonatal birth weight were mediated via four paths. The direct effects (coefficient: 0.056) showed opposite signs compared to indirect effects (coefficient: −0.127) in this path analysis. It meant that the negative effects of the previous cesarean section were suppressed by other factors which bring positive effects.
Conclusion: This study showed that previous cesarean section had negative effects on neonatal birth weight with increasing incidence of placenta previa and preterm birth. But these effects were suppressed by other positive factors, such as maternal body mass index, just after the child policy updated in China.

Statement of significance

Problem or issue

Chinese child policy was updated from one child policy to two child policy. Pregnant women with previous cesarean section increased suddenly and bring new medical risk to Chinese clinicians.

What is already known

Previous cesarean section was a high risk for maternal and neonatal outcomes, but it was unclear that if it would bring lower neonatal birth weight.

What this paper adds

1. The neonatal birth weight of the woman with previous cesarean section was lower than the woman without previous cesarean section. But this effect was not significant in the multiple linear regression analysis when included previous cesarean section, placental previa, maternal body mass index, maternal age and gestational age as factors.
2. Our path analysis model showed that the effects of previous cesarean section on neonatal birth weight were mediated by placental previa, preterm birth and maternal body mass index, and demonstrated a suppression effect with opposite signs between direct and indirect effects.

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1. Introduction

The rate of cesarean section (C/S) had increased dramatically in both developed and developing countries in the past decades, increasing from 16.0% in a typical developed country in the early 1990s to about 50% in some countries in 2010s.[1–3] WHO reported that the rate of C/S in China was the highest and that China also had the highest rate of C/S without medical indication.[2] The Chinese C/S rate averaged 54.9% in 2014 and in some hospitals was up to 80%.[4] Since the One-child Policy was revised to a Two-child policy in 2013,[5] the number of pregnancies with previous C/S suddenly increased and previous C/S became a new medical risk for obstetrics in China.

Previous C/S, with a rate of repeated C/S from 52.7% to 87%,[6–8] has been reported to be associated with maternal/neonatal morbidity and mortality, including ante-partum hemorrhage caused by placental problems,[6,9] anemia, preeclampsia, uterine rupture and hysterectomy,[9,10] preterm birth, low birth weight, small for gestational age, low Apgar scores, neonatal asphyxia,[7,11] stillbirth and unexplained stillbirth.[6,12] Low birth weight (LBW), defined as birth weight less than 2500 g in term pregnancies, has been proved to be influenced by previous C/S.[6] The mechanisms of adverse effects of C/S on the neonatal birth weight of the subsequent pregnancy are not clearly understood. Studies speculated with devascularization of uterine vessels and increased vascular resistance because of scarring,[13] placenta previa caused by previous C/S with changes in uterine structure and immune function that occur with onset of labor.[14]

One of the main causes of placenta previa is previous C/S. However, some researchers found that previous C/S did not have a significant effect on placenta previa [15]. Placenta previa has been found to be associated with LBW.[6,16–19] Preterm birth (neonatal delivery at less than 37 completed weeks of gestation) was shown to come more frequently after previous C/S and placenta previa in some results, with or without LBW,[6,7,16–18,20] but other outcomes showed that previous C/S had no significant effects on preterm birth rate.[10,11]

Path analysis, conducted using the statistical software MPlus in this case, is one of many procedures of a structural equation model. It allows the researcher to specifying a set of relationships between variables and analyses. The MPlus statistical software can be carried out for observed variables that are continuous, censored, binary, ordered categorical (ordinal), unordered categorical (nominal), counts, or combinations of these variable types.[21] Path analysis is an extension of the regression model and is used to test the fit of the correlation matrix against two or more causal models being compared by the researchers.[22,23] Structural equation modeling has been widely used to account for gestational age, which is a strong predictor of neonatal birth weight and has been shown in many studies to be an important intermediate in the causal pathway between an exposure and birth.[24,25]

The aim of this study was to test if a previous cesarean section influenced the neonatal birth weight under Chinese background with high C/S and updated child policy. A model of associations linking previous C/S, placenta previa, gestational age, and neonatal birth weight was established. The hypothesized model was tested through path analysis by evaluating direct effects of any path, or indirect effects of a combination of paths, on the overall fit of this model (see Fig. 1). The model is informed by the following hypotheses:

H1. Placenta previa and gestational age is influenced by previous C/S.

H2. Neonatal birth weight is influenced by previous C/S, placenta previa, gestational age.

