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Influence of Previous Cesarean Section on Subsequent Pregnancy Complications in Hunan, China: A Retrospective Cohort Study

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Abstract

Aim: Under the introduction of the two-child policy, women with second pregnancies having a previous cesarean section have suddenly increased. The two-child policy has provided a new chance for studying the previous cesarean section, which is considered a new medical risk in China. This study aimed to examine the previous cesarean sections influence on pregnancy complications among women with singleton delivery in their second pregnancies.

Method: A total of 2018 eligible women with second pregnancies who had a singleton delivery from January 2015 to October 2017 were studied retrospectively. Data on the previous delivery mode for the first pregnancy, maternal characteristics and pregnancy complications for the second pregnancy were obtained from the electronic medical records. Chi-square test was used to describe and obtain the significant maternal characteristics according to the previous mode of delivery. The pregnancy complications associated with previous cesarean section was analyzed with binary logistic regression.

Results: Of 2018 eligible women with singleton delivery in their second pregnancy, 942 (46.7%) had a previous cesarean section (study group) while 1076 (53.3%) also had a previous vaginal delivery (reference group). Previous cesarean section had an increase risk on the following pregnancy complications; Gestational Diabetes Mellitus (GDM) (Adjusted Odds Ratio [aOR]: 1.438; 95% CI, 1.093-1.894), fetal anomaly (aOR: 14.258; 95% CI, 4.213-48.248), and placenta previa (aOR: 2.890; 95% CI, 1.623-5.148).

Conclusion: This study demonstrates that the previous cesarean section is associated with increased risk of GDM, fetal anomaly and placenta previa on second singleton pregnancy after the implementation of the universal two-child policy in China.

Keywords: Cesarean section; China; Pregnancy complications; Second pregnancy; Two-child policy

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Introduction

Cesarean Section (CS) is the most common obstetrical operation known worldwide. Over the past decades, the rate of CS has increased both in developing and developed countries. The WHO issued a disclosure in 1985, stating the CS regional rates must not exceed 10% to 15% [1,2]. Nonetheless, China is one of the countries with the prevalence of CS averagely of 46.2% over the past decades that are higher than the recommended threshold. Coincidentally, this high prevalence of CS began during the implementation period of the one-child policy introduced in 1979 to reduce the then growing population in China. CS is considered safe under medical indications, but most women who had CS under the one-child policy opted for it without any medical indications [1,3]. In 2015, the one-child policy was replaced with the universal two-child policy. This new policy has encouraged most couples to consider having a second child. As a result, it suddenly increased the number of pregnancies with an obstetrical history of previous CS [4,5]. Hence, previous CS has become a new medical risk for clinicians in China.

A study on previous CS and its association with adverse pregnancy outcomes has been studied extensively in other countries. However, literature on such studies in China is sparse, mainly due to

the one-child policy, which could not allow for subsequent pregnancies that could be used to access previous CS's influence on pregnancy complications. However, these previous studies' findings have been reported to be associated with some pregnancy complications [1,2], but the results were inconsistent. Some studies have indicated previous CS to be associated with pregnancy complications such as pregnancy-induced hypertension disorders [6-8], placenta previa [7-10], placenta abruption, placenta accreta/adhesions [8,9]. In contrast, other studies showed that previous CS had no significant effect on placenta disorders such as placenta previa [6,11], placenta abruption [7,9] and placenta accrete [12].

Furthermore, other pregnancy complications are not well known to be associated with previous CS due to the limited number of studies on these outcomes. Few studies have reported an increased risk for Gestational Diabetes Mellitus (GDM) [7] and polyhydramnios [6,7] in pregnancy after CS when compared with vaginal delivery. Also, a previous study indicated high incidence of pregnant women with a previous CS diagnosed with fetal anomaly when compared with women with previous vaginal delivery [13]. Studies conducted to support the hypothesis of previous CS association with GDM, polyhydramnios, and fetal anomaly remains sparse to the best of our knowledge. Given the limited evidence on the influence of previous CS on these pregnancy complications such as GDM, polyhydramnios and fetal anomaly and the inconsistencies in the association between previous CS and the placenta disorders shown in other studies, there is a need for research attention on these pregnancy complications to update clinicians and women on the risk associated with CS.

