The Effects of Birth Spacing After Cesarean Delivery on Pregnancy Outcomes: A Retrospective Cohort Study

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Abstract

The changing family planning policy from One-Child to Two-Child Policy, led to a significant increase in the proportion of pregnancies with variant interpregnancy intervals (IPIs) after previous cesarean section (CS). To examine the relationship between IPI and perinatal outcomes, we conducted a retrospective cohort study of 1854 women having a history of CS and delivered in 2016 at West China Second University Hospital. With an IPI of 24-59 months as the reference, the associations between various IPIs (<24, 60-119, and ≥120 months) and pregnancy outcomes were examined by multivariate logistic regression analysis with multiple models. We found that IPI <24 months significantly increased the risk of anemia in late pregnancy (aOR 2.09, 95% CI 1.21-2.62, p = 0.008). IPI <24 months was associated with a higher risk for incomplete uterine rupture (OR 1.30, 95% CI 1.05-1.61), IPI ≥60 months was related to a lower risk for incomplete uterine rupture (IPI = 60-119 months: OR 0.77, 95% CI 0.62-0.95; IPI ≥120 months, OR 0.59, 95% CI 0.38-1.08), and women with IPI ≥120 months were more likely to develop gestational hypertension (GHP) (p = 0.036) and gestational diabetes mellitus (GDM) (p = 0.001). These effects became nonsignificant after adjusting possible confounders. This study revealed that IPI may combine with other factors to affect GHP, GDM, and uterine rupture in the subsequent pregnancy after previous CS.

Introduction

According to the recommendations of the World Health Organization (WHO), the interval from previous live birth and subsequent conception should be a minimum of 2 years, regardless of the previous delivery mode[1]. In 2016, when the universal one-child policy was replaced with the two-child policy, all couples in China were allowed to have a second child[2]. Because the one-child policy had been in place for 36 years in China, this change was very likely to increase the number of high-risk parturients with typical risk factors such as advanced maternal age (AMA) and a long interpregnancy interval (IPI). Additionally, there has also been a sharp increase in pregnancies with previous cesarean section (CS) due to the high CS rates over recent decades in China[3,4]. Consequently, it is a great challenge for obstetricians in China to manage the growing number of high-risk parturients with multiple risk factors, such as AMA, a long IPI, and previous CS, which have been demonstrated to increase the risk of adverse pregnancy outcomes, such as uterine rupture[5,6], gestational hypertension (GHP)[7,8], gestational diabetes mellitus (GDM)[9], preterm delivery, low birth weight (LBW) and neonatal intensive care unit (NICU) admission[10-15].

We performed a preliminary systematic review of the association between IPI and adverse pregnancy outcomes after previous CS and found that pregnancy spacing after previous CS was related to the risk of uterine rupture, the probability of a successful vaginal birth after CS (VBAC), and the risk of placenta previa[16]. However, we cannot conclude the optimal IPI after previous CS because different measurements and categorizations of birth spacing were used in previous studies. Furthermore, 36 years after implementing the one-child policy, China implemented the two-child policy broadly; as a result, the number of pregnant women with long IPIs increased significantly, and this family planning policy caused

the number of pregnancies and deliveries among Chinese women to be quite different from those of other countries. Thus, there is no relevant research conducted exclusively for Chinese women. Therefore, we conducted this large retrospective cohort study to explore the association between IPI after previous CS and adverse pregnancy outcomes.

Methods

This retrospective cohort study was conducted at West China Second University Hospital (Sichuan University), a tertiary care hospital. Women with a history of CS who gave birth from January 2016 to December 2016 at West China Second University Hospital were included in this cohort. This study was approved by the Research Ethics Committee, Chengdu, China (ref. number 2016-010; date of approval 2016-05-25) and written informed consent was obtained from all subjects. All experiments and methods were performed in accordance with relevant guidelines and regulations. Data were obtained from the electronic medical system and were supplemented by information from medical records. Two trained abstractors were instructed to review and abstract data from the medical chart.

Our primary analyses included all women who had at least one previous CS at 28 to <42 weeks of gestation and delivered at 28 to <42 weeks of gestation. We excluded women who met the following criteria: (1) underwent uterine surgery other than CS; (2) did not receive routine antenatal care; (3) had multiple pregnancies; and (4) had fetal malformations.

IPI was defined as the number of months between the date of last cesarean operation and the conception date of the subsequent delivery, which was estimated by the delivery date of the index pregnancy minus its gestational age at birth. The IPI was categorized into four groups: less than 24 months, 24 to 59 months, 60 to 119 months, and 120 months or greater.

