Dynamic Change of Placenta Previa From Second Trimester to Delivery: a Retrospective Longitudinal Study Cohort

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Abstract

Introduction: Placenta previa contributes greatly to severe antenatal and post-partum hemorrhage in obstetrics. Previous studies have mainly focused on the risk factors of placenta previa, and very limited studies have reported which factors may affect the dynamic outcome of placenta previa in the second trimester. The aim of this study was to investigate the impact of maternal and neonatal characteristics on dynamic change of placenta previa from second trimester to delivery.

Methods: A retrospective longitudinal sub-cohort investigation was carried out among 510 pregnant women with placenta previa in second trimester of pregnancy from the Longitudinal Placenta Previa Study (LoPPS). Logistic regression analysis was used to discover the connections between maternal covariates and dynamic change process of placenta. Multivariable linear regression analysis was used to detect the associations between perioperative characteristics and the volume of intraoperative bleeding.

Results: Among the pregnant women with major placenta previa in the second trimester, 28.8% of them were without placenta previa at delivery, and 25.5% morphed into minor placenta previa. There was significant correlation between placenta previa type and pre-pregnancy BMI (Beta: 0.141, 95% CI: 0.046,0.235. $p=0.003$), gestational age (Beta: -0.355, 95% CI: -0.507, -0.204. $p<0.001$) and times of prior cesarean section (Beta: 0.161, 95% CI: 0.050,0.271. $p<0.001$).

Conclusion: 71.2% of the pregnant women with major placenta previa in the second trimester were still with placenta previa at delivery, and the proportion may be higher in pregnant women suffering previous cesarean section and with high pre-pregnancy BMI.

Introduction

Placenta previa (PP) is characterized by the abnormal placenta covering the endocervical os[1, 2], and the incidence of placenta previa in the third trimester is reportedly between 0.30% and 5.6%[3, 4]. It is not only a major contributor to severe antenatal and post-partum hemorrhage (PPH) in obstetrics, but also associated with serious maternal and adverse fetal outcomes, including morbid adherence of the placenta, thrombophlebitis, preterm labor, septicemia[5–9].

The placement of the placental edge determines whether the placenta is major or minor[9–11]. In the major placenta previa, the placenta overlaps the internal cervical os completely or partially, while the minor placenta previa is < 20 mm from the internal cervical os[12]. Low-lying or marginal placenta previa is another term for minor placenta previa. Complication rates are greater in major placenta previa than in minor placenta previa. Compared to women with minor placenta previa, women with major placenta previa experience greater antepartum and postpartum hemorrhage, premature births and hysterectomies[13–16].

In clinical work, we noticed that some pregnant women with major placenta previa diagnosed by ultrasonic imaging in the second trimester of pregnancy would morph into minor placenta previa in the third trimester of pregnancy, and some women were even without placenta previa. However, previous studies have mainly focused on the risk factors of placenta previa[8, 17, 18], and very limited studies have reported which factors

may affect the dynamic outcome of placenta previa in the second trimester. Finding the possible factors can be instrumental in improving the safety of mother with PP, and reducing the incidence of adverse pregnancy outcomes[19, 20].

Therefore, in the present study, we aimed to investigate the pregnancy and perioperative characteristics of mothers with placenta previa. Given the findings reported for our cohort, we also aimed to study the dynamic change of placenta previa from second trimester to delivery and determine the impact of maternal and neonatal characteristics on placenta previa.

Methods

Study design and participants

The present study was embedded in the Longitudinal Placenta Previa Study (LoPPS), an ongoing pregnancy and birth cohort study conducted in Chengdu, which aims to determine the relative contributions of genes and environment to the development and prognosis of placenta previa[21, 22]. This retrospective cohort study was conducted at the Chengdu Women's and Children's Central Hospital and included all women diagnosed with placenta previa during their second trimester pregnancy between January 2019 and December 2020. During the study period, the total times of delivery per year ranged between 15000 and 19000. The LoPPS placenta previa study, which was established in January 2018, attempts to unravel the complicated interplay between genes and the environment in specifying development and prognosis of placenta previa (Chinese Clinical Trial Registration Number: ChiCTR2100054068). It was approved by the Ethics Committee of the Chengdu Women's and Children's Central Hospital (No. 201830). And further verify the results of our retrospective study through an ongoing prospective research (Chinese Clinical Trial Registration Number: ChiCTR2100052428). Written informed consent was obtained from all participants. This subgroup study included pregnant women with an ultrasound confirmed placenta previa in the second trimester. Twin pregnancies were eliminated from this study due to the high rate of poor outcomes[23]. Therefore, the state of the placenta previa in singleton pregnancies was studied in this study. Mothers who had chronic metabolic diseases or were taking immunosuppressants were not included in the study. Infants with severe malformations or genetic disorders were also excluded from the study.

