Original Article

Vasa previa: Perinatal outcomes in singleton and multiple pregnancies

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SUMMARY Vasa previa (VP) is a rare and life-threatening condition for the fetus. It is associated with increased perinatal mortality rates. The current study sought to retrospectively analyze the perinatal outcomes of VP in singleton and multiple pregnancies between January 1, 2013 and December 31, 2019 at a tertiary hospital in west China. One hundred and fifty-seven cases of VP were identified, including 131 singletons, 23 twins and 3 triplets. VP in 20 cases was diagnosed at delivery. There were 183 live births. Neonatal mortality was significantly higher in cases with no prenatal diagnosis (9.7% vs. 1.3%, p = 0.035). There was a significantly higher rate of NICU admission, premature infant and neonatal pneumonia in cases with prenatal diagnosis (p < 0.05). Among twin pregnancies with VP as a prenatal diagnosis, there were significantly earlier gestational age at admission (31.1 vs. 34.1 weeks, p = 0.000) and delivery age (33.4 vs. 35.3 weeks, p = 0.000) than those among singleton pregnancies. The neonatal mortality in twins with prenatal diagnosis was significantly higher than that in singletons (0% vs. 6.9%, p = 0.037). Early hospitalization of VP in the third trimester may be reasonable. The data suggest that the timing of elective delivery at 34-36 weeks in singletons and 32-34 weeks in twins may be suitable. It should be emphasized to make corresponding optimal delivery time according to individual differences for the women, especially in twin pregnancy.

Keywords vasa previa (VP), prenatal diagnosis, no prenatal diagnosis, singleton and multiple pregnancies, perinatal outcomes

1. Introduction

Vasa previa (VP) is a rare condition in which the umbilical vessels, unprotected by either placental tissue or Wharton's jelly, run through the membranes over the internal cervical os and under the fetal presenting part. The estimated incidence varies from 0.2 to 0.60 per 1,000 pregnancies (*1-3*). Previa vessels laceration may result in blood loss and catastrophic fetal distresses or stillbirth/ neonatal death (*4,5*), which is associated with increased perinatal mortality.

Risk factors for VP are velamentous cord insertion, second-trimester low-lying placenta or placenta praevia, conception by assisted reproductive technologies, bilobed and succenturiate lobe placentas situated in the lower uterine segment, and multiple pregnancies (3, 6, 7).

Antenatal diagnosis of VP and delivery by planned cesarean section before the rupture of the membranes is recommended with the survival rate increased to 97-99%; however, survival rates in cases without antenatal diagnosis are poor, even in cases with emergency cesarean section, the neonatal survival rate is less than

50% (2).

According to the image of VP by color Doppler ultrasound, two varieties have been described (8): Type 1, in which there was a single placental lobe with a velamentous cord insertion, and Type 2, in which the vessels over the cervix were connecting between lobes of a placenta with multiple lobes. Recently, Suekane highlighted a new type of VP as Type 3, which is with a boomerang orbit and without velamentous insertion nor bilobed/accessory placenta (9).

The aims of this study were to *i*) analyze the outcomes of VP in singleton and multiple pregnancies; *ii*) investigate the clinical characteristics of patients with prenatal diagnosed VP or VP diagnosed at delivery.

2. Patients and Methods

A retrospective cohort study was conducted in patients with VP, which delivered between January 1, 2013 and December 31, 2019 at a tertiary hospital in west China. The study was approved by the Ethics committee of West China Second University Hospital (No. 2020129). Informed consent was not required because the study was conducted retrospectively. Medical records of pregnant women were reviewed by the authors.

2.1. Diagnosis of VP

Prenatal diagnosis of VP were evaluated by transabdominal or transvaginal ultrasound (10) and suspected VP in ultrasonography confirmed by MRI.

Patients with antenatal diagnosis of VP or diagnosis at delivery *via* clinical and/or pathologic investigation were reviewed. Placental pathological examination was performed to confirm the diagnosis of VP (11). Cases with antenatal diagnosis of VP but not verified at delivery were excluded.