Maternal outcomes included anemia in late pregnancy, GHP, GDM, an abnormal placental position, pernicious placenta, placenta accreta, placental abruption, premature rupture of membranes (PROM), uterine rupture (including incomplete and complete uterine rupture), postpartum hemorrhage (PPH), and hysterectomy. According to the WHO guidelines, anemia in late pregnancy was defined as a hemoglobin concentration less than 110 g/L between 32 and 42 weeks of gestation[41]. The definitions of gestational hypertension complied with the consensus statement from the International Society of Study of Hypertension in Pregnancy (ISSHP)[42]. The definitions of GDM (where Grade A1 indicates that blood glucose is well controlled by nondrug therapy during pregnancy and Grade A2 indicates that blood glucose should be controlled by drugs during pregnancy) complied with the WHO criteria[43]. Uterine rupture was measured during CS by experienced obstetricians, and complete rupture was defined as a tear through all layers of the uterine wall, and incomplete rupture was defined as a tear in the muscular layers with intact serosa or amniotic membranes[44]. Adverse fetal outcomes included preterm birth, admission to the NICU, low 1-min Apgar score, and LBW. LBW was defined as a birth weight less than 2500 g, and a low 1-min Apgar score was defined as an Apgar score of less than 10 during 1 minute after birth evaluated by a professional obstetrician.

The demographic and clinical characteristics of the four groups may be significantly different, and these factors may be potential confounding factors affecting the association between IPI and perinatal outcomes. We established multivariable logistic regression analysis models to adjust for these factors and then analyzed the effect of the IPI after CS on adverse maternal and fetal outcomes. Since previous studies have confirmed that emergency CS significantly increases the risk of adverse perinatal outcomes[45], we established analysis models to separately analyze the relationships between IPI after emergency CS or elective CS and pregnancy outcomes by using a multivariable logistic regression method.

Sociodemographic characteristics and adverse pregnancy outcomes were compared among the four groups, the chi-squared test was used for categorical variables, and one-way analysis of variance was used for continuous variables. Multivariable logistic regression analysis was separately conducted for the association between different IPIs and each pregnancy outcome after controlling for the known and suspected confounding factors, and the analysis used an IPI of 24-59 months as the reference category, as it was the recommended IPI by WHO guidelines[1]. Data analyses were performed using the software package SPSS statistics version 21.0 (SPSS Inc.) A p-value < 0.05 for both sides was considered significant.

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

Results

A total of 1854 deliveries with a history of CS were reported at West China Second University Hospital (Sichuan University) between January 1, 2016, and December 31, 2016. According to the exclusion criteria, 192 women were excluded: 51 cases without routine antenatal care, 85 cases of multiple pregnancy, 44 cases of fetal malformation, and 12 cases of uterine surgery other than CS. The final sample size for this retrospective cohort study was 1662, and these women were categorized into 4 groups according to different IPIs: 121 women with an IPI of < 24 months, 583 women with an IPI of 24 to 59 months, 712 women with an IPI of 60 to 119 months, and 246 women with an IPI of 120 months or greater (Figure 1).

Maternal characteristics. In the entire cohort, the mean maternal age was 33.3 years (SD 2.9), and women with an IPI of 120 months or greater were significantly older than the other three groups, with a value of 37.1 years (SD 3.0). To test the collinearity of the interpregnancy interval and maternal age, we performed a collinearity diagnostic, which indicated low collinearity between the two factors. Women with an IPI of 120 months or greater had a higher prevalence of gravidity ≥ 3 than the other four groups while having a lower prevalence of parity ≥ 2 and prior CS ≥ 2 and a smaller gestational age at delivery. In addition, significant differences were found among the four groups in terms of the distributions of maternal body mass index (BMI) ($p = 0.005$) and educational status ($p < 0.001$). Women with an IPI of less than 24 months had a history of 2 CSs or more, and among them, the proportion (3.5%) of in vitro fertilization and

embryo transfer (IVF-ET) was higher than the rates among the other three groups. There were no significant differences in the distribution of history of vaginal delivery or in the proportion of pregnant women with chronic hypertension or pregestational diabetes mellitus (PGDM) among the four groups. Only 2.8% (n = 47) of women achieved VBAC, and the rates of emergency CS and CS with indications were not different across the four groups (Table 1).

Univariate analysis of the correlation between IPIs and pregnancy outcomes. Compared with the other three groups, women with an IPI of 120 months or greater had a higher rate of GHP (6.1%, p < 0.036) and GDM (34.9%, p = 0.001). There were statistically significant differences in the incidence of uterine rupture among the four groups (p = 0.041), and the proportion of uterine rupture in women with an IPI of 120 months or greater (4.9%, n = 12) was significantly lower than that among women in the other three groups. No significant difference was found across the four groups regarding to maternal outcomes, including anemia, low placenta, placenta previa, pernicious placenta, placenta accreta, placental abruption, PROM, PPH, and hysterectomy. Groups with an IPI of less than 24 months (4.1%, n = 5) and an IPI of 120 months or greater (6.1%, n = 15) were more likely to deliver before 34 weeks of gestation (p = 0.002). Babies in the group of women whose IPI was equal to or greater than 120 months had significantly lower birth weights (p = 0.017) and shorter birth lengths (p = 0.035) than those in the other three groups. No significant difference was found across the four groups regarding to perinatal outcomes, including low 1-min Apgar score, LBW and admission to the NICU (Table 2).