Data collection

In the routine prenatal examination during 24-28 gestational weeks, standardized questionnaires were used to collect maternal sociodemographic data (age, height, pre-pregnancy weight, occupation, parity, mode of conception), lifestyle behaviors before pregnancy (smoking and alcohol use) and pre-existing conditions. The standardized questionnaire of the LoPPS cohort study was self-designed and detailed information is available in Supplemental File 1. Medical records were used to collect information on pregnancy complications and maternal and neonatal outcomes, such as gestational age, pregnancy-induced illness, primigravid, gravidity, parity, times of prior cesarean delivery, times of prenatal bleeding, gestational age of first prenatal bleeding, times of abortion, intraoperative bleeding, neonatal birthweight and birth-length.

Statistical methods

All statistical analyses were performed with SPSS version 25.0 (IBM, Armonk, NY, USA). The chi-squared or Fisher's exact test was used to assess categorical data, which are reported as a count and a percentage. The means and standard deviations of continuous variables were calculated using the Student's t-test, LSD Student's t test,

one-way analysis of variance, or the nonparametric test. Multiple ordered logistic regression analysis was used to detect the associations between maternal and neonatal characteristics and the types of placenta previa and placenta accreta. Covariates were selected according to the significantly different variables in univariate analysis and the factors reported in previous studies that would affect dependent variable. All tests were two-tailed, and $p < 0.05$ was considered statistically significant.

Results

The selection process for this study population is presented in Figure 1. A total of 622 second trimester of pregnant women with major placenta previa from LoPPS were initially recruited into this subgroup study. After excluding mother-offspring pairs that did not match the inclusion criteria and did not give birth in our hospital, the final analysis included 510 mother-offspring pairs. The descriptive data of the study participants are shown in **Table 1**. The average maternal age at recruitment was 31.49 ± 4.25 years, and the average gestational age was 37.51 ± 1.92 weeks. The mean birth weight of all neonates was 2887.86 ± 527.03 g. Furthermore, 13.9% of mothers conceived via assisted reproductive technology (ART), and 99.2% of maternal parity was ≤ 2 due to Chinese two-child policy. During pregnancy, 28.8% pregnant women with major placenta previa in the second trimester had no placenta previa in the third trimester, and 25.5% morphed to minor placenta previa. Finally, 130 cases (25.5%) of minor placenta previa and 233 cases (45.7%) of major placenta previa were included in the analysis.

In the major placenta previa group, over half of the mothers had prenatal bleeding and were complicated with preterm birth, and 100% delivered by cesarean section; this group had the highest times of prenatal bleeding, with the lowest gestational age, birthweight and rate of assisted reproductive technology (**Table 2**).

In our cohort, there were significant differences in pre-pregnancy BMI ($p < 0.001$), mode of conception ($p = 0.006$), gestational weight gain ($p < 0.001$), gestational age ($p < 0.001$), preterm birth ($p < 0.001$), ICP ($p = 0.037$), times of prior cesarean section ($p = 0.022$), prenatal bleeding rate ($p < 0.001$), times of prenatal bleeding ($p < 0.001$), mode of delivery ($p < 0.001$), neonatal birthweight ($p < 0.001$), and birthlength ($p = 0.009$) among the no, minor and major placenta previa group (**Table 2**). After adjusting for the maternal age, GDM, GHD, FGR, times of gravidity, times of parity and times of abortion, the results revealed a correlation between placenta previa type and pre-pregnancy BMI (Beta: 0.141, 95% CI: 0.046, 0.235. $p = 0.003$), gestational age (Beta: -0.355, 95% CI: -0.507, -0.204. $p < 0.001$) and times of prior cesarean section (Beta: 0.161, 95% CI: 0.050, 0.271. $p < 0.001$) (**Figure 2**).