The implementation of the universal two-child policy provides an ideal situation to study previous CS's influence on pregnancy complications. Therefore, this study examines previous CS's influence on pregnancy complications such as Gestational Diabetes Mellitus, polyhydramnios, fetal anomaly, Pregnancy Induced Hypertension (PIH), placenta disorders (placenta previa, placenta abruptions and placenta accreta among women with singleton delivery in the second pregnancies.

Methods

Subject's section

This study used clinical data of 2018 women with singleton delivery in the second pregnancies delivered between January 2015 and October 2017 at the Third Xiangya Hospital of Central South University. These women were identified from the electronic medical records and enrolled in the study. The 2018 women were selected based on the following inclusion criteria: (i) women who had live delivery at ≥ 24 weeks gestation; (ii) had singleton delivery for both the first and this second pregnancy. Women were excluded if they do not meet the criteria above or; (i) women whose pregnancy were as a result of Artificial Reproductive Technology (ART); (ii) women whose records had missing information on the previous mode of delivery, pregnancy complications in the second pregnancy as well as maternal characteristics of second pregnancies.

Clinical data on the previous delivery mode, maternal characteristics and the pregnancy complications in the second pregnancy were retrieved from the electronic medical records and further validated and maintained by our research team. Women with a singleton pregnancy with previous CS in the first pregnancy were categorized as the study group. In contrast, those with spontaneous vaginal delivery for the first pregnancy were categorized as the reference group.

We obtained ethical approval for this study from the Xiangya School of Nursing and the Institutional Review Board from the Third Xiangya Hospital of Central South University, Hunan, China.

Definitions of variables

Maternal characteristics included demographic and obstetric information such as maternal age at second pregnancy, Body Mass Index (BMI), which was obtained from the weight and height of the pregnant woman at the first prenatal booking and was calculated as (weight in kg)/(height in m^2), the number of prenatal care visits ≥ 4 (standard prenatal care according to doctor's suggestion), Interpregnancy Interval (IPI) was also defined as the interval of years between the first delivery and the second pregnancy, history of Terminations of Pregnancy (TOP) before this second pregnancy and preexisting medical conditions which were all diagnosed by an obstetrician (pre-pregnancy diabetes, chronic hypertension, angiocardiography, anemia, systemic lupus erythema, asthma, fibroid, ovarian and fallopian cyst, syphilis, hypothyroidism and hyperthyroidism). The continuous variables of the maternal characteristics were further sub-grouped into categories.

The pregnancy complications for this study are defined as disorders or diseases that occur during the second pregnancy period. Hence the pregnancy complications that obstetricians diagnosed were selected for this study and included Gestational Diabetes Mellitus (GDM), Polyhydramnios, Fetal anomaly, Pregnancy Induced Hypertension (PIH), Placenta Previa, Placenta abruption, Placenta accreta. Gestational Diabetes Mellitus GDM was diagnosed using a 2-h, 75 g oral glucose tolerance test [14]. Polyhydramnios was defined as an abnormally sizeable amniotic fluid of 24 cm or greater during pregnancy and diagnosed through ultrasound examination [15]. The fetal anomaly was defined as a delivery defect or congenital malformation during the intrauterine life and can be identified prenatally or at delivery (WHO). Pregnancy Induced Hypertension (PIH) was defined as diastolic blood pressure >90 mmHg on two occasions, four hours apart or a single reading of >110 mmHg from 20 weeks gestation [16]. Placenta previa is an implantation of the placenta over or near the internal opening of the cervix. Placental abruption is the premature separation of a usually implanted placenta from the uterus, and placenta accrete refer to the clinically apparent morbidly adherent placenta [17].