Multivariable logistic regression analysis of the associations among anemia, GHP, GDM and IPI. With an IPI of 24-59 months as the reference category, our analysis suggested that an IPI of less than 24 months was related to an increased risk of developing anemia in late pregnancy (adjusted odds ratio (aOR) 2.09, 95% CI 1.21-2.62, p = 0.008), while an IPI of 60 to 119 months or 120 months or greater was not associated with anemia in the third trimester (IPI of 60 to 119 months, aOR 1.37, 95% CI 0.94-1.98, p = 0.098; IPI of 120 months or greater, aOR 1.39, 95% CI 0.81-12.38, p = 0.232). IPIs of less than 24 months, 60 to 119 months, and 120 months or greater had no significant effect on the risk of developing GHP or GDM (Table 3).

Multivariable logistic regression analysis of the associations between other pregnancy outcomes and IPIs. Multivariable logistic regression analysis using an IPI of 24-59 months as the reference category was conducted to examine the associations between different IPIs and adverse perinatal outcomes among 1662 women with previous CS. Model 1 did not adjust for any confounding factors (Table 4), while model 2 adjusted for maternal age, maternal BMI, educational status, assisted reproductive technology (ART), number of previous CSs, previous vaginal delivery and previous emergency CSs (Table 5). In model 1, an IPI of less than 24 months significantly increased the risk of incomplete uterine rupture (OR 1.30, 95% CI 1.05-1.61), while an IPI of 60 to 119 months (OR 0.77, 95% CI 0.62-0.95) and 120 months or greater (OR 0.59, 95% CI 0.38-1.08) significantly reduced the risk of incomplete uterine rupture. In model 2, after adjustments for some confounders, the results suggested that the IPI was not a risk factor for incomplete uterine rupture. In models 1 and 2, we found that IPI had no effect on other adverse

perinatal outcomes, including pernicious placenta, abnormal placental position, PROM, PPH, hysterectomy, low 1-min Apgar score, and admission to the NICU.

Studies have confirmed that emergency CS can significantly increase the risk of adverse perinatal outcomes[17]. The other four models were established by using multivariable logistic regression analysis to analyze the relationship between the IPI of 552 women with emergency CS and that of 1099 women with elective CS and perinatal outcomes separately. Model 3 did not adjust for any confounding factors in women with emergency CS (Table 6), while model 4 adjusted for maternal age, maternal BMI, educational status, ART, number of previous CSs, and previous vaginal delivery (Table 7). In models 3 and 4, the association between IPI and incomplete uterine rupture among women with emergency CS always remained nonsignificant ($p > 0.05$). Model 5 did not adjust for any confounding factors among women with elective CS (see Supplementary Table S1), while model 6 adjusted for maternal age, maternal BMI, educational status, ART, number of previous cesarean sections, and previous vaginal delivery (see Supplementary Table S2). In model 5, IPI was a risk factor for incomplete uterine rupture ($p = 0.048$). An IPI of less than 24 months significantly increased the risk of incomplete uterine rupture (OR 1.35, 95% CI 1-1.82), and an IPI of 60 to 119 months (OR 0.74, 95% CI 0.55-1) or 120 months or greater (OR 0.55, 95% CI 0.3-0.99) significantly reduced the risk of incomplete uterine rupture (see Supplementary Table S1). In model 6, after adjustments for some confounders, we found that the IPI of women with a history of selected CS was not a risk factor for incomplete uterine rupture ($p = 0.131$) (see Supplementary Table S2).

Discussion

Because birth spacing might affect maternal health status and nutrient concentrations, it is plausible that the IPI after CS is associated with perinatal outcomes. Some studies have recognized the increased risk of anemia in women with IPIs shorter than 6 to 24 months regardless of a history of CS[18-20]. A study found that a short IPI of <18 months after CS was related to a greater risk of anemia[21]. Our study indicates that an IPI of <24 months increased the risk of anemia in late pregnancy. Anemia among women with a short IPI is a status of total iron depletion, which is seen to be the consequence of inadequate time from previous delivery to replenish the iron stores[22].