According to the image of VP by color Doppler ultrasound, VP was diagnosed as follows: Type 1 VP, in which there was a single placental lobe and the fetal vessels run freely through the membranes over the cervix or within 2 cm from the internal cervical os; Type 2 VP, in which the vessels were connected between lobes of a placenta with multiple lobes over the cervix or within 2 cm from the internal cervical os (8,12); Type 3 VP, in which fetal vessels were boomerang orbit and without velamentous insertion nor bilobed/accessory placenta (9).

2.2. Data collection

Maternal collected data included demographic characteristics, gestational age at diagnosis, delivery age, obstetric history, complications, indications of delivery, mode of delivery, delivery documents, pathologic reports, and blood loss at delivery. Neonatal data included gestational age at delivery, birth weight, Apgar scores, neonatal death, admission to the NICU, and major neonatal conditions.

2.3. Statistical analysis

Descriptive statistics, such as frequency, percentage, and mean, standard deviation (SD), and the range were used for the presentation of variables. Parameters were analyzed using two-tailed student's *t*-test, Chi-squared test or Fisher's exact probability test, and Spearman test. Statistical analyses were performed with SPSS version19.0 (SPSS Inc, Chicago, IL). A *p* value < 0.05 was considered statistically significant.

3. Results

3.1. Study participants

During the study period, 79,647 pregnant women were delivered at our institution. One hundred and fifty-seven patients had VP, and 26 cases (16.56%) were multiple pregnancies, as 10 monochorionic diamniotic (MCDA) twin pregnancy, 13 dichorionic diamniotic (DCDA) twin pregnancy, 2 dichorionic triamniotic (DCTA) triplet pregnancy, and 1 trichorionic triamniotic (TCTA) triplet pregnancy. The incidence of VP was 1.97 per 1,000 pregnancies. Maternal age was 31.7 ± 4.9 years.

The classifications of VP were: Type 1 141cases (89.8%) (Figure 1), Type 2 12 cases (7.6%) (Figure 2), and Type 3 4 cases (2.6%) (Figure 3). Among the cases, 137 cases (87.3%) were diagnosed antenatally, 20 cases (12.7%) were diagnosed at delivery.

In prenatal diagnosis cases, there were 120 singleton pregnancies, 16 twin pregnancies (MCDA 7, DCDA 9) and 1 triplet pregnancy (TCTA 1). One hundred thirtytwo cases (96.4%) were diagnosed by ultrasound and 5 cases were diagnosed by MRI.

In cases without prenatal diagnosis, there were 11 singleton pregnancies, 7 twin pregnancies (MCDA 3, DCDA 4) and 2 triplet pregnancies (DCTA 2).

One hundred and fifty-one cases (96.2%) had one or more identifiable placental and/or maternal risk indications. Velamentous cord insertion (70.1%) and low-lying placenta or placenta previa (59.2%) were two of the most prevalent. Maternal demographics and pregnancy characteristics are presented in Table 1.

3.2. Management during pregnancy in prenatal diagnosis group

Among the prenatal diagnosis cases, 22 cases were conceived by assisted reproduction technology, as 7 twins, 14 singletons and 1 triplet pregnancy. The diagnosis gestational age (GA) in singletons was $26.6 \pm$ 4.9 weeks, 66.7% in the second trimester, and 33.3% in the third trimester. In twins, GA at diagnosis was $24.4 \pm$ 4.1 weeks, 81.2% in the second trimester of pregnancy, 18.8% in the third trimester. In twin pregnancies, selected termination of abnormal fetus was performed at 17+3weeks in one DCDA twin; one fetus death (not with VP) presented at 28+6 weeks in one MCDA twin; one fetus (not with VP) was dead at 27 weeks due to severe fetal growth retardation in one DCDA twin.

One hundred and thirty-seven cases were monitored closely until delivery. The gestational age at admission



Figure 1. Images of Type 1 vasa previa.



Figure 2. Images of Type 2 vasa previa.