The study's covariates included significant maternal characteristics and the possible pregnancy complications (in the second pregnancy) known in the published literature as risk factors of the pregnancy complications in this study (potential confounders). For significant maternal characteristics that were used as covariates, we excluded pre-pregnancy diabetes and chronic hypertension when analyzing for GDM and PIH, respectively. We considered potential risk factors for the following: GDM (PIH [18]), polyhydramnios (fetal anomaly [19], GDM [20]) and PIH (placenta disorders [21], GDM [22]).

Statistical analyses

The maternal characteristics were described and summarized by frequencies and percentages. Chi-square and Fisher's exact test was used to compare the groups. Probability values of <0.05 were considered statistically significant. We used univariate and multivariate logistic regression to ascertain the influence of previous CS on pregnancy complications. The influence of the covariates was analyzed. First, maternal age, Body Mass Index (BMI) at booking,

history of pregnancy termination, and significant preexisting medical condition (diabetes, chronic hypertension, asthma, fibroid, ovarian and fallopian cyst) were added as covariates. For the covariates of GDM and PIH, we excluded pre-pregnancy diabetes and chronic hypertension, respectively. Then potential risk factors for GDM (placenta disorders, PIH), polyhydramnios (fetal anomaly, GDM) and PIH (placenta disorders, GDM) were further analyzed. We presented the logistic regression results as crude and adjusted Odds Ratios (ORs) with 95% Confidence Intervals (CIs). The data was analyzed using SPSS 25.0 (IBM Corp., Armonk, NY, USA).

Results

Maternal characteristics

Among the 2018 eligible women with singleton second pregnancy, 942 (46.7%) had experienced one previous CS, while the remaining 1076 (53.3%) had one previous vaginal delivery.

Women with previous CS were older and had advanced age (≥ 35 years) than women with previous vaginal delivery. Those with previous CS had a higher BMI >25.0 kg/m^3 and a longer IPI (5years and above) than those with previous vaginal delivery. Both women with previous CS and previous vaginal delivery had the recommended number of prenatal visits ≥ 4 visits. The history of pregnancy termination was slightly higher among those with previous CS than those with previous vaginal delivery. Furthermore, women with previous CS had a higher rate of preexisting medical diseases such as diabetes, hypertension, asthma, fibroid, cyst of the ovary and fallopian tube than those with previous vaginal delivery (Table 1).

Table 1: Maternal characteristics of women with second pregnancies by the first previous mode of delivery in Hunan, China.

Previous Mode of delivery, n (%)			
Maternal characteristics	**Previous vaginal delivery n= 1076**	**Previous CS n=942**	**P value**
Age, (years)			
<35	716 (66.5)	447 (47.5)	<0.001
≥ 35	360 (33.5)	495 (52.5)	
BMI on admission (kg/m²)			
<18.5	1 (0.1)	1 (0.11)	<0.001
18.5-24.9	359 (33.4)	198 (21.0)	
25.0-29.9	606 (56.3)	558 (59.2)	
≥ 30	110 (10.2)	185 (19.6)	
IPI (years)			
>2	365 (33.9)	149 (15.8)	<0.001
2-4	262 (24.3)	217 (23.0)	
≥ 5	449 (41.7)	578 (61.1)	
Prenatal care visit ≥ 4	938 (87.2)	796 (84.5)	0.085
History of termination of pregnancy	625 (58.1)	625 (66.4)	<. 001
Preexisting medical conditions			
Pre-gestational Diabetes	21 (2.0)	44 (4.7)	0.001
Chronic Hypertension	8 (0.7)	19 (2.0)	0.013
Angiocardioparthy	68 (6.3)	54 (5.7)	0.581
Anaemia	52 (4.8)	43 (4.6)	0.777
Systemic lupus erythema	4 (0.4)	9 (1.0)	0.941
Asthma	13 (1.2)	23 (2.4)	0.037
Fibroid	22 (2.0)	35 (3.7)	0.024
Fallopian and ovarian cyst	11 (1.0)	39 (4.1)	<0.001
Syphilis	3 (0.3)	10 (1.1)	0.47
Hypothyroidism	21 (2.0)	15 (1.6)	0.543
Hyperthyroidism	16 (1.5)	12 (1.3)	0.683

BMI: Body Mass Index; IPI: Interpregnancy Interval

Analysis of previous CS on pregnancy complications

Regarding the pregnancy complications, women with previous CS had a significantly higher rate of Gestational Diabetes Mellitus, fetal anomaly and placenta previa when compared with those with previous vaginal delivery. When these pregnancy complications were analyzed using the univariate binary logistic regression (odd crude ratio), they were all associated with previous CS (Table 2).