Many studies have reported the association between birth spacing and adverse neonatal outcomes[15], while limited studies have been conducted exclusively for women with a history of a previous CS. A large meta-analysis of multiparous women in 2006 concluded that IPIs of <18 months and of ≥ 60 months had the highest risk for preterm birth[15]. Moreover, Class et al used cousin and sibling comparisons and revealed that an IPI of 60 months or greater had elevated risks for preterm delivery (< 37 weeks)[23]. Compared with an IPI of 24-59 months, our results implied that the rate of premature delivery before 34 weeks increased in the group of women with an IPI of <24 months and of ≥120 months. Due to the substantial growth of parturients with extremely long IPIs after implementation of the revised reproductive policy in China, we separately analyzed the association between adverse perinatal outcomes

and IPIs of ≥120 months, which was not addressed in the non-Chinese studies. Zhu et al attributed the relationship between long intervals and adverse perinatal outcomes to “physiological regression”, the hypothesis being that women’s reproductive capacity after delivery physiologically declines and gradually reaches the levels of primigravid women[24]. The reason for the lack of an association between a short IPI after previous CS and adverse perinatal outcomes could be the small proportion (7.28%) of short IPIs in this study.

The relationship between IPI after CS and abnormal placental position was reported in two studies, which reported that both were unrelated[25,26]. Our investigation also indicated no association between abnormal placental position and IPI. The association between a short IPI and an increased risk of inadequate healing of uterine scars has been recognized[27]. Although our analysis included maternal age as a potential confounder, we still attribute the association between a long IPI and abnormal placental position to the physiological changes in the uterus in AMA. Several studies have observed an increased occurrence of placenta previa among women with AMA and thought that AMA may lead to compromised uteroplacental blood flow, thus increasing the risk of placental previa[28-30]. We found that since only 9 patients were pregnant within 1 year after CS and none of them had abnormal placental positions, there may be a bias.

Our investigation demonstrated that the incidence of GHP and GDM was significantly increased among women with IPIs of ≥120 months. Nevertheless, the effect was nonsignificant after adjustment. Hanley et al showed that women with a longer IPI were more likely to develop GDM or GHP[31], but the study took women with multiple pregnancies as its own control, and maternal age increased with increasing in IPI. In our study, women with an IPI of ≥120 months were significantly older than those in the other three groups, and nearly 80% of these women had a gestational age of over 35 weeks. In addition, overweight and obesity have also been proven to be risk factors for GHP and GDM[18,19]. However, in our study, there were no significant differences in the proportions of high maternal BMI among the four groups. Therefore, the correlation between GHP, GDM and IPI may be affected by maternal aging.

Repeat CS is acknowledged to increase the risk of maternal complications[32], and TOLAC is an option for women with a scarred uterus. Successful TOLAC can avoid numerous surgery-related morbidities and is beneficial to subsequent pregnancies. However, failed TOLAC is related to an increased risk of uterine rupture, which is detrimental for both the parturient and the fetus[33,34]. A systematic study reported that the median incidence of complete uterine rupture was 1% among women with previous CS[35], but the range of incidences of incomplete uterine rupture was wide at 2.1%-10.1%[36,37]. In this study, 8.7% (n = 145) of women were found to have incomplete uterine rupture during the operation, while no complete uterine rupture was reported. Previous studies indicated that the risk of complete uterine rupture increased with AMA, grandmultiparity (≥ 6), an extremely short IPI and macrosomia[6,38-40]. We found that the IPI of women with a history of emergency CS was not related to the occurrence of uterine rupture, while in the group of women with a history of selected CS, the risk of incomplete uterine rupture decreased in the groups with IPIs of 60-119 months and ≥120 months. Studies have reported a

significantly increased risk of uterine rupture during emergency CS, but mothers with elective repeat cesarean section (ERCD) had almost no risk of uterine rupture (0-0.004%)[39]. We assumed that the risk of uterine rupture was underestimated for elective CS, mitigating the risk of uterine rupture.

One of the strengths of this study is its focus on the effects of extremely long IPIs, which is in accordance with the current birth policy in China. Our results suggest that shorter and longer IPIs should be a risk factor in subsequent pregnancy for women with a history of CS. In addition, our analysis of the adverse pregnancy outcomes related to IPI is relatively systemic, comprising scar-related morbidities and common pregnancy morbidities. The main limitation of our study is its retrospective design, which precludes a power analysis. Moreover, the rate of trial of labor after cesarean (TOLAC) was only 2.87% (*n* = 47), and the incidence of uterine rupture may be underestimated. We could not accurately analyze the effects of IPI on the success of VBAC or the risk of uterine rupture for the small proportion of women with TOLAC. A larger, prospective study would have to be carried out to identify candidates for TOLAC and provide intensive prenatal care to guarantee safety during TOLAC. Our previous systematic evaluation found that an IPI of more than 6-8 months after CS can reduce the risk of adverse maternal and neonatal outcomes, which is quite different from the results of this study. Our conclusions regarding a short IPI are based on a small sample size and should thus be interpreted with caution. Given that the WHO recommends an IPI of ≥24 months, further studies of a short IPI would have to be in a prospective design.

Conclusion

Our study indicates that an IPI of <24 months is related to a greater risk of anemia in late pregnancy. IPI may synergize with other factors to increase the risk of incomplete uterine rupture. An extremely long IPI of ≥120 months is related to higher risks of GHP and GDM due to increasing maternal age. An optimal IPI and gestational age should be considered for families planning to have a second baby.