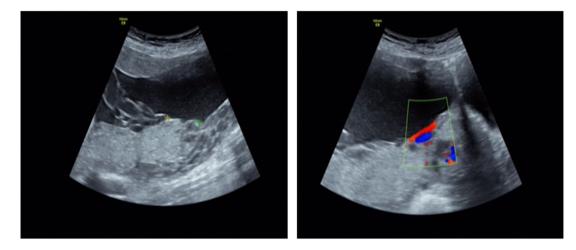


Figure 3. Images of Type 3 vasa previa.

| Table 1. Maternal demographics and | pregnancy characteristics of vasa previa |
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| Variables | All cases $(n = 157)$ | Prenatal diagnosis ($n = 137$) | No prenatal diagnosis ($n = 20$) | p value |
|---|-----------------------|----------------------------------|------------------------------------|-------------|
| Maternal age (y) | 31.7 ± 4.9 | 31.7 ± 4.8 | 31.2 ± 5.3 | 0.642 |
| \geq 35 years old, <i>n</i> (%) | 39 (24.8) | 33 (24.1) | 6 (30.0) | 0.768 |
| BMI (kg/m^2) | 25.7 ± 2.5 | 25.6 ± 2.5 | 26.3 ± 2.5 | 0.248 |
| Gravidity | 2 (1-8) | 3 (1-8) | 2 (1-5) | 0.031 |
| Primipara, n (%) | 100 (63.7) | 84 (61.3) | 16 (80.0) | 0.105 |
| Singleton, n (%) | 131 (83.4) | 120 (87.6) | 11 (55.0) | 0.001 |
| Risk factor | | | | |
| Multiple pregnancy, n (%) | 26 (16.6) | 17 (12.4) | 9 (45.0) | 0.001 |
| ART, n (%) | 28 (17.8) | 25 (18.2) | 3 (15.0) | 0.967 |
| Low-lying placenta or placenta previa, n (%) | 93 (59.2) | 88 (64.2) | 5 (25.0) | 0.001 |
| Velamentous cord insertion, n (%) | 110 (70.1) | 100 (73.0) | 10 (50.0) | 0.036 |
| Bilobate or succenturiate placenta, n (%) | 12 (7.6) | 12 (8.8) | 0 (0.0) | 0.354 |
| At least one risk factor [#] , n (%) | 151 (96.2) | 134 (97.8) | 17 (85.0) | 0.028^{*} |

Data are presented as mean ± standard deviation or proportion (%). BMI: Body Mass Index; ART: assisted reproduction technology. [#]includes multiple pregnancy, ART pregnancy and placental factor. ^{*}Fisher's Exact Test.

was 33.7 ± 2.3 weeks with delivery age 35.1 ± 1.6 weeks. All were performed as cesarean section (CS), 35 cases with emergency CS, and 102 cases with planned CS. There were 15.3% cases before 34 weeks, 72.3% between 34 and 36 weeks, and 12.4% at term. A total of 120 cases (87.6%) received either 1 or 2 courses of

antenatal steroids.

In 120 singleton cases, 83 (69.2%) patients were hospitalized with no symptoms, which included 33 cases of hospitalization at 32.6 ± 1.4 weeks (range 29-34 weeks) with delivery at 34.7 ± 1.5 weeks (range 30-38 weeks), 50 cases of hospitalization at 35.4 ± 1.3 weeks

(range 34-40 weeks) with delivery at 36.1 ± 1.2 weeks (range 34-40 weeks of gestation). Thirty-seven cases had emergency admissions due to premature rupture of membranes (PROM), vaginal bleeding, abnormal fetal monitoring and threatened premature labor, with delivery at 34.7 ± 1.2 weeks (range 32-39 weeks).

Among 16 twin cases, 7 patients were hospitalized with no symptoms at 32.6 ± 1.3 weeks (range 30-35 weeks) with delivery at 33.9 ± 1.0 weeks (range 32-36 weeks). Nine cases had emergency admissions due to vaginal bleeding, abnormal fetal monitoring and threatened premature labor, with delivery at 33.0 ± 1.1 weeks (range 31-35 weeks).

In singleton pregnancies, emergency caesarean delivery was performed in 28 cases due to PROM (3 cases), vaginal bleeding (3 cases), abnormal fetal monitoring (2 cases), severe preeclampsia (1 case), in labor (19 cases). In twin pregnancies, emergency caesarean section was performed due to vaginal bleeding (2 cases), abnormal fetal monitoring (2 cases) and in labor (2 cases). In a triplet pregnancy an emergency caesarean section was performed for severe preeclampsia.