During the perioperative period, significant differences in emergency cases ($p = 0.019$), balloon occlusion ($p < 0.001$), anesthesia mode ($p = 0.032$), bleeding volume ($p = 0.008$), urine volume ($p = 0.035$), fluid transfusion

volume ($p<0.001$), intrauterine balloon ($p<0.001$), placenta accreta ($p<0.001$), placenta perforation ($p<0.001$), neonatal asphyxia ($p=0.013$), 1-minute Apgar score ($p=0.037$), antibiotic use time ($p=0.017$), 24-hour bleeding volume ($p=0.004$), febrile morbidity ($p=0.029$), postoperative hemoglobin concentration ($p=0.042$) were found among the no, minor and major placenta previa group (**Table 3**). Linear regression analysis was further used to investigate relative factors for intraoperative bleeding. After adjusting for the maternal age, gestational age, pre-pregnancy BMI, incision mode, the results revealed a correlation between intraoperative bleeding and duration of surgery, and type of placenta previa (Beta: 85.638, 95% CI: 29.920,171.322. $p=0.019$). The volume of intraoperative bleeding was positively correlated with the duration of surgery, with the bleeding volume increasing 19.616 mL when the duration of surgery increased by 1 minute (Beta: 19.616, 95% CI: 4.726,30.505. $p=0.028$) (**Table 4**).

It is worth noting that 62.7% of pregnant women complicated with placenta accreta in the major placenta previa group, which is the main population of postpartum hemorrhage. Therefore, the maternal characteristics were further analyzed by the degree of placental accreta. There were significant differences in mode of conception ($p=0.032$), gestational weight gain ($p<0.001$), gestational age ($p<0.001$), preterm birth ($p<0.001$), GHD ($p=0.002$), primigravid ($p=0.036$), gravidity ($p=0.026$), parity ($p=0.003$), times of prior cesarean section ($p<0.001$), prenatal bleeding rate ($p=0.038$), intraoperative bleeding ($p<0.001$), birthweight ($p<0.001$), and birthlength ($p<0.001$) among the no accreta, accreta, increta and percreta group (**Table 5**). Ordered logistic regression was further used to explore maternal risk factors for placental accreta. After adjusting for the maternal age, pre-pregnancy BMI, GHD, ICP and FGR, the results revealed a correlation between the degree of placenta accreta and gestational age (Beta: -0.323, 95% CI: -0.539, -0.106. $p=0.004$), GHD (Beta: 0.740, 95% CI: 0.147,1.334. $p=0.014$) and times of prior cesarean section (Beta: 1.136, 95% CI: 0.574,1.699. $p<0.001$) (**Figure 3**).

Discussion

In this retrospective preliminary study, we investigated the pregnancy and perioperative characteristics of mothers with placenta previa. Given the findings reported for our cohort, we also aimed to study the dynamic change of placenta previa from second trimester to delivery and determine the impact of maternal and neonatal characteristics on placenta previa.

In our cohort, the pregnant women with major placenta previa confirmed by ultrasound in the second trimester were included in our study. As the gestational weeks progressed, partial pregnant women's placenta previa disappeared while partial morphed into minor placenta previa. But a considerable proportion of pregnant women (45.7%) were still diagnosed as major placenta previa. This is conformity with the Green Top Guideline No. 27a from BJOG[4]. As such, it demonstrates the importance of managing and educating pregnant women with verified major placenta previa in the second stage of pregnancy. Pregnant women with placenta previa in our cohort can be effectively controlled and treated in advance, ensuring their safety during pregnancy.

