Different Methods for Termination of Mid-trimester Pregnancy With Placenta Previa

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Research Article

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Abstract

Objective: Investigate the different methods for termination at mid-trimester in pregnant women with placenta previa.

Methods: A retrospective study was conducted on 264 cases for termination at mid-pregnancy in our hospital, and 34 cases with placenta previa were set as the observation group, and 230 cases with normal placenta were set as control group. Among them, the preferred methods of termination at first were Mifepristone combined with Misoprostol/Rivanol in the observation group, and Mifepristone combined with Misoprostol/Rivanol/cervical double balloon (CDB) in the control group. If the volume of prenatal bleeding was up to 100 mL in the observation group, emergency artery embolization (UAE) was implemented to stop bleeding, then CDB plus with curettage were used in order. If it failed to induce in the control group, CDB was used subsequently followed with Misoprostol/Rivanol. Then, all those cases were set as the comprehensive-induce group, and the others were set as the simple-induce group.

Results: the average maternal age, the number of gravidity/parities, the rate of cesarean section, the hospitalization days and cost, the induction time, the rate of postpartum hemorrhage, puerperal infection were higher in the observation group than those in the control group(p<0.05). There were 4 cases used UAE+CDB+curettage in the observation group and 6 cases used CDB after Misoprostol/Rivanol in the control group. The duration time of termination, the rate of postpartum hemorrhage and transferring to ICU, hospitalization days and cost in the comprehensive-induce group were significantly higher than those in the simple-induce group (p<0.05). All cases were delivered through vaginal successfully.

Conclusion: We should pay more attention to the complications of prenatal bleeding, postpartum hemorrhage, puerperal infection during the induction at mid-trimester in pregnant women with placenta previa. Emergency UAE + CDB +curettage is a good combination method in prenatal hemorrhage of placenta previa during termination, and CDB was a good tool for cervical ripen with immature cervical condition in mid-trimester for induction of labor.

Background

Placenta previa refers to the placenta attaching to the lower uterine segment, at a relatively low or completely covering the cervix, which is confirmed when ultrasound shows that the edge of the placenta is within 2 cm of the cervix. [1]. If a pregnant woman with placenta previa needs to undergo termination of mid-pregnancy due to severe fetal malformation, stillbirth and serious maternal complications, the risks of massive hemorrhage, disseminated intravascular coagulation (DIC), hysterectomy and other adverse outcomes can be high, or even the safety of maternal life will be endangered [2, 3]. With the development of prenatal diagnosis technology, an increasing number of fetal anomalies are found during mid-pregnancy by ultrasound or karyotype analysis or microarray [4]. If those women were combined with placenta previa, cesarean delivery or even hysterectomy would be necessary just in case of hemorrhage during the process of termination, which will have a strong impact on patient's physical and mental health [5, 6]. Uterine artery embolization (UAE) has been widely used for postpartum hemorrhage, cesarean scar pregnancy, placenta increta and many other aspects [3,7–8]. Some researchers reported that UAE was used for the prevention of hemorrhage during the termination of pregnancy

for pregnant women combined with placenta previa [2, 9], but the problem is the overuse of UAE which also bring more complication such as irregular menstruation [10]. How to successfully terminate mid-pregnancy combined with placenta previa, and reduce the amount of bleeding and protect the patient's reproductive function is a big challenge.

In our study, we retrospectively analyzed the pregnant women with placenta previa who underwent termination of mid-pregnancy in our hospital within 1 year from January 1st, 2017 to December 31th, 2017, and discussed the labor inducing methods used among them.

Methods

1.Participants and methods

This study was conducted from January 1st, 2017 to December 31th, 2017 in our hospital, a tertiary-care teaching hospital in Wuhan city, Hubei province, in the central of China.

1.1 Ethical approval

The study protocol was a retrospective research, the study protocol was approved by the Ethics Committee of Maternal and Child Health Hospital of Hubei Province ([2019]IEC (XM008)). All parturient women requiring termination of pregnancy in this work signed informed consent.

1.2 Data sources

This retrospective study was based on the maternity departments of a tertiary- level public hospital in Wuhan city, Hubei province, China. This is a big birth center, with annual number of newborn babies of around 25, 000 in recent 5 years. The delivery data were collected from the hospital's information system from January 1st, 2017 to December 31th, 2017. A total of 295 cases were included in our study, of which 10 cases had incomplete information, 21 cases of spontaneous abortion were excluded. Therefore, a complete data of 264 cases were finally included (accounting for 89.5% of total data). Of all, 37 cases were stillbirth, 213 cases were malformations confirmed by ultrasound or/and chromosomal abnormalities, and 14 cases were severe complications and having inability to continue the pregnancy. According to placenta position, patients with placenta previa were collected in the observation group (n=34), those without placenta previa collected in the control group (n=230). **(Fig 1)**