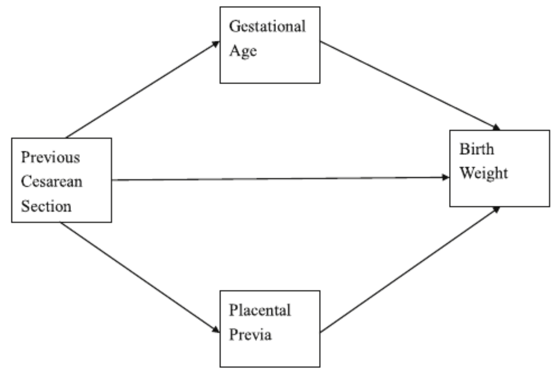

Fig. 1. Hypothesized model of study.

H3. The effect of previous C/S on neonatal birth weight is mediated by placenta previa.

H4. The effect of previous C/S on neonatal birth weight is mediated by gestational age.

2. Methods

This was a retrospective analysis. Data used in this study were limited to singleton births of the second pregnancy between 24 weeks 0 days and 42 weeks 6 days of gestation from July 1, 2015 to June 30, 2016 in Xiangya Hospital, the Second Xiangya Hospital and the Third Xiangya Hospital of Central South University (CSU). All the information was collected from electronic medical records (EMR) maintained by each hospital. Discharge diagnoses for every delivery were coded using the International Classification of Diseases, 10th Revision (ICD-10), Clinical Modification. For avoiding the influence from the factors which was existed before, we excluded pregnancies with previous LBW and SGA recorded in the EMR.

We used the following information as baseline characteristics of women included in the study: maternal age, marital status, education level, tobacco use, alcohol use, maternal body mass index (BMI). Maternal BMI was calculated from the weight and height of the pregnant women recorded in the EMR when they admission for delivery. The rates of previous C/S and repeated C/S were recorded. Placenta previa was defined as placenta covering all, or part of the internal cervix diagnosed by ultrasound during the second or third trimester. As a routine check, placenta previa was confirmed immediately prior to delivery by an ultrasound. Gestational age was determined using menstrual history and first trimester ultrasound. All births were attended by licensed health care providers including midwives and obstetricians. Birth weight was measured on a pediatric scale which was calibrated before each measurement and rounded to the nearest 10 g and recorded in the EMR by midwives or nurses.

Descriptive statistics (frequencies, percentages, means, standard deviations and ranges) were calculated to obtain descriptions of the sample characteristics and main variables. Multiple linear regression analysis was used to analyze the relationship between variables using SPSS 21.0 (IBM Corp., Armonk, NY) statistical software. Multiple linear regression models were based on backward elimination of nonsignificant variables and adjusted for the following predictors: maternal age and BMI at delivery, placental previa, gestational age and previous C/S. A P value of 0.05 was regarded as statistically significant. Data were also exported to Mplus (version 7.11) for modeling the hypothesized associations and path analysis in a sample of 3466 second-pregnancies. Along with a binary mediate variable (placenta previa), a model of an example of a path analysis with a continuous dependent variable and a categorical mediating variable were used.[21] Loadings on the independent variable (previous C/S), dependent variable (birth weight) and mediate variables (placenta previa and gestational age), confidence intervals, and standard errors were computed using the bootstrap procedure on 5000 samples. With a "baseline model" for categorical outcomes, fit indices were obtained by TYPE = GENERAL in the ANALYSIS command. Model fit was evaluated using the comparative fit index (CFI, with the criterion of CFI >0.96), the root-mean-square-error of approximation (RMSEA, with the criterion of <0.05) and the weighted root-mean-square residual (WRMR, criterion <1.0).[26] Parameter estimates were calculated and represent the strength of the path between two variables (standardized and unstandardized regression coefficients, standard error SE, *P*-value, indirect effects and 95% confidence intervals). R-square was used to evaluate the variance of each variable explained in the model.