After the multivariate logistic regression (adjustment for the covariates, which include significant maternal characteristics and potential risk factors), there was an association between previous CS with GDM, fetal anomaly and placenta previa. Comparing the adjusted odds ratio of the pregnancy complications among women with previous CS and previous vaginal delivery (reference group), women with previous CS were 1.44 times more likely to have GDM (95% CI, 1.09-1.89) and 14.26 times more likely to have fetal anomaly (95% CI, 4.21-48.25). Furthermore, women with previous CS were 2.89 times more likely to have placenta previa (95% CI, 1.62-5.15) than those with previous vaginal delivery. In contrast, polyhydramnios, pregnancy-induced hypertension, placenta abruption and placenta accreta were the pregnancy complications that were not associated with previous CS compared with previous vaginal delivery in our study (Table 3).

Discussion

This study examined previous CS's influence on pregnancy complications among women having their second pregnancy under the Chinese two-child policy's implementation. The main findings of this study indicated that GDM, fetal anomaly and placenta previa are the pregnancy complications associated with previous CS independent of maternal age, BMI at admission, IPI, history of termination of pregnancy, significant preexisting medical conditions and potential risk factors (pregnancy complications in the second pregnancy that are confounders) for the pregnancy complications in this study.

This paper has shown that previous CS is associated with increased risk of GDM, fetal anomaly and placenta previa but not polyhydramnios, PIH, placenta abruption, and placenta accreta. To our knowledge, this is the first study to support the hypothesis of previous CS's influence with GDM and also the first recent study to show an association between previous CS and fetal anomaly.

Pregnant women with previous CS were 1.44 times at high risk of GDM. The results of Hu's study also presented this relationship [7], although there is an unknown exact biological relationship between previous CS and GDM. Nonetheless, there has been speculation that inefficient placenta function due to abnormal trophoblastic invasion that may occur due to the uterine changes induced by prior CS can interfere with uteroplacental blood flow leading to subsequent gestational complications, including GDM [23]. Furthermore, a normal placenta's buffer action against hyperglycemia in the mother [24] may impede due to placenta insufficiency as a result of placenta abnormalities associated with previous CS. Therefore, this may cause GDM in pregnancy. Also, placenta hypoxia associated with

Table 2: Crude odd ratios for pregnancy complications associated with previous cesarean section in the second pregnancy, Hunan, China.

Previous Mode of delivery, n (%)								
Pregnancy complications	**Previous vaginal delivery n=1076**	**Previous CS n=942**	**B**	**S. E**	**Wald X^2**	**P**	**OR**	**95% CI**
GDM	112 (10.4)	156 (16.6)	0.535	0.133	16.248	0	1.708	1.317- 2.216
Polyhydramnios	2 (0.2)	4 (0.4)	0.829	0.867	0.913	0.339	2.29	0.418- 12.531
Fetal anomaly	3 (0.3)	44 (4.7)	2.864	0.598	22.899	0	17.525	5.423- 56.638
PIH	43 (4.0)	51 (5.4)	0.319	0.212	2.257	0.133	1.375	0.908- 2.084
Placenta previa	18 (1.7)	46 (4.9)	1.104	0.282	15.372	0	3.018	1.737- 5.241
Placenta Abruption	9 (0.8)	6 (0.6)	-0.274	0.529	0.269	0.604	0.76	0.269-2.143
Placenta Adhesion	118 (11.0)	102 (10.8)	0.014	0.143	0.01	0.921	0.986	0.745- 1.305

B: Unstandardized Regression Weight/ Coefficient of the Constant; S.E: Standard Error; Wald X^2: Chi-square test; *P*: Significant Value; OR: Odds Ratio; CI: Confidence Interval; GDM: Gestational Diabetes Mellitus; PIH: Pregnancy Induced Hypertension

Table 3: Adjusted odd ratios for pregnancy complications associated with previous cesarean section in the second pregnancy, Hunan, China.