1.3 Labor inducing methods

All patients requiring induced labor were managed by the same obstetric group. All of selected cases were assessed by three prenatal diagnosis experts. The labor inducing procedures were improved by fetal biological parents in the outpatient department. After admission, pregnant woman, her spouse and other family members (parents of both parties) were fully informed by obstetricians about her condition, labor inducing procedures and the possible risks in labor induction, and were asked to sign the informed consent for induction of labor. After that, blood routine, urine routine, coagulation function, liver and kidney function were tested. The placentas of all cases were routinely examined by vaginal ultrasound. The labor inducing method was adopted based on gestational weeks, cervical Bishop score, amniotic fluid volume, placental attachment site. At first,

there were three labor inducing methods, one is combined application of Mifepristone and Misoprostol. Mifepristone was taken orally with a total dose of 300 mg (50mg, Bid*3d)，then vaginal medication of Misoprostol was carried out at 8am on the 4th day (100ug, Q6h). Such scheme was mainly used for pregnant women whose gestational age was less than or equal to 16 weeks. Second, combined use of Mifepristone and ethacridine lactate (Rivanol). After oral administration of Mifepristone with a total dose of 300mg (50mg, Bid* 3D), Rivanol 100mg was injected into the amniotic cavity under ultrasound guidance. Such treatment scheme was mainly used for pregnant women whose gestational age was more than 16 weeks without oligohydromnios or liver/kidney dysfunction. Third, Mifepristone combined with cervical double balloon (CDB). Mifepristone was taken orally with a total dose of 300 mg (50mg, Bid*3d), then CDB (80mL intrauterine, 80mL extrauterine of vagina) was carried out for 12-24h. Such scheme was mainly used for pregnant women combined with oligohydromnios or liver/kidney dysfunction, but placenta previa was the contraindication for use of CDB.

If the volume of prenatal bleeding was up to or equal to 100 mL in the observation group, emergency artery embolization (UAE) was implemented to stop bleeding, then CDB plus with curettage were used in order. If it failed to induce in the control group, CDB was used subsequently followed with Misoprostol/Rivanol. Then, all those cases were set as the comprehensive-induce group, and the others were set as the simple-induce group.

CDB [11]: The patient emptied the bladder and took the lithotomy position, then the obstetricians gently placed the speculum into the vagina, disinfected the cervix, inserted the CDB into the cervix until both balloons entered the cervical canal, injected 40 mL of normal saline into the "U" balloon, then pulled the "V" balloon out of the cervical external orifice and injected 40 mL of normal saline into it. At last, two balloons were added in turn until the volume of both balloons reached 80 mL. If the patient was unbearable for 80 mL, 10-20 mL of normal saline should be drawn out from both balloons.

UAE [12]: Patients were placed in the supine position, disinfected and draped in the inguinal area, and Lidocaine was given for local anesthesia before surgery. The surgeon punctured the right femoral artery according to Seldinger's method, inserted the 5F catheter sheath and catheter into the left uterine artery until arterial subtraction, perfused Gentamicin 80,000 units, and embolized with gelatin sponge. The right uterine artery was cannulated, perfused and embolized too. After the operation, the catheter and sheath were pulled out, the local pressure bandage was applied, the right lower limb was immobilized for 24h, perioperative antibiotics were given to prevent infection.

In the observation group, if prenatal bleeding was up to 100 mL, emergency artery embolization (UAE) was implemented to stop bleeding, then cervical double balloon (CDB) plus with curettage were used in order [11]. In the control group, if the first two methods of Misoprostol/ Rivanol failed to deliver fetus and placenta, it is necessary to combine with CDB for termination of pregnancy. If all those combination methods were invalid to make the pregnant woman deliver fetus and placenta, a cesarean section was required.

- **Observational indexes**

The observational indexes included maternal age, gravidity, parity, body mass index, terminated gestational week, the history of cesarean section, placenta position, method of labor induction, induction time, antenatal

hemorrhage, postpartum hemorrhage, curettage, manual removal of placenta, puerperal morbidity, and proportion of ICU cases, impatient days and hospitalization cost.

The induction time

The induction time of mifepristone combined with Misoprostol was from the insertion of the first tablet of Misoprostol to the deliver fetus and placenta. The induction time of Mifepristone combined with Rivanol was from intra-amniotic injection of Rivanol to deliver fetal and placenta. The induction time of Mifepristone combined with CDB was from placing CDB to the deliver fetal and placenta. The induction time of the comprehensive-induce cases was from the first using of Misoprostol or Rivanol to the deliver fetal and placenta.