3. Results

The total number of live births in the three Xiangya hospitals during the study period was 10,674. We excluded the first pregnancies (N = 7148), multiple gestations (N = 27), records of previous LBW and SGA (combined N = 33). The EMR system was established in 2010 in China,[27] so the records of the previous pregnancies were incomplete; some of the records of previous pregnancies were taken from the narratives of pregnant women or their families. Analyses were then limited to 3466 births for second pregnancies. Of the 3466 second pregnancies, the mean age was 32.14 years (from 18 to 45years), the mean gestational age was 270.3 days (from 28 weeks 4 days to 41 weeks 6 days). Of the 47.23% (N = 1637) pregnant women who had a previous C/S, 85.28% (N= 1396) of them had a repeated C/S. Comparing with women who had not had a previous C/S, the women with previous C/S had a high rate of placenta previa, a high level of maternal BMI, a decreased gestational age and low neonatal birth weight delivery (see Table 1). When neonatal birth weight was used as a dependent variable and significant variables were put into the multiple linear regression model, three predictors were included in the final model (see Table 2). Neonatal birth weight decreased with placental previa, lower gestational age and maternal BMI. Both maternal age and previous C/S were excluded from the model.

After analyzing the data with the hypothetical model shown in Figs. 1 and 2, we determined that the hypothetical model proposed for this study did not demonstrate a perfect fit with data derived from the whole sample. The imperfect fit was demonstrated by a RMSEA of 0.112 and a WRMR of 2.004. Applying the result of multiple linear regression analysis, the information from the

Table 2
Predictors of neonatal birth weight using multiple linear regression analysis based on backward elimination of nonsignificant variables.

	Variables	B	95%CI	*P*
Full model	Placental previa	−0.212	−0.277 to −0.146	0.000
	Previous C/S	0.010	−0.016 to 0.036	0.440
	BMI	0.031	0.027–0.035	0.000
	Maternal age	0.002	−0.002 to 0.005	0.337
	Gestational age	0.178	0.171–0.186	0.000
Final model	Placental previa	−0.208	−0.273 to −0.143	0.000
	BMI	0.032	0.028–0.036	0.000
	Gestational age	0.178	0.170–0.185	0.000

Significance: $P < 0.05$.

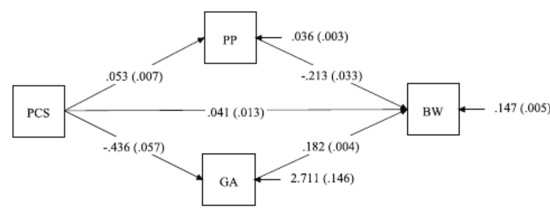

Fig. 2. Effect sizes of path analysis. The effect of previous CS on birth weight, placental previa, gestational age, and the effects of placental previa, gestational age on birth weight are presented. PCS: previous cesarean section. PP: placental previa. GA: gestational age. BW: birth weight.

literature review and our clinical experience, we modified the model with another path, which is shown in Fig. 3. This model described other two paths. One was from previous C/S to maternal BMI, showing the influence on neonatal birth weight, the other one was from previous C/S to placenta previa, on through gestational age, showing the influence on neonatal birth weight. This change improved the model fit with a RMSEA of 0.049, a CFI of 0.992 and a WMRM of 0.960, which indicated a good fit of the data to the modified model.

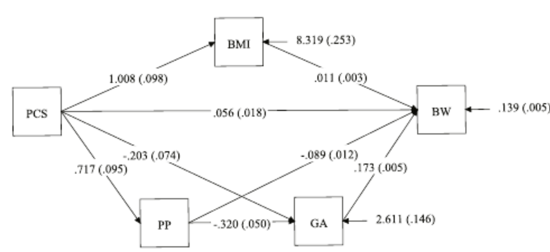

Fig. 3. Trimmed model of trust based on data analysis.

Table 1
Comparison of baseline characteristics of women with and without previous C/S in Hunan, China in 2016.

Maternal characteristics	Previous C/S 1637 (47.23)	No previous C/S 1819 (52.76)	*P*-value
Maternal age at delivery (years) mean (SD)	32.54 (3.96)	31.79 (4.04)	<0.001
Married %	1627 (99.9)	1815 (99.8)	0.495
≤ High school education %	142 (8.7)	127 (7.0)	0.058
Tobacco use	0	0	
Alcohol use	0	0	
BMI: body mass index mean (SD)	27.68 (2.94)	26.67 (2.83)	<0.001
Current C/S %	1396 (85.28)	276 (15.2)	<0.001
Placenta previa %	108 (6.6)	24 (1.3)	<0.001
Neonatal birth weight (kg) mean (SD)	3.306 (0.502)	3.352 (0.477)	0.006
Gestational age (days) mean (SD)	268.83 (1.62)	271.85 (1.67)	<0.001

Significance: $P < 0.05$.

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Table 3
Fit indices for the path analysis model.