There are conflicting studies on the relationship between pre-pregnancy BMI levels and severity of placenta previa. Anas M Fallatah et al observed a strong positive association between pre-pregnancy BMI and

placenta previa severity while Matias C Vieira found nothing[24, 25]. In our cohort, we determined that high pre-pregnancy BMI significantly increased the severity of placenta previa. Even after accounting for the various relative factors, the data still indicated that there was a correlation between pre-pregnancy BMI and of placenta previa type, which contradicts the results of Matias C Vieira. In the study of Matias C Vieira, pre-pregnancy BMI appeared to be associated with an increased risk of having the most severe kind of placenta previa. However, this association was lost after other risk factors such as previous cesarean delivery were taken into account. This is most likely due to the distinct rates of previous cesarean deliveries in the two studies. The rate of cesarean section in Anas M Fallatah's study in Saudi Arabia reaches more than 40%, which is comparable to the rate of China[26, 27]. However, the rate is less than 20% in Matias C Vieira's study in England. Further well-designed studies are required to confirm the findings and evaluate any potential mechanisms linking pre-pregnancy BMI and severity of placenta previa.

In our cohort, a substantial correlation between gestational hypertension disorder and placenta accreta was noticed, which was consistent with previous studies[28, 29]. The actual pathogenesis of hypertensive disorders complicating pregnancy is uncertain. A potential etiology is decreased interaction between the trophoblasts and the endometrium/decidua. Because women who present with placenta accreta have frequently had previous cesarean deliveries or curettage or both, placenta tissue damage from past instrumentation is thought to play a role in placenta accreta[30–32]. It means that pregnant women diagnosed with placenta previa in the second trimester need more rigorous blood pressure tests and more attention should be paid to the history of previous cesarean section and abortion to reduce the severity of placenta accreta. For pregnant women with hypertension complicated accompanied by placenta previa, MRI may be used to further elucidate the condition of placental accreta.

According to previous studies, the incidence of unfavorable pregnancy outcome has been progressively increasing due to a rise in the cesarean delivery rate. The major risk factor for women who have had previous cesarean deliveries is placenta accreta and placenta covering the uterus scar[33–35]. China, in particular, is a huge country with a high cesarean section rate, with up to more than 46% of pregnant women having non-clinically indicated cesarean sections due to Chinese cultural customs. To minimize the rate of cesarean section and to eliminate the high-risk element of placenta previa, more scientific medical publicity and education are needed[35–37].

The merits of our study are the specialized study population and large standard sample size. The participants were screened by strict inclusion and exclusion criteria. Twin pregnant women were not selected due to a higher risk of maternal and fetal complications, a higher rate of preterm birth and a lower neonatal birthweight. Additionally, the placental position of pregnant women as well as maternal and neonatal birth outcomes were tracked throughout pregnancy, resulting in a rather comprehensive study design. Due to the low natural incidence of placenta previa, it is time consuming to obtain participants. As a result, it is difficult to recruit and follow up such a large sample of pregnant women with placenta previa at a single hospital for two years. Our hospital, which treats a huge number of pregnant women with serious complications, is one of the largest and most professional women's and children's Hospitals in Southwest China. As a result, we are able to examine such important diseases with huge samples. The total times of delivery annually during the study period ranged from 15000 to 19000 in our hospital.

This preliminary study adds to our understanding of dynamic change of placenta previa from second trimester to delivery, but it has numerous limitations that should be considered. First, compared with that of similar studies in common diseases of pregnancy, the sample size in this study was relatively modest. Second, The current research is a retrospective study, it is more appropriate to follow up pregnant women from the second trimester of pregnancy prospectively, and collect maternal serum sample during prenatal examination to detect the changes of various metabolic indexes during pregnancy. Third, due to China's geomorphic diversity and ethnic diversity, the related variables of placenta previa, such as the living region altitude and nationality, were limited. To further understand the relevant maternal and neonatal factors in China among pregnancy populations with placenta previa, a large-scale study involving more regions and nationalities conducted in multiple centers is required.

In summary, this study suggested that 71.2% of the pregnant women with major placenta previa in the second trimester were still with placenta previa at delivery, and the proportion may be higher in pregnant women suffering previous cesarean section and with high pre-pregnancy BMI.