ICU transfer criteria

The cases with massive hemorrhage during induction of labor required intrauterine balloon tamponade, UAE, or suspected sepsis.

1.5 Statistical analysis

Statistical analysis was performed with software SPSS (v.19.0, SPSS Inc, Chicago, IL, USA). Measurement data were presented in from of means standard deviation, T test and Wilcoxon test were conducted for statistical comparison of groups, while Chi-square analysis and Fisher's exact test were conducted for enumeration data. The difference was considered statistically significant when $p<0.05$.

Results

2.1 The comparison of general information of maternity

The average maternal age in the observation group was 31.5y, and that in the control group was 29.5y, and there was a significant difference between the two groups (p 0.05). The number of gravidity or parity in the observation group was higher than that in the control group(p 0.05). The rate of cesarean section was 35.3% (12/34) in the observation group, which was higher than that 19.6%(45/230) in the control group (p 0.05). The impatient days and hospitalization cost (RMB) in the observation group were higher than those in the control group ($p<0.05$). There were no differences in the gestational weeks of termination, body mass index (BMI) before termination of pregnancy, and the rate of maternity insurance between in the two groups ($p> 0.05$). The data are presented in **Table 1**.

2.2 Different methods of labor induction

In the observation group, 5 cases (14.7%) were induced by Mifepristone combined with Misoprostol, 29 cases (85.3%) were induced by Mifepristone combined with Rivanol at first. In the control group, there were 24 cases (10.4%) by Mifepristone with Mifepristone, 203 cases (88.3%) by Mifepristone with Rivanol, and 3 cases (0.4%) by Mifepristone with CDB at first, respectively. There was no significant difference between the two groups in terms of the method of labor induction ($p> 0.05$).

In the observation group, there were 4 cases induced by the comprehensive-induce methods of UAE+CDB+curettage for prenatal bleeding more than 100mL (100 mL,150 mL,180 mL and 200 mL), while there were 6 cases induced by comprehensive-induce methods of adding CDB after Misoprostol or Rivanol. The rate of comprehensive-induce method had difference between in the two groups ($p< 0.05$). The data are shown in **Table 2**. All women in the both groups underwent vaginal delivery and no case chose cesarean delivery.

2.3 The duration time and complications of labor induction in the two groups

The median induction time in the observation group was 35.0h, which was longer than that in the control group (30.0h) ($p<0.05$). The amount of postpartum hemorrhage within 2 hours after delivery in the observation group was 335.3 mL, which was larger than that in the control group (269.2 mL, $p<0.05$), and the rates of postpartum hemorrhage, puerperal infection, UAE and ICU in the observation group were higher than those in the control group ($p< 0.05$). There was no difference in the rate of manual placenta removal between the two groups ($p>0.05$) (**Table 3**).

In the observation group, 4 patients had a one-time prenatal hemorrhage and the amount of bleeding was more than 100mL (100 mL,150 mL,180 mL and 200 mL). In the control group, none of the women had antenatal hemorrhage.

2.4 The comprehensive-induce and simple-induce methods

There were 4 cases using UAE+CDB+curettage in the observation group and 6 cases using CDB after Misoprostol or Rivanol in the control group, so there were 10 cases in the comprehensive-induce group, the others 254 cases were in the simple-induce group. The median duration time in the comprehensive-induce group was 37.5h, and that in the simple-induce group was 30.0 h, there was a significant difference between them ($p>0.05$). The rate of prenatal hemorrhage was 30% (3/10) in the comprehensive-induce group, which was significantly higher than that in the simple-induce group (0.4%, 1/254) ($p< 0.05$); the rate of postpartum hemorrhage was 50.0% (5/10) in the comprehensive-induce group, which was higher than that in the simple-induce group [2.4% (6/254), $p<0.05$)]. The rate of puerperal infection was 80.0% (8/10) in the comprehensive-induce group, which was higher than that in the simple group [2.4% (6/254), $p<0.05$)] (**Table 4**).

Discussion

Advanced maternal age (age greater than 35 years old), multiparity, smoking, history of curettage, assisted reproductive technology, prior cesarean section, and prior placenta previa may increase the incidence of placenta previa [13-15]. The common complications of placenta previa include placenta accrete spectrum (PAS), uncontrolled antepartum/postpartum hemorrhage, so blood transfusion, hysterectomy, ICU care may need [16,17]. Placenta previa affects 0.5% to 3% of third trimester pregnancies, which may be a factor leading to increasing rate of cesarean section [18]. In our study, the rate of placenta previa was 12.9% (34/264) and the maternal age, gravidity, parity, rate of cesarean section in the women with placenta previa were higher than normal. These may be due to following reasons. First of all, placental migration may occur throughout pregnancy, nearly 90% of hypo placentas (early stage) eventually grows into the uterus for more blood supply in the third trimester [19]. In our study, the average gestation age of pregnant women was 22.3 weeks, if the pregnancy continues, the position of placenta may change to normal in the third trimester. Second, with the

beginning of China's universal two-child policy, more and more multiparous women with advanced maternal age, prior cesarean section, history of curettage have more chance to terminate pregnancy for stillbirth, fetal malformation, serious maternal complications [13]. Last, our birth center is a maternal emergency center, pregnant women with high risk of placenta previa are more likely to choose our hospital.