	Model 1	Model 2
RMSEA root-mean-square error of approximation	0.112	0.049
CFI comparative fit index	0.978	0.992
WRMR weighted-root-mean-square residual	2.004	0.960

The direct effects between the variables of the modified model are described in Fig. 3. This model shows that previous C/S is correlated with placenta previa (coefficient 0.717, standard error, SE 0.095, $P < 0.001$), increased maternal BMI (coefficient 1.008, SE 0.098, $P < 0.001$) and reduced gestational age (coefficient −0.203, SE 0.074, $P = 0.006$), and in turn, high rate placenta previa (coefficient −0.089, SE 0.012, $P < 0.001$) and lower gestational age (coefficient 0.173, SE 0.005, $P < 0.001$) were correlated with lower neonatal birth weight, higher maternal BMI (coefficient 0.011, SE 0.003, $P < 0.001$) were correlated with higher neonatal birth weight, and in the path placenta previa also reduced gestational age (coefficient −0.320, SE 0.050, $P < 0.001$). Previous C/S showed a positive direct effect on neonatal birth weight with a coefficient of 0.056 (SE 0.018, $P < 0.001$), however, the sum indirect effects of three different paths was inconsistent with a coefficient of −0.127 (see Table 3). Within a mediation model, this had been recognized as suppression on effects when the direct and mediated effects of an independent variable on a dependent variable had opposite signs.[28–30]

Coefficient of determination (R-square) was used to evaluate the variance explained by each variable in the model. Placenta previa was explained 11.3% ($R^2 = 0.113$), gestational age was explained at 5.4% ($R^2 = 0.055$), maternal BMI was explained at 3.0%, and finally, neonatal birth weight was explained 42.1% in this model. Overall, this path analysis model explained about 61.8% of the variance in neonatal birth weight when babies were delivered by a woman with previous C/S.

4. Discussion

4.1. Main findings

In this study, when comparing with no previous C/S pregnancy, the neonatal birth weight of pregnant women with previous C/S was significant lower. But previous C/S was excluded from the multiple linear regression model of neonatal birth weight. Then we tested a model that explained the effects of previous C/S on neonatal birth weight were mediated by placenta previa, maternal BMI and gestational age. After the model was modified, four different indirect paths were found, including that: (a) previous C/S was associated with higher maternal BMI and maternal BMI was associated with higher neonatal birth weight; (b) previous C/S increased the incidence of placenta previa and low neonatal birth weight was associated with placental previa; (c) previous C/S decreased gestational age, which caused low neonatal birth weight; and (d) previous C/S increased the incidence of placenta previa; in turn, placenta previa decreases gestational age, which contributes to low neonatal birth weight. This model demonstrated a suppression effect with opposite signs between direct and indirect effects.

4.2. Interpretation

4.2.1. The effects of previous C/S on neonatal birth weight

Previous C/S demonstrated negative effects on neonatal birth weight in some studies,[6,13,33] but not in others.[7,11] Our findings suggest a path of the effects from previous C/S to neonatal birth weight. Meanwhile, a suppression effect was demonstrated in this path. MacKinnon et al.[29] used an example to explain the suppression effect. In a suppression effect, the independent variable has positive influence on dependent variable, but it also has negative influence on dependent variable through another variable called mediator. Combined, these two hypothetical effects may cancel each other out, resulting in a total effect of independent variable on dependent variable being equal to zero, or opposite signs. The suppression effect demonstrated in our findings could be used to explain the inconsistent results in previous research. The indirect effects of previous C/S on neonatal birth weight mediated by placenta previa and gestational age were negative, but the direct effects were positive. In this study, the combination effects of previous C/S were negative with $|ab/c'| = 2.28$, and we got the same results comparing between pregnancies with previous C/S and pregnancies without previous C/S (see Table 1).

4.2.2. The effects of previous C/S on placenta previa

Our findings showed that previous C/S is related to higher likelihood of placenta previa, and this was supported by many studies.[9,16,17,34,35] Interestingly, one study examined placental migration by trans-abdominal ultrasound from 12 to 32 weeks gestation and concluded there was no significant difference in the incidence of placenta previa between groups with or without previous CS.[15] But after calculating the rate of placenta previa based on the data in the authors' Table 3, we found that the rate of placenta previa in women with previous C/S (1.22%) was two-fold greater than in women without previous C/S (0.65%), which echoed findings of a meta-analysis study (0.87% in women with previous C/S and 0.44% in women without previous C/S) between April 2000 and February 2009 in England.[34] In this study, we presented data showing a higher rate of placenta previa (6.6% in women with previous C/S and 1.3% in women without previous C/S) than other studies. This might be caused by the development of chronic complications after C/S with a long inter-pregnancy interval,[36] which might be related to the national policy change from the One-child Policy to the Two-child Policy from 2013.