Declarations

Acknowledgments

All the analyses, interpretations and conclusions that were derived from the data source and included in this article are those of the authors. This study was supported by West China Second University Hospital (Sichuan University).

Contribution to authorship

R. Z. was involved in the conception and planning of the study, interpretation of the data, and critical revision of the article; Q. X. was involved in carrying out of the study, writing the first draft and critical revision of the article; L. Y. was involved in the interpretation of the data, and co-writing of the article; Q. W. and W. X. was involved in acquisition, analysis of the data; X. W. was involved in analysis of the data and revision of the article.

Disclosure of interests

None of the authors has a conflict of interest.

Details of ethics approval

Ethical approval was obtained from the Research Ethics Committee, Chengdu, China (ref. number 2016-010; date of approval 2016-05-25).

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Tables

Table 1. Baseline Maternal Characteristics in the Four Groups Categorized by Interpregnancy Interval.

Maternal Parameters	IPI of < 24 mon (n = 121)	IPI of 24-59 mon (n = 583)	IPI of 60-119 mon (n = 712)	IPI of ≥120 mon (n = 246)	*P* value
Maternal age at index conception (y)	30.75±3.5	31.43±3.31	33.88±3.2	37.14±2.95	< 0.001
≥ 35	16 (13.2)	86 (14.8)	284 (39.9)	195 (79.3)	0.001
< 35	105 (86.8)	497 (85.2)	428 (60.1)	51 (20.7)	
Education (y)					< 0.001
≤ 12	9 (7.4)	36 (6.2)	52 (7.4)	23 (9.4)	
13-16	10 (8.3)	48 (8.3)	74 (10.5)	34 (13.9)	
≥ 17	102 (84.3)	497 (85.5)	578 (82.1)	188 (76.7)	
BMI, No. (Kg/m^2)					0.005
< 18	19 (15.7)	74 (12.7)	55 (7.7)	14 (5.7)	
18-23.9	80 (66.1)	395 (67.8)	525 (73.7)	173 (70.3)	
24-27.9	22 (14.9)	93 (16)	116 (16.3)	51 (20.7)	
> 28	4 (3.3)	21 (3.6)	16 (2.2)	8 (3.3)	
Number of previous pregnancies					< 0.001
≥ 3	66 (54.5)	366 (62.8)	530 (74.4)	218 (88.6)	
< 3	55 (45.5)	217 (37.2)	182 (25.6)	28 (11.4)	
Parity ≥ 2	16 (13.2)	38 (6.5)	26 (3.7)	10 (4.1)	< 0.001
Prior cesareans ≥ 2	16 (13.2)	33 (5.7)	21 (2.9)	5 (2.0)	0.001
Prior vaginal birth	4 (3.3)	8 (1.4)	11 (1.5)	6 (2.4)	0.384
IVF-ET	2 (3.5)	6 (1.0)	4 (0.6)	3 (1.2)	0.007
Preexisting hypertension	2 (1.7)	2 (0.3)	4 (0.6)	4 (1.6)	0.128
Preexisting diabetes	0 (0)	3 (0.5)	2 (0.3)	2 (0.8)	0.60
Gestational age at delivery (weeks)	38.05±1.75	38.07± 1.81	38.12± 1.76	37.72± 2.21	0.027

Mode of delivery					0.178
Repeated cesarean section	117 (96.7)	560 (96.1)	696 (97.8)	242 (98.4)	
Vaginal birth after CS	4 (3.3)	23 (3.9)	16 (2.2)	4 (1.6)	
Type of repeated cesarean section					
Emergency cesarean section	38 (32.2)	179 (31.9)	220 (31.6)	87 (36.0)	0.641
CS with indications	45 (37.2)	191 (34)	216 (31)	85 (35.1)	0.403

Data are expressed as mean ± SD, or n (%) with p-value from exact chi-square.

IPI, interpregnancy interval.

BMI, body mass index; IVF-ET, in vitro fertilization and embryo transfer.

Table 2. Rates of Maternal and Neonatal outcomes in the Four Groups Categorized by Interpregnancy Interval.