When a patient is admitted, routine sonography is applied before a digital examination. Transvaginal sonogram is superior to a transabdominal sonogram [1,19]. At present, the common methods for termination of pregnancy in China include Mifepristone and Misoprostol for the patients with the gestational age less than and equal to 16 weeks or intra-amniotic injection of ethacridine lactate (Rivanol) for those with gestational age over 16 weeks and CDB for oligohydromnior or liver/kindey dysfunction with normal placenta [20,21]. For pregnant women with prior cesarean or/and placenta previa but without placenta percreta, both the Mifepristone-Misoprostol and Mifepristone-Rivanol are effective and safe methods for the termination of mid-trimester pregnancy [22]. As an acceptable method of labor induction, CDB can be safely applied to pregnant women who undergo vaginal delivery with term pregnancy [23], or to those with history of cesarean section [24]. CDB is also a safe and effective method for labor induction with oligohydramnios or hepatorenal function impairment in the mid-trimester [25]. In our observation, the common methods for termination of pregnancy in the mid-trimester using Mifepristone combined with Misoprostol or Rivanol are effective (88.2%, 30/34) with placenta previa, and the common methods using Mifepristone combined with Misoprostol or Rivanol or CDB (97.4%, 224/230) with normal placenta. Due to the risk factor of placenta position in the patients with placenta previa in the mid-trimester, the induction time, the amount of prenatal and postpartum hemorrhage within 2 hours after delivery, and the rates of postpartum hemorrhage, puerperal infection, UAE and ICU were higher than the patients with normal placenta position. The rate of needing comprehensive-induce methods of UAE+CDB+curettage was higher in the patients with placenta previa (8.8%, 4/34) than that with normal placenta needing CDB after Mifepristone combined with Misoprostol or Rivanol(2.6%, 6/230). We should pay more attention to deal with placenta previa when need termination of pregnancy in mid-trimester.

For the placental factors, the rate of prenatal hemorrhage in the pregnant women with placenta previa is higher than that with normal placenta during the induction of labor in mid-trimester [26,27]. In our observation, there were 4 cases occur prenatal hemorrhage in the cases with placenta previa but no one in the cases with normal placenta. How to prevent and deal with prenatal hemorrhage is the key. In recent years, the combination of UAE and conventional medical or instrument labor induction methods has become a new treatment scheme widely studied in clinical practice [7,9,28]. Prophylactic UAE before curettage in patients with cesarean scar pregnancy is safe and effective [7]. However, whether to use emergency or prophylactic UAE for termination of mid-pregnancy with placental previa still remains debated [9,28]. He et al [9] analyzed 85 cases with complete placenta previa for termination of second-trimester pregnancy, in which 20 cases were treated with cesarean delivery, 30 cases were treated with Mifepristone+Rivanl+UAE, and 35 patients were induced by Mifepristone+Rivanol. The results showed that the total amount of blood loss during induction and labor was lowest, the incidence of fever was highest in cases using Mifepristone+Rivanol+UAE, but 13 patients underwent emergency UAE and 2 patients underwent emergency cesarean section in the cases using Mifepristone+Rivanol. Wang et al [28] found the patients with complete placenta previa who underwent mid-trimester pregnancy termination by labor induction with prophylactic UAE(n=15) and without prophylactic UAE(n=10), the rate of success abortion, the bleeding volume, induction-to-abortion time had no significant

difference, but the hospital stay was longer and pyrexia was more common in the cases with prophylactic UAE. So prophylactic UAE was not recommended for second-trimester abortion with complete placenta previa. In our clinical observation, among 34 cases with placental previa, only 4 cases needed emergency UAE to stop bleeding successfully. This may be related to the following factors:The technology of UAE in our hospital is mature, and can be carried out quickly within 30 minutes. Prenatal blood loss was more than or equal to 100 mL when we decided to implement emergency UAE. there was no case of bleeding caused by placenta percreta.