Abbreviations

BMI: Body mass index; CI: Confidence interval; GDM: Gestational diabetes mellitus; ICP: Intrahepatic cholestasis of pregnancy; LoPPS: Longitudinal Placenta Previa Study; OR: Odds ratio; ART: Assisted reproductive technology; GHD: Gestational hypertension disorder; WHZ: Z-score for weight-for-height; WAZ: Z-score for weight-for-age; HAZ: Z-score for height-for-age; BAZ: Z-score for BMI-for-age

Declarations

Ethics approval and consent to participate

The experimental design and procedures were approved by the Ethics Committee of the Chengdu Women's and Children's Central Hospital (No. 201830). All methods were performed in accordance with the relevant guidelines and regulations. Written informed consent was obtained from all participants.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

XL and SW designed the research protocol; XL and TL conducted the study; XL and RD analyzed the data; XL drafted the manuscript; XY, LW, WX, CF critically revised the manuscript; XY, SW provided funding resources. All authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

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Data availability

The datasets generated and analysed during the current study are not publicly available due to our ongoing prospective study but are available from the corresponding author on reasonable request.

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Tables

Table 1

Description of the maternal and neonatal characteristics

Variables	Total
Mothers	510
Maternal age (year)	31.49±4.25
Pre-pregnancy BMI (kg/m2)	23.44±3.69
Mode of conception	
Natural conception	439(86.1%)
Assisted reproductive technology	71(13.9%)
Gestational weight gain (kg)	12.70±2.58
Gestational age (week)	37.51±1.92
Preterm birth	180(35.3%)
Type of placenta previa	
Without placenta previa	147(28.8%)
Minor placenta previa	130(25.5%)
Major placenta previa	233(45.7%)
Gravidity	
1	137(26.9%)
2	101(19.8%)
3	118(23.1%)
4+	154(30.2%)
Parity	
0	138(27.1%)
1	236(46.2%)
2	132(25.9%)
3+	4(0.8%)
Infants	
Sex(male)	246(48.2%)
Birthweight (g)	2887.86±527.03
Birthlength(cm)	47.88±2.93

Table 2

Variables	Without	Minor	Major	p-value
Mothers	N=147	N=130	N=233	
Age (year)	31.40±4.17	31.70±4.10	31.38±4.34	0.490a
Pre-pregnancy BMI (kg/m ²)	21.51±3.35	22.34±3.56	24.06±3.62	<0.001a
Mode of conception				0.006b
Natural conception	108(73.5%)	115(88.5%)	216(92.7%)	
ART	39(26.5%)	15(11.5%)	17(7.3%)	
Gestational weight gain (kg)	13.28±3.47	12.25±3.22	11.20±3.37	<0.001a
Gestational age (week)	38.77±1.64	37.27±1.88	36.09±1.82	<0.001a
Preterm birth	12(8.2%)	39(30.0%)	129(55.4%)	<0.001b
Pregnancy-induced illness				
GDM	16(10.9%)	14(10.7%)	37(15.8%)	0.188b
GHD	4(2.7%)	4(3.1%)	7(3.0%)	0.663c
ICP	12(8.2%)	11(8.5%)	7(3.0%)	0.037b
FGR	6(4.1%)	7(5.4%)	8(3.4%)	0.371b
Primigravid	58(39.5%)	34(26.2%)	63(27.0%)	0.075b
Gravidity	2(2)	3(3)	3(3)	0.183d
Parity	1(2)	1(2)	2(1)	0.094d
Times of prior cesarean section	0(1)	0(1)	1(1)	0.022d
Prenatal bleeding rate	19(12.9%)	35(26.9%)	138(59.2%)	<0.001b
Times of prenatal bleeding	0(1)	1(1)	3(2)	<0.001d
Gestational age of first prenatal bleeding	29.33(4.06)	29.94(6.45)	28.11(6.92)	0.597d
Times of abortion	1(1)	1(2)	2(2)	0.571d
Mode of delivery (cesarean section)	73(49.7%)	115(88.5%)	233(100.0%)	<0.001b
Infants				
Birthweight (g)	3057.35±511.36	2976.91±541.08	2744.31±524.21	<0.001a
Birthlength (cm)	49.10±2.74	48.38±2.21	47.65±2.70	0.009a

BMI body mass index, ART assisted reproductive technology, GDM gestational diabetes, GHD gestational hypertension disorder, ICP intrahepatic cholestasis of pregnancy, FGR fetal growth restriction.