Previous Mode of delivery, n (%)								
Pregnancy complications	**Previous vaginal birth n=1076**	**Previous CS n=942**	**B**	**S. E**	**Wald X^2**	**P**	**OR**	**95% CI**
GDM †	112 (10.4)	156 (16.6)	0.364	0.14	6.715	0.01	1.438	1.093 - 1.894
Polyhydramnios ‡	2 (0.2)	4(0.4)	0.439	0.948	0.215	0.643	1.551	0.242 - 9.946
Fetal anomaly	3 (0.3)	44 (4.7)	2.657	0.622	18.253	0	14.258	4.213 - 48.248
PIH ¶	43 (4.0)	51 (5.4)	-0.081	0.232	0.123	0.725	0.922	0.585 -1.452
Placenta previa	18 (1.7)	46 (4.9)	1.061	0.294	12.994	0	2.89	1.623 - 5.148
Placenta abruption	9 (0.8)	6 (0.6)	-0.758	0.569	1.777	0.183	0.469	0.154 - 1.428
Placenta Accreta	118 (11.0)	102 (10.8)	-0.042	0.151	0.078	0.78	0.959	0.714- 1.288

B: Unstandardized Regression Weight/ Coefficient of the Constant; S.E: Standard Error; Wald X^2: Chi-Square Test; P: Significant Value; aOR: Adjusted Odds Ratio; CI: Confidence Interval; GDM: Gestational Diabetes Mellitus; PIH: Pregnancy Induced Hypertension

aOR, Models first adjusted for maternal age, BMI at admission, IPI, history of pregnancy termination, preexisting medical conditions (pre-gestational diabetes, chronic hypertension fibroid, ovarian and fallopian cyst and asthma). Pre-gestational diabetes was not added to the covariates of GDM and chronic hypertension was also not added to the covariates of PIH

†Further adjusted for PIH in the second pregnancy

‡Further adjusted for fetal anomaly and GDM in the second pregnancy

¶Further adjusted for placenta previa, placenta abruption, placenta adhesion and GDM in the second pregnancy

placenta insufficiency may also affect the glucose transporters found in the placenta's syncytiotrophoblast, responsible for increasing glucose transport from the mother to the placenta [25]. This placenta insufficiency may result in hyperglycemia in the maternal circulation that may contribute to GDM. GDM in previous pregnancy can be recurrent in the subsequent pregnancy. However, a study [7] indicated that recurrent GDM in previous pregnancy does not significantly reduce previous CS's influence on GDM. Also, advanced maternal age and overweight or obesity is identified as risk factors for gestational diabetes mellitus. Although most of the women with previous CS were of advanced maternal age and were overweight, we adjusted for these confounders. Nevertheless, there remained an association between previous CS and GDM. However, further studies elucidating the current findings on the relationship between previous CS and GDM and the possible biological and physiological relationship need to be appraised.

Furthermore, previous CS showed a significant impact on the fetal anomaly in our study. To our knowledge, this is the first recent study that shows the association between previous CS and fetal anomaly. These findings of this study, might be due to the increased risk of placenta disorders associated with previous CS, which can predispose the women to placenta insufficiency that may affect the fetus's normal development leading to increased risk for fetal anomaly [26,27]. It could also be speculated that the risk of fetal anomaly may be due to the uterine cavity changes induced by a uterine scar from previous CS, which can alter the uterus's anatomy that predisposes women to have a fetal anomaly. Although advanced maternal age, pre-gestational diabetes, and chronic hypertension are considered high-risk fetal anomaly factors, there remained a higher risk for fetal anomaly associated with previous CS when adjusted for our studies. However, most of the pregnancies with fetal anomaly were terminated at the first or second trimester, which may not represent the exact number of women with a fetal anomaly. Therefore, more studies focusing on the association between previous CS and fetal anomaly need to be conducted in the future.