The patient with comprehensive-induce methods to terminate the pregnancy in the mid-trimester had more complications of prenatal hemorrhage (30% vs 0%), postpartum hemorrhage (50.0% vs 2.4%), puerperal infection (80.0% vs 2.4%), the main reason is the patients with prenatal hemorrhage or immature cervical conditions [29]. After UAE, the uterus was hypoxic, the placenta and fetus remained in the uterus, which may lead to intrauterine infection, fever, and even septicemia. So, CDB was performed to ripen cervix. Curettage was carried out subsequently to remove the placenta tissue and fetus of by ultrasound monitoring during the best period of hemostasis after UAE. This combination of induction methods with UAE+CDB+curettage is effective for prenatal hemorrhage in the patients of placenta previa [11]. After using Mifepristone combined with Misoprostol or Rivanol in the patients of normal placental, the ripening of cervical is still difficult in some cases. CDB may be a remedy measure to promote cervical ripening after drugs induction, and properly extending the time of CDB from 12 h to 24 h can reduce the chance of surgical induction of dilatation and evacuation in mid-trimester [30]

Conclusions

For the pregnant women with placenta previa in mid-pregnancy, the conventional induction method is useful, but the risk for complications such as antepartum hemorrhage, PPH, infection will be higher. UEA +DBC and curettage maybe a new method to deal with antepartum hemorrhage for pregnant women with placenta previa, and CDB was a good tool for cervical ripen with immature cervical condition in mid-trimester for induction of labor.

Declarations

Ethics approval and consent participate

- The study conformed to the guidelines explained in the Declaration of Helsinki and was approved by the Ethics Committee of Maternal and Child Health Hospital of Hubei Province ([2019]IEC (XM008)). A waiver for the requirement of informed consent from the patients whose records were analyzed was granted by the Chair of the Committee on the grounds of being a minimal risk study.

Consent for publication

-Not applicable

Availability of data and materials

- Access to the qualitative data should be given upon request to the corresponding author after taking any necessary precautions to safeguard participants' privacy and confidentiality.

Competing interests

-The authors declare that they have no competing interests

Conflict of interest statement

We declare that we do not have any commercial or associative interest that represents a conflict of interest in connection with the work submitted

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Author's Contributions

- QL, SW, YZ conceived the study, analyzed the data, interpreted the results, and drafted the manuscript. FT, YZ conceived the study, drafted the manuscript. SD, RL analyzed the data and revised the manuscript. All authors read and approved the final manuscript.

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References

1. Jain V, Bos H, Bujold E. Guideline No. 402: Diagnosis and Management of Placenta Previa. J Obstet Gynaecol Can. 2020 Jul;42(7):906-917.e1. doi: 10.1016/j.jogc.2019.07.019. PMID: 32591150
2. Feng Y, Li XY, Xiao J, Li W, Liu J, Zeng X, Chen X, Chen KY, Fan L, Kang QL, Chen SH. Risk Factors and Pregnancy Outcomes: Complete versus Incomplete Placenta Previa in Mid-pregnancy. Curr Med Sci. 2018 Aug;38(4):597-601. doi: 10.1007/s11596-018-1919-9. Epub 2018 Aug 20. PMID: 30128867
3. Aoki M, Tokue H, Miyazaki M, Shibuya K, Hirasawa S, Oshima K. Primary postpartum hemorrhage: outcome of uterine artery embolization. Br J Radiol. 2018 Jul;91(1087):20180132. doi: 10.1259/bjr.20180132. Epub 2018 Apr 18. PMID: 29641227
4. Zhuang J, Chen C, Jiang Y, Luo Q, Zeng S, Lv C, Wang Y, Fu W. Application of the BACs-on-Beads assay for the prenatal diagnosis of chromosomal abnormalities in Quanzhou, China. BMC Pregnancy Childbirth. 2021 Jan 28;21(1):94. doi: 10.1186/s12884-021-03589-9. PMID: 33509128