Perinatal outcome	IPI of < 24 mon (n = 121)	IPI of 24-59 mon (n = 583)	IPI of 60-119 mon (n = 712)	IPI of ≥ 120 mon (n = 246)	*P* value
Anemia	22 (18.2)	57 (9.8)	90 (12.6)	32 (13)	0.057
GHP	15 (4.2)	5 (2.6)	22 (3.1)	15 (6.1)	0.036
GDM	21 (18.2)	120 (20.6)	156 (21.9)	86 (34.9)	0.001
Grade A1	17 (14.9)	107 (18.4)	136 (19.1)	79 (32.1)	
Grade A2	4 (3.3)	13 (2.2)	20 (2.8)	7 (2.8)	
Placenta inherence	5 (8.9)	46 (7.9)	50 (7.0)	21 (8.5)	0.9
Placental position					0.256
Normal	107 (88.4)	522 (89.5)	637 (89.5)	215 (87.4)	
Low placenta	9 (7.4)	18 (3.1)	31 (4.4)	16 (6.5)	
Partial or marginal placenta previa	1 (0.8)	10 (1.7)	16 (2.2)	4 (1.6)	
Complete placenta previa	4 (3.3)	33 (5.7)	28 (3.9)	11 (4.5)	
Pernicious placenta	7 (5.8)	40 (6.9)	40 (5.6)	19 (7.7)	0.629
Placenta accreta	11 (9.1)	46 (7.9)	50 (7.0)	21 (8.5)	0.787
PROM	17 (14)	68 (11.7)	108 (15.2)	29 (11.8)	0.258
Uterine rupture	12 (9.9)	63 (10.8)	58 (8.1)	12 (4.9)	0.041
Placental abruption	2 (1.7)	3 (0.5)	2 (0.3)	4 (1.6)	0.258
Postpartum hemorrhage	5 (4.1)	35 (6.0)	43 (6.0)	16 (6.5)	0.835
Hysterectomy	2 (1.7)	6 (1.0)	7 (1.0)	3 (1.2)	0.921
Preterm birth	16 (13.2)	72 (12.3)	77 (10.8)	39 (15.9)	0.282
Preterm birth < 34 weeks	5 (4.1)	15 (2.6)	11 (1.5)	15 (6.1)	0.002
Birth weight (g)	3247±499	3233±522	3290±502	3174±558	0.017
Birth length (cm)	49.25±2.39	48.99±2.89	49.23±2.52	48.68±2.89	0.035
LBW	3 (5.5)	38 (6.5)	40 (5.6)	26 (10.6)	0.071
1-min Apgar score <10	5 (4.1)	3 (5.3)	28 (3.9)	13 (5.3)	0.625
NICU admission	17 (12.7)	57 (9.8)	72 (10.1)	28 (11.4)	0.519

Data are expressed as mean ± SD, or n (%) with p-value from exact chi-square.

IPI, interpregnancy interval.

GDM, gestational diabetes mellitus; GHP, gestational hypertension; PROM, premature rupture of membrane.

LBW, the birth weight of newborns is less than 2500g; NICU, neonatal intensive care.

Table 3. Association among Anemia, GHP, GDM and IPI in the Three Groups with IPI of <24, 60-119 and ≥ 120 months.

	IPI of <24 mon (n = 121)		IPI of 60-119 mon (n = 712)		IPI of ≥ 120 mon (n = 246)	
	aOR (95% CI)	*P* value	aOR (95% CI)	*P* value	aOR (95% CI)	*P* value
Anemia	2.09 (1.21-3.62)	0.008	1.37 (0.94-1.98)	0.098	1.39 (0.81-2.38)	0.232
GHP	1.91 (0.67-5.45)	0.227	1.06 (0.53-2.13)	0.874	1.65 (0.69-3.98)	0.262
GDM	1.28 (0.73-2.23)	0.395	1.21 (0.89-1.64)	0.218	0.86 (0.58-1.3)	0.482

IPI, interpregnancy interval.

aOR, adjusted odds ratio; CI, confidential index; GHP, gestational hypertension; GDM, gestational diabetes mellitus.

Adjusted for maternal age, maternal body mass index, education status, gravidity, number of previous cesarean section.

Table 4. Association between other Perinatal Outcomes and IPI in the Three Groups with IPI of <24, 60-119 and ≥ 120 months.

	Index	IPI of <24 mon (n = 121)	IPI of 60-119 mon (n = 712)	IPI of ≥ 120 mon (n = 246)	P value
		aOR (95% CI)	aOR (95% CI)	aOR (95% CI)	
Abnormal placental position	0.084	0.92 (0.77-1.1)	1.09 (0.91-1.3)	1.18 (0.82-1.97)	0.366
Pernicious placenta with or without placenta accreta	0.015	0.98 (0.79-1.22)	1.02 (0.82-1.26)	1.03 (0.67-1.98)	0.889
PROM	0.032	0.97 (0.82-1.14)	1.03 (0.87-1.22)	1.07 (0.76-1.63)	0.074
Uterine rupture	-0.265	1.30 (1.05-1,61)	0.77 (0.62-0.95)	0.59 (0.38-1.08)	0.014
Postpartum hemorrhage	0.060	0.94 (0.72-1.23)	1.06 (0.81-1.39)	1.13 (0.66-2.58)	0.662
Hysterectomy	0.054	0.95 (0.74-1.21)	1.06 (0.83-1.35)	1.11 (0.68-2.36)	0.666
1-min Apgar score <10	-0.252	1.28 (0.62-2.73)	0.78 (0.37-1.61)	0.61 (0.13-2.9)	0.504
NICU admission	-0.004	1.00 (0.82-1.23)	1.00 (0.81-1.22)	0.99 (0.66-1.91)	0.966

IPI, interpregnancy interval.

aOR, adjusted odds ratio; CI, confidential index; PROM, premature rupture of membrane.