Among the placenta disorders, only placenta previa has an association with previous CS in our study. Previous CS was associated with an increased risk of placenta previa with an adjusted Odds Ratio (ORs) of 2.89, higher than some previous studies [7,28,29]. These previous studies have indicated the association between previous CS and placenta previa, but the Odd Ratios (ORs) were lesser than our study. However, parity and multiple gestations, considered to increase the risk of placenta previa in a previous study [30], were excluded from our study. Furthermore, when adjusted for the covariates (significant maternal characteristics), which were also considered potential confounders to placenta previa in previous studies [28,31], it remained a higher risk. This higher Odd Ratio (OR) may be due to the study conducted with data from a tertiary hospital where women with high-risk pregnancies such as placenta previa are referred to. Currently, the exact cause of placenta previa is unknown. However, placenta previa is hypothesized to be related to a failure of apparent placental migration, impaired differential growth of the lower uterine

segment, and deficient decidua basalis in the presence of previous surgery injury [10,32].

However, polyhydramnios was not associated with previous CS in our study; this is in variance with previous studies [6,7]. The difference might be attributed to the small number of pregnant women with polyhydramnios in our study, which contributed to a small effect size that did not associate previous CS and polyhydramnios. This is supported by the wide Confidence Interval (CI) observed in its Odds Ratio (OR). Furthermore, among the placenta disorders associated with previous CS in the previous studies, placenta abruption and placenta accreta did not show any association with previous CS. This finding is in variance with other previous studies [1,8-10]. An observation of no increased risk between previous CS and Pregnancy Induced Hypertension (PIH) existed in our study. This may be due to a smaller number of women with PIH in our study which could not predict the association.

Our study also confirms the high CS rate of 46.7% in the first delivery as the previous CS. This finding is congruent with the WHO study, which indicated China to be the country with the highest CS rate of 46.2% among the 24 Asian countries. This present study is one of the few studies conducted after the two-child policy that examines previous CS's influence on pregnancy complications. This study also adjusted for several confounding factors that could have influenced our result. The study was conducted three years after implementing the two-child policy that accurately represents pregnancy complications among women with a second pregnancy.

The present study also had some limitations, primarily due to the retrospective nature of the design. Firstly, misclassification of the pregnancy complications may exist just as other administrative databases, which can lead to bias, but this may have occurred randomly and therefore could have the tendency of reducing the bias that could have occurred in this study.

Secondly, some details of information on the first pregnancy, such as the pregnancy outcomes and indications for previous CS, were not present due to the transitioning from paper medical records entry to electronic medical records. Information regarding their first pregnancy, which happened very long ago, was not captured. There can be a reduction of bias from lack of indication for the previous CS since most women during the one-child policy had CS without any medical reasons [1,3]. Also, some women did not have their first child at our hospital; hence the available details of the first pregnancy were obtained from maternal self-report, of which there could be a presence of recall bias.

Thirdly, the BMI used for the study was BMI at admission for delivery, which may not represent the exact BMI since the fetus's weight could have influenced maternal BMI at admission. Lastly, there could be selection bias since most women who had obstetric complications in their first pregnancy might opt for a tertiary hospital or be referred to a tertiary hospital to seek medical help during their subsequent pregnancy.

Conclusion

In conclusion, our study revealed the association of previous first CS with pregnancy complications such as GDM, fetal anomaly and placenta previa on singleton pregnancy among women having their second child under the universal two-child policy. Hence, this study provides the needed information for obstetricians, nurses and midwives to acquaint themselves with knowledge pertaining to pregnancy complications and provides intensive management and follow-ups of women with previous CS to ensure a healthy mother and baby throughout the pregnancy and delivery periods. Such information obtained from this study could help the decision-making process regarding CS for the health care providers and expectant mothers alike, mainly when there are no clear medical indications for CS.

Data Availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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