5. Saccone G, Migliorini S, Crocetto F, Della Corte L, Cancellieri E, Improda L, Improda FP, Maruotti GM, Cancelmo G, Imbimbo C, Bifulco G, Zullo F, Berghella V. Risk of unscheduled delivery in women with placenta accreta according to planned gestational age at delivery. J Matern Fetal Neonatal Med. 2021 Jan 27:1-4. doi: 10.1080/14767058.2021.1878493. Epub ahead of print. PMID: 33504230
6. Xie RH, Zeng S, Zhou L, Wen S, Liao Y, Walker M, Wen SW, Lei H. Comparison of Adverse Maternal and Neonatal Outcomes in Women Affected by Placenta Previa With and Without a History of Cesarean Delivery: A Cohort Study. J Obstet Gynaecol Can. 2021 Jan 23:S1701-2163(21)00062-1. doi: 10.1016/j.jogc.2020.12.022. Epub ahead of print. PMID: 33497780
7. Tian H, Li S, Jia W, Yu K, Wu G. Risk factors for poor hemostasis of prophylactic uterine artery embolization before curettage in cesarean scar pregnancy. J Int Med Res. 2020 Oct;48(10):300060520964379. doi: 10.1177/0300060520964379. PMID: 33467974.
8. Sentilhes L, Kayem G, Chandraharan E, Palacios-Jaraquemada J, Jauniaux E; FIGO Placenta Accreta Diagnosis and Management Expert Consensus Panel. FIGO consensus guidelines on placenta accreta spectrum disorders: Conservative management. Int J Gynaecol Obstet. 2018 Mar;140(3):291-298. doi: 10.1002/ijgo.12410. PMID: 29405320.
9. He F, Yin WC, Chen BJ, Gong JJ, Chen DJ. [Clinical investigation in the methods for complete placenta previa labor induction in the second trimester]. Zhonghua Fu Chan Ke Za Zhi. 2020 May 25;55(5):317-321. Chinese. doi: 10.3760/cma.j.cn112141-20191124-00639. PMID: 32464719
10. Czuczwar P, Stępniak A, Wrona W, Woźniak S, Milart P, Paszkowski T. The influence of uterine artery embolisation on ovarian reserve, fertility, and pregnancy outcomes - a review of literature. Prz Menopauzalny. 2016 Dec;15(4):205-209. doi: 10.5114/pm.2016.65665. Epub 2017 Feb 8. PMID: 28250724
11. Tang F, Du S, Zhao Y, Sun G, Lin Y, Li R, Wu X. Clinical analysis of uterine artery embolization combined with double balloon catheter plus curettage for patients with placenta previa who underwent pregnancy termination and suffered antenatal massive hemorrhage in the 2nd trimester: Three case reports. Medicine (Baltimore). 2019 Jan;98(4):e14266. doi: 10.1097/MD.0000000000014266. PMID: 30681626
12. Li Y, Gong L, Wu X, Gao H, Zheng H, Lan W. Randomized controlled trial of hysteroscopy or ultrasonography versus no guidance during D&C after uterine artery chemoembolization for cesarean scar pregnancy. Int J Gynaecol Obstet. 2016 Nov;135(2):158-162. doi: 10.1016/j.ijgo.2016.04.019. Epub 2016 Aug 5. PMID: 27634054
13. Correa-de-Araujo R, Yoon SSS. Clinical Outcomes in High-Risk Pregnancies Due to Advanced Maternal Age. J Womens Health (Larchmt). 2020 Nov 13. doi: 10.1089/jwh.2020.8860. Epub ahead of print. PMID: 33185505.
14. Coutinho CM, Giorgione V, Noel L, Liu B, Chandraharan E, Pryce J, Frick AP, Thilaganathan B, Bhide A. Effectiveness of contingent screening for placenta accreta spectrum disorders based on persistent low-lying placenta and previous uterine surgery. Ultrasound Obstet Gynecol. 2021 Jan;57(1):91-96. doi: 10.1002/uog.23100. PMID: 32865834.
15. Jeon H, Min J, Kim DK, Seo H, Kim S, Kim YS. Women with Endometriosis, Especially Those Who Conceived with Assisted Reproductive Technology, Have Increased Risk of Placenta Previa: Meta-analyses. J Korean Med Sci. 2018 Jul 30;33(34):e234. doi: 10.3346/jkms.2018.33.e234. PMID: 30127709;