Abnormal placental position, including low placenta, partial and complete placenta previa.

Table 5. Association between other Perinatal Outcomes and IPI in the Three Groups with IPI of <24, 60-119 and ≥ 120 months.

	Index	IPI of <24 mon (n = 121)	IPI of 60-119 mon (n = 712)	IPI of ≥ 120 mon (n = 246)	P value
		aOR (95% CI)	aOR (95% CI)	aOR (95% CI)	
Abnormal placental position	0.139	0.87 (0.71-1.06)	1.15 (0.94--1.4)	1.32 (0.89-1.97)	0.169
Pernicious placenta with or without placenta accreta	0.103	0.90 (0.71-1.14)	1.11 (0.88-1.41)	1.23 (0.77-1.98)	0.395
PROM	0.059	0.94 (0.78-1.13)	1.06 (0.88-1.28)	1.13 (0.78-1.63)	0.527
Uterine rupture	-0.193	1.21 (0.96-1.53)	0.82 (0.65-1.04)	0.68 (0.43-1.08)	0.102
Postpartum hemorrhage	0.162	0.85 (0.62-1.15)	1.18 (0.87-1.53)	1.38 (0.75-2.58)	0.303
Hysterectomy	0.145	0.87 (0.65-1.14)	1.16 (0.87-1.53)	1.34 (0.77-2.36)	0.312
1-min Apgar score <10	-0.272	1.31 (0.59-3.08)	0.76 (0.32-1.7)	0.58 (0.11-2.9)	0.516
NICU admission	0.102	0.90 (0.72-1.13)	1.11 (0.89-1.38)	1.23 (0.79-1.91)	0.365

IPI, interpregnancy interval.

aOR, adjusted odds ratio; CI, confidential index; PROM, premature rupture of membrane.

Abnormal placental position, including low placenta, partial and complete placenta previa.

Aadjusted for maternal age, maternal body mass index, education status, assisted reproductive technology, number of previous cesarean section, previous vaginal delivery, previous emergency cesarean section.

Table 6. Association between IPI and other Perinatal Outcomes in Women with Emergency Cesarean Section.

	Index	IPI of <24 mon (n = 121)	IPI of 60-119 mon (n = 712)	IPI of ≥ 120 mon (n = 246)	P value
		aOR (95% CI)	aOR (95% CI)	aOR (95% CI)	
Abnormal placental position	0.119	0.89 (0.63-1.24)	1.13 (0.81-1.57)	1.27 (0.66-2.48)	0.482
Pernicious placenta with or without placenta accreta	-0.036	1.04(0.73-1.47)	0.96 (0.68-1.37)	0.93 (0.46-1.88)	0.840
PROM	0.028	0.97 (0.74-1.28)	1.03 (0.78-1.35)	1.06 (0.61-1.83)	0.843
Uterine rupture	-0.249	1.28 (0.94-1.75)	0.78 (0.57-1.06)	0.61 (0.33-1.12)	0.113
Postpartum hemorrhage	0.215	0.81 (0.47-1.37)	1.24 (0.73-2.14)	1.54 (0.53-4.57)	0.430
Hysterectomy	0.265	0.77 (0.46-1.25)	1.30 (0.8-2.16)	1.70 (0.64-4.66)	0.293
1-min Apgar score <10	-0.503	1.65 (0.5-6.42)	0.61 (0.16-2.01)	0.37 (0.02-4.05)	0.428
NICU admission	0.035	0.97 (0.69-1.35)	1.04 (0.74-1.46)	1.07 (0.55-2.12)	0.838

IPI, interpregnancy interval.

aOR, adjusted odds ratio; CI, confidential index; PROM, premature rupture of membrane.

Abnormal placental position, including low placenta, partial and complete placenta previa.

Table 7. Association between IPI and other Perinatal Outcomes in Women with Emergency Cesarean Section.

	Index	IPI of <24 mon (n = 121)	IPI of 60-119 mon (n = 712)	IPI of ≥ 120 mon (n = 246)	P value
		aOR (95% CI)	aOR (95% CI)	aOR (95% CI)	
Abnormal placental position	0.160	0.85 (0.59-1.22)	1.17 (0.82-1.69)	1.38 (0.68-2.86)	0.382
Pernicious placenta with or without placenta accreta	0.057	0.95 (0.64-1.38)	1.06 (0.72-1.56)	1.12 (0.52-2.43)	0.772
PROM	0.068	0.93 (0.69-1.25)	1.07 (0.8-1.44)	1.15 (0.64-2.08)	0.653
Uterine rupture	-0.157	1.17 (0.84-1.63)	0.86 (0.61-1.19)	0.73 (0.38-1.42)	0.354
Postpartum hemorrhage	0.195	0.82 (0.44-1.49)	1.21 (0.67-2.27)	1.48 (0.45-5.14)	0.528
Hysterectomy	0.192	0.83 (0.47-1.42)	1.21 (0.71-2.14)	1.47 (0.5-4.56)	0.494
1-min Apgar score <10	-0.572	1.77 (0.47-8.86)	0.56 (0.12-2.14)	0.32 (0.01-4.58)	0.426
NICU admission	0.321	0.73 (0.49-1.06)	1.38 (0.94-2.04)	1.90 (0.89-4.17)	0.102

IPI, interpregnancy interval.

aOR, adjusted odds ratio; CI, confidential index; PROM, premature rupture of membrane.