^aAverage and standard deviation. One-way Analysis of Variance

^bNumber (percentage). Chi-squared Test

^cNumber (percentage). Fisher Exact Test

^dMedian (interquartile range). Kruskal-Wallis Test

Table 3

Description of the perioperative characteristics by type of placenta previa

Variables	Without N=73	Minor N=115	Major N=233	p-value
Preoperation				
Emergency cases	6(8.22%)	18(15.6%)	61(26.2%)	0.019b
Hemoglobin concentration	116.64±11.62	117.05±12.51	115.35±12.81	0.224a
Balloon occlusion	0(0%)	2(1.7%)	28((12.0%))	<0.001c
Anesthesia mode	2(2.7%)	3(2.6%)	20(8.6%)	0.032c
Intraoperation				
Incision mode (Longitudinal incision)	2(2.7%)	2(1.7%)	15(6.4%)	0.175c
Bleeding volume	560.27±278.53	664.96±325.87	776.39±507.02	0.008a
Duration of surgery	45.24±19.98	46.68±21.80	49.81±20.46	0.174a
Urine volume	120(60)	130(60)	145(70)	0.035d
Fluid transfusion volume	1220(430)	1455(490)	1820(570)	<0.001d
Blood product transfusion	1(1.4%)	1(0.9%)	7(3.0%)	0.140c
Intrauterine balloon	26(35.6%)	65(56.5%)	171(73.4%)	<0.001b
Placenta accreta	24(32.9%)	57(49.6%)	146(62.7%)	<0.001b
Placenta perforation	2(2.7%)	7(6.1%)	66(28.3%)	<0.001c
Uterine artery ligation	0(0%)	2(1.7%)	11(4.7%)	0.149c
Caesarean hysterectomy	0(0%)	0(0%)	2(0.9%)	0.540c
Neonatal asphyxia	1(1.4%)	5(4.3%)	28(12.0%)	0.013c
Apgar score				
1 min	10(1)	9(1)	8(1)	0.037d
5 min	10(0)	10(1)	9(2)	0.382d
10 min	10(0)	10(0)	9(2)	0.420d
Postoperation				
Antibiotic use time	24(12)	24(24)	48(24)	0.017d
Transfer to ICU	1(1.4%)	1(0.9%)	3(1.3%)	1.000c
24-hour bleeding volume	674.20±354.50	768.45±348.22	894.93±526.01	0.004a
Febrile morbidity	6(8.2%)	14(12.2%)	50(21.6%)	0.029b
Hemoglobin concentration	102.19±11.03	102.35±11.14	98.80±15.77	0.042a

Hemoglobin reduction	14.77±4.29	15.64±5.37	17.67±6.21	0.126a
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^aAverage and standard deviation. One-way Analysis of Variance

^bNumber (percentage). Chi-squared Test

^cNumber (percentage). Fisher Exact Test

^dMedian (interquartile range). Kruskal-Wallis Test

Table 4

Association between maternal and perioperative characteristics and volume of intraoperative bleeding

Variables	Beta	95% CI	P-value	VIF
R ² =0.423				
Maternal age (year)	-1.575	(-3.633,0.483)	0.133	1.234
Gestational age (week)	0.857	(-0.04,1.673)	0.080	1.422
Pre-pregnancy BMI (kg/m2)	-16.188	(-95.963,63.588)	0.690	1.092
Emergency cases	52.684	(-19.988,125.356)	0.155	1.082
Duration of surgery	19.616	(4.726,30.505)	0.028	1.296
Preoperative balloon occlusion	45.52	(-69.536,160.575)	0.437	1.161
Mode of anesthesia	-43.246	(-168.969,82.476)	0.499	1.085
Type of placenta previa	85.638	(29.920,171.322)	0.019	1.289
Incision mode	32.122	(-36.73,100.974)	0.359	1.277