16. Dai YM, Wei J, Wang ZQ, Zhang XB, Cheng L, Gu N, Hu YL. [Intrauterine balloon tamponade combined with temporary abdominal aortic balloon occlusion in the management of women with placenta accreta spectrum:a randomized controlled trial]. Zhonghua Fu Chan Ke Za Zhi. 2020 Jul 25;55(7):450-456. Chinese. doi: 10.3760/cma.j.cn112141-20200225-00135. PMID: 32842248
17. Anderson-Bagga FM, Sze A. Placenta Previa. 2020 Jun 27. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan–. PMID: 30969640.
18. Long SY, Yang Q, Chi R, Luo L, Xiong X, Chen ZQ. Maternal and Neonatal Outcomes Resulting from Antepartum Hemorrhage in Women with Placenta Previa and Its Associated Risk Factors: A Single-Center Retrospective Study. Ther Clin Risk Manag. 2021 Jan 12;17:31-38. doi: 10.2147/TCRM.S288461. PMID: 33469297;
19. Obstetrics Subgroup, Chinese Society of Obstetrics and Gynecology,Chinese Medical Association. [Guidelines for the diagnosis and management of placenta previa (2020)]. Zhonghua Fu Chan Ke Za Zhi. 2020 Jan 25;55(1):3-8. Chinese. doi: 10.3760/cma.j.issn.0529-567X.2020.01.002. PMID: 32074766.
20. Qian J, Jing X, Wu S, Zheng S, Li Y, Ren M, Di W, Shen H, Dong B, Chang Q, Shi H, Yao C, Song W, Huang Z. [Efficacy and safety of mifepristone combined with misoprostol for termination of pregnancy between 8 and 16 weeks of gestation]. Zhonghua Fu Chan Ke Za Zhi. 2015 Jul;50(7):505-9. Chinese. PMID: 26311640.
21. Obstetrics Subgroup, Chinese Society of Obstetrics and Gynecology, Chinese Medical Association. [Guideline of cervical ripening and labor induction during the third trimester pregnancy]. Zhonghua Fu Chan Ke Za Zhi. 2014 Dec;49(12):881-5. Chinese. PMID: 25608986.
22. Pharmacoeconomic Review Report: Mifepristone and misoprostol (Mifegymiso) [Internet]. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2017 May. PMID: 30512907.
23. Beckmann M, Acreman M, Schmidt E, Merollini KMD, Miller Y. Women's experience of induction of labor using PGE2 as an inpatient versus balloon catheter as an outpatient. Eur J Obstet Gynecol Reprod Biol. 2020 Jun;249:1-6. doi: 10.1016/j.ejogrb.2020.03.031. Epub 2020 Apr 4. PMID: 32311627.
24. Korb D, Renard S, Morin C, Merviel P, Sibony O. Double-balloon catheter versus prostaglandin for cervical ripening to induce labor after previous cesarean delivery. Arch Gynecol Obstet. 2020 Apr;301(4):931-940. doi: 10.1007/s00404-020-05473-x. Epub 2020 Mar 5. PMID: 32140810.
25. Li N, Wu P, Zhao J, Feng L, Qiao FY, Zeng WJ. Effectiveness and safety of double-balloon catheter versus intra-amniotic injection of ethacridine lactate for termination of second trimester pregnancy in patients with liver dysfunction. J Huazhong Univ Sci Technolog Med Sci. 2015 Feb;35(1):129-134. doi: 10.1007/s11596-015-1401-x. Epub 2015 Feb 12. PMID: 25673206.
26. Pei R. Reply to the Comment: Prophylactic Uterine Artery Embolization in Mid-trimester Pregnancy Termination for Placenta Previa: Required for all Patients? Cardiovasc Intervent Radiol. 2017 Mar;40(3):476-477. doi: 10.1007/s00270-016-1554-4. Epub 2016 Dec 28. PMID: 28032132.
27. Matsubara S, Takahashi H, Baba Y. Prophylactic Uterine Artery Embolization in Mid-trimester Pregnancy Termination for Placenta Previa: Required for All Patients? Cardiovasc Intervent Radiol. 2017 Mar;40(3):474-475. doi: 10.1007/s00270-016-1553-5. Epub 2016 Dec 27. PMID: 28028579.
28. Wang Y, Hu C, Pan N, Chen C, Wu R. Prophylactic uterine artery embolization in second-trimester pregnancy termination with complete placenta previa. J Int Med Res. 2019 Jan;47(1):345-352. doi:

10.1177/0300060518801455. Epub 2018 Oct 14. PMID: 30318981;

29. Tu YA, Chen CL, Lai YL, Lin SY, Lee CN. Transcervical double-balloon catheter as an alternative and salvage method for medical termination of pregnancy in midtrimester. Taiwan J Obstet Gynecol. 2017 Feb;56(1):77-80. doi: 10.1016/j.tjog.2015.12.024. PMID: 28254231.
30. Peng J, Li R, Du S, Yin H, Li M, Zheng X, Wu S, Zhao Y. Induction of labour in mid-trimester pregnancy using double-balloon catheter placement within 12 h versus within 12-24 h. BMC Pregnancy Childbirth. 2021 Jan 6;21(1):17. doi: 10.1186/s12884-020-03513-7. PMID: 33407258;

Tables

Due to technical limitations, table 1 is only available as a download in the Supplemental Files section.

Table 2 Methods of inducing labor in observation group and control group

Group	n	Mifepristone with Rivanol [n]	Mifepristone with Misoprostol [n]	Mifepristone with CDB [n]	Comprehensive-induction (n)	Comprehensive-induction (%)
Observation group	34	29	5	0	4	11.8
Control group	230	203	24	3	6	2.6
Z		0.965			6.814	
P		0.617			0.002	

CDB: cervical double balloon

Chi-square analysis and Fisher's exact test were used

Due to technical limitations, table 3 is only available as a download in the Supplemental Files section.