Abnormal placental position, including low placenta, partial and complete placenta previa.

Adjusted for maternal age, maternal body mass index, education status, assisted reproductive technology, number of previous cesarean section, previous vaginal delivery.

Figures

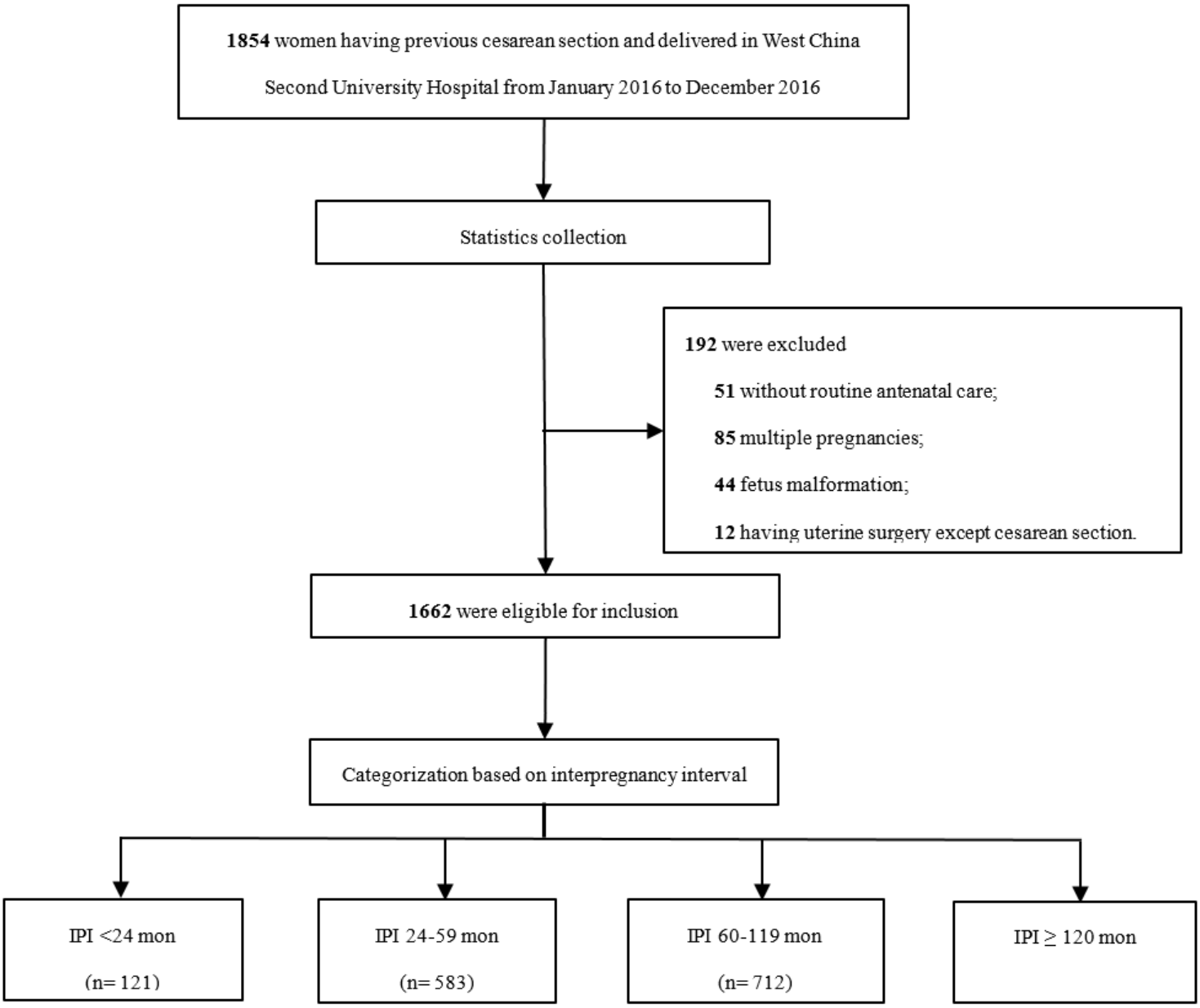

Figure 1

Flow chart of sample selection and statistics collection

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