Table 5

Description of the maternal and neonatal characteristics by placenta accreta

Variables	None	Accreta	Increta	Percreta	p-value
Mothers	N=159	N=157	N=87	N=18	
Age (year)	31.73±3.39	31.73±4.36	31.71±4.54	32.78±5.62	0.183b
Pre-pregnancy BMI (kg/m2)	23.61±3.99	23.32±3.21	24.02±3.39	23.92±3.35	0.409b
Mode of conception					0.032 ^d
Natural conception	134(84.3%)	142(90.4%)	85(97.7%)	18(100.0%)	
ART	25(15.7%)	14(8.9%)	2(2.3%)	0(0%)	
Gestational weight gain (kg)	13.07±2.85	12.46±2.89	12.23±3.37	11.26±2.62	<0.001 ^b
Gestational age (week)	37.74±1.16	36.21±1.30	36.02±1.49	35.00±1.91	<0.001 ^b
Preterm birth	58(36.5%)	96(61.1%)	68(78.2%)	18(100.0%)	<0.001 ^a
Pregnancy-induced illness					
GDM	28(17.6%)	30(19.1%)	17(19.5%)	3(16.7%)	0.809d
GHD	4(2.5%)	2(1.3%)	3(3.4%)	4(22.2%)	0.002 ^d
ICP	6(3.8%)	7(4.5%)	3(3.4%)	0(0%)	0.956d
FGR	4(2.5%)	5(3.2%)	1(1.1%)	1(5.6%)	0.424d
Primigravid	32(20.1%)	21(13.4%)	10(11.5%)	1(5.6%)	0.036d
Gravidity	2.86±1.61	3.52±1.91	3.66±1.82	4.22±1.16	0.026b
Parity	1(1)	1(1)	2(1)	2(2)	0.003 ^c
Times of prior cesarean section	0.41±0.51	0.50±0.69	0.76±0.66	1.28±0.57	<0.001 ^b
Prenatal bleeding rate	49(30.8%)	84(53.5%)	43(49.3%)	9(50.0%)	0.038a
Times of prenatal bleeding	0.82±1.14	1.21±1.59	1.02±1.34	0.94±1.21	0.521b
Gestational age of first	26.89(3.28)	29.71(6.61)	29.96(3.39)	28.11(8.29)	0.735c

prenatal bleeding					
Times of abortion	1.05±1.65	1.44±1.46	1.56±1.49	1.39±1.03	0.212 ^b
Intraoperative bleeding	605(280)	780(510)	1060(730)	1880(960)	<0.001 ^c
Infants					
Birthweight (g)	2913.64±425.50	2810.62±418.37	2683.97±379.50	2477.78±388.15	<0.001 ^b
Birthlength (cm)	49.32±1.98	48.31±2.78	47.55±2.05	46.06±3.13	<0.001 ^b

BMI body mass index, ART assisted reproductive technology, GDM gestational diabetes, GHD gestational hypertension disorder, ICP intrahepatic cholestasis of pregnancy, FGR fetal growth restriction.

^aNumber (percentage). Chi-squared Test

^bAverage and standard deviation. One-way Analysis of Variance

^cMedian (interquartile range). Kruskal-Wallis Test

^dNumber (percentage). Fisher Exact Test

Figures

Figure 1

The selection process for this study.

Figure 2

After adjusting for the maternal age, GDM, GHD, FGR, times of gravity, times of parity and times of abortion, multiple logistic regression revealed a correlation between placenta previa type and pre-pregnancy BMI (Beta: 0.141, 95% CI: 0.046,0.235. p=0.003), gestational age (Beta: -0.355, 95% CI: -0.507, -0.204. p<0.001) and times of prior cesarean section (Beta: 0.161, 95% CI: 0.050,0.271. p<0.001).

Figure 3

Ordered logistic regression was further used to explore maternal risk factors for placental accreta. After adjusting for the maternal age, pre-pregnancy BMI, GHD, ICP and FGR, the results revealed a correlation between the degree of placenta accreta and gestational age (Beta: -0.323, 95% CI: -0.539, -0.106. $p=0.004$), GHD (Beta: 0.740, 95% CI: 0.147, 1.334. $p=0.014$) and times of prior cesarean section (Beta: 1.136, 95% CI: 0.574, 1.699. $p<0.001$).

Supplementary Files

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- [SupplementaryFile1.docx](#)