Table 4: The complications between in the comprehensive-induction and simple-induction groups

Group	N	Induction time （h, Median（25-75%）	Prenatal hemorrhage （n, %）	postpartum hemorrhage （n, %）	Puerperal infection (n, %)
Comprehensive-induction	10	37.5, 23-103.3	3, 30.0	5,50.0%	8, 80.0
Simple-induction	254	30.0, 21.6-36.0	1, 0.4	6 ,2.4	6, 2.4
Z		-2.293	56.516	54.680	115.482
P		0002	0.000	0.000	0.000

PPH: postpartum hemorrhage; CDB: cervical double balloon

Wilcoxon test, Chi-square analysis and Fisher’s exact test were used

Figures

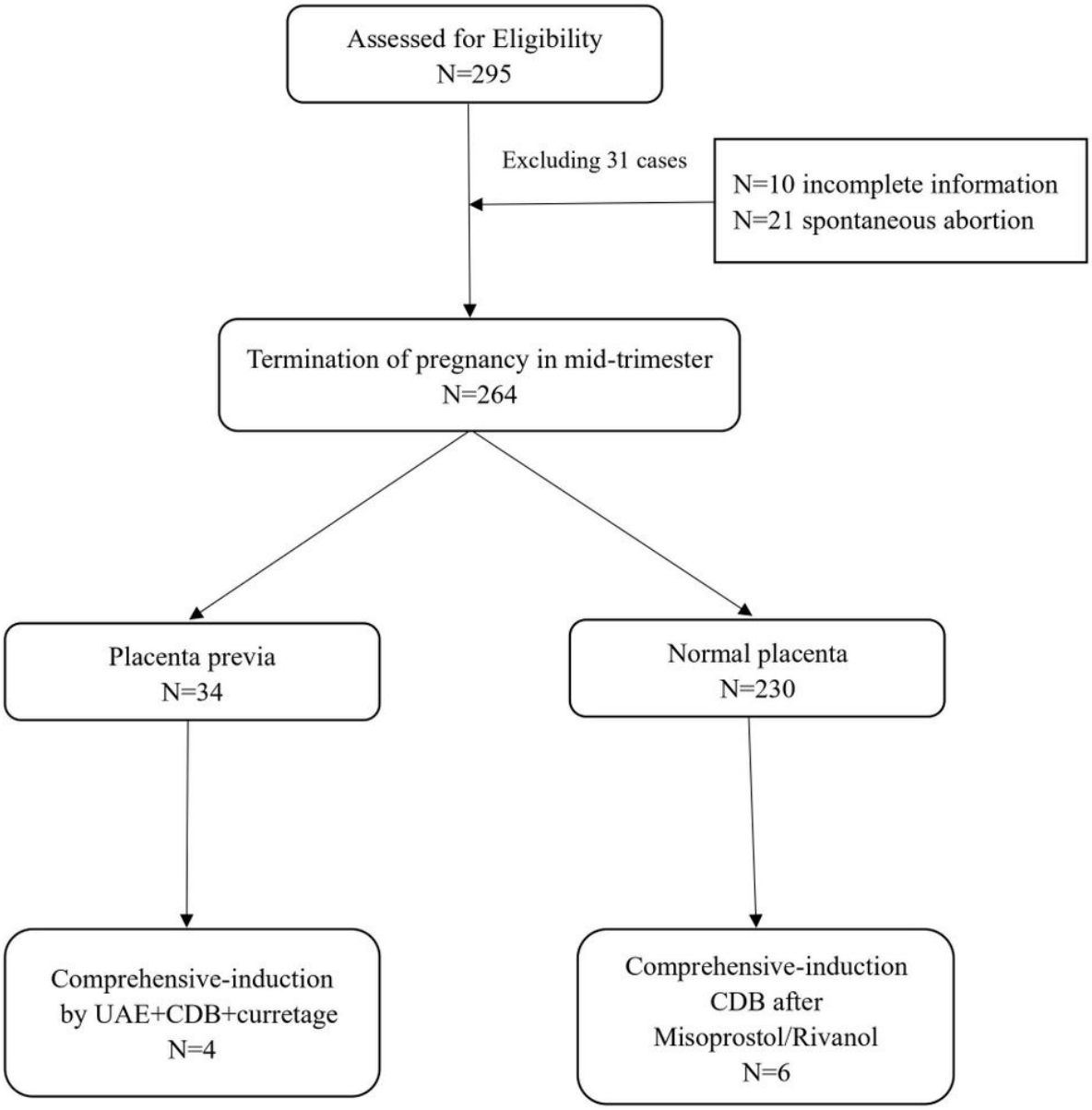

Fig 1: Flowchart demonstrating

Figure 1

According to placenta position, patients with placenta previa were collected in the observation group (n=34), those without placenta previa collected in the control group (n=230). (Fig 1)

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Table1.docx
- Table3.docx