4.2.3. The effects of previous C/S on gestational age

We found a negative association between previous C/S and gestational age, and this association was mediated by placenta previa. This was consistent with previous studies that had found an increased risk of preterm delivery among pregnant women with previous C/S and placenta previa.[6,7,16–18,20,33] The results in Table 4 show that the indirect negative effects of the path from previous C/S to placenta previa to gestational age to neonatal birth weight

Table 4
Effects from previous C/S to neonatal birth weight using path analysis.

Mediation pathway	Indirect effects (ab)	Direct effects (c')	|ab/c'|
Previous C/S – placenta previa – birth weight	−0.064		
Previous C/S – gestational age – birth weight	−0.035		
Previous C/S – placenta previa – gestational age – birth weight	−0.040		
Previous C/S – BMI – birth weight	0.011		
Sum	−0.127	0.056	2.28

were higher than those of the path from previous C/S to gestational age to neonatal birth weight. This indicates that placenta previa would be the main reason for prophylactic preterm deliveries stemming from medical balancing in pregnant women with previous C/S.

4.2.4. The effects of maternal BMI in this path analysis model

The effects of maternal BMI were findings out our hypothetical model.

5. Strengths and limitations

One of the strengths of this study was that we did a first look of the relationship between previous C/S and neonatal birth weight after the child policy was updated in China. And we collected data from hospitals in China, where the rate of C/S without medical indication is the highest.[2] This might have reduced the bias coming from previous medication indication of C/S.

Another one was that we used path analysis to support the direct and indirect association between previous C/S and neonatal birth weight. The outcomes provided evidence for the hypothesized explanations that placenta previa and prophylactic preterm deliveries caused by previous C/S would increase neonatal morbidity (low neonatal birth weight in this study), and part of prophylactic preterm deliveries came from placenta previa.[13,15,17,31] The results also showed that both the direct effects and the indirect effect through maternal BMI were positive on neonatal birth weight. One possible reason of these positive effects was that pregnant women with previous C/S would pay more attention on self-care, like balanced nutrition, from conceiving to delivering when they recognized the high risks. The other possible reason was the result of a self-selection process by healthier women who were taking advantage of the new Two-child Policy. Same as our other study showed that advanced maternal age was not found to be a high-risk factor for adverse perinatal outcomes as usual after child policy updated.[32]

This study had several limitations. First, we included data from only three hospitals in Hunan, China; therefore, the generalizability of the results is limited. Secondly, part of the medical records for previous delivery was incomplete due to the EMR implementation schedule in the hospitals whose records we studied. Finally, this was just a first look study after child policy updated, conditions would change later.

6. Clinical implications

Our study suggested that under the background of child policy updated, with the increasing high risk of previous C/S, previous C/S showed combined negative effects on neonatal birth weight, but besides the negative effects of placenta previa and prophylactic preterm deliveries, the direct effect of previous C/S was positive. The BMI of the pregnant woman was higher than no previous C/S pregnant woman and coming with higher neonatal birth weight. These results remind that previous C/S, as a medical high risk, also aroused the self careful of the pregnant woman.

7. Conclusion

In this paper, we presented the association between previous C/S and neonatal birth weight. The negative effects were due to previous C/S, which increases incidence of placenta previa and preterm birth. But these effects were suppressed by other positive effects, such as maternal BMI.

Ethical approval

The data set was provided by the Department of Hospital Administration of Central South University. The study received approval by the Institutional Review Board of the Third Xiangya Hospital, Central South University, March 17th, 2015 (2015-S179).

Disclosure of interests

The authors have no relevant disclosures.

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Contribution to authorship

CxQ and SyT conceived, planned, and designed the study. CxQ wrote the first draft of the manuscript. YlD and WtC supervised the project, interpreted the data, oversaw the writing of the paper, and edited the manuscript. CmM and SM abstracted the dataset. WyW and JrC validated and analyzed the data under supervision of YlD. All authors contributed to data analysis, interpretation of the results, and manuscript revisions. All authors reviewed and approved the submitted manuscript.

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