The management in cases with prenatal diagnosis is shown in Table 2 and Table 3.

3.3. Management during pregnancy in not prenatal diagnosis group

Among the cases diagnosed at delivery, the admission

age was 35.6 ± 3.6 weeks (range 27-40 weeks), with delivery at 36.3 ± 3.0 weeks (range 28-40 weeks), and 12 cases with delivery at term.

Seventeen cases had CS, 12 cases with planned CS, 5 cases with emergency CS due to PROM with velamentous cord insertion, PROM with twin pregnancy, intrahepatic cholestasis of pregnancy with twin pregnancy, twin-twin transfusion syndrome and severe preeclampsia.

Vaginal delivery was performed in 3 cases, including 2 singleton pregnancies with velamentous cord insertion delivery at term and 1 DCTA triplet pregnancy in labor at 28+1 weeks with PROM.

3.4. Perinatal outcomes between type1 and type 2 VP

Among the cases of Type 1 VP, one hundred twentyone cases were diagnosed prenatally. Gestational age at diagnosis was 26.1 ± 4.8 weeks, 71.1% in the second trimester, and 28.9% in the third trimester. The gestational age at admission was 33.9 ± 2.6 weeks with delivery age 35.2 ± 1.9 weeks. 138 cases (97.9%) had cesarean section.

Among the cases of Type 2 VP, they were all diagnosed prenatally. The gestational age at admission was 33.7 ± 1.5 weeks with delivery age 35.0 ± 1.6 weeks. All cases had cesarean section.

Except for 4 cases of Type 3 VP, perinatal outcomes between Type 1 and Type 2 VP cases are shown in detail in Table 4.

Table 2. Perinatal outcomes in cases with vasa previa

Variables Prenatal diagnosis (n = 137)No prenatal diagnosis (n = 20)p value Prenatal hemorrhage, n (%) 21 (15.3) 1 (5.0) 0.369 GA at admission (wks) 33.7 ± 2.3 35.6 ± 3.6 0.002 Corticosteroids for fetal lung maturity, n (%) 120 (87.6) 12 (60.0) 0.005 GA at delivery (wks), n (%) 35.1 ± 1.6 36.3 ± 3.0 0.004 28-31 6/7 3 (2.2) 2 (10.0) 0.000^{*} 32-33 6/7 18 (13.1) 0(0.0)34-36 6/7 99 (72.3) 6 (30.0) > 3717 (12.4) 12 (60.0) Mode of delivery, n (%) 0.002 Vaginal delivery 0(0.0)3 (15.0) Cesarean delivery 137 (100.0) 17 (85.0) Planning cesarean delivery 102 (74.5) 12 (70.6) 0.961 Emergency cesarean delivery 35 (25.5) 5 (29.4) Neonatal outcomes Number of fetus Live births, n 152 31 5 min Apgar < 7, n (%) 2 (1.3) 2 (6.5) 0.134 Premature infant, n (%) 135 (88.8) 17 (54.8) 0.000Birth weight (g) $2,\!374.5\pm439.2$ $2,\!380.7\pm 665.6$ 0.961 NICU, n (%) 85 (55.9) 11 (35.5) 0.038 NICU LOS (days) 8 (1-49) 6 (5-50) 0.503 Neonatal mortality, n (%) 2(1.3)3 (9.7) 0.035 19 (12.5) RDS, n (%) 2 (6.5) 0.513 53 (34.9) 0.041 Pneumonia, n (%) 5 (16.1) IVH, *n* (%) 14 (9.2) 2 (6.5) 0.883 Anemia, n (%) 19 (12.5) 3 (9.7) 0.891

GA: gestational age; RDS: Respiratory distress syndrome; IVH: Intraventricular hemorrhage; LOS: Length of stay. *Fisher's Exact Test.

| Variables | Singleton | Twin | <i>p</i> value |
|--|---------------------|---------------------|----------------|
| Total | 120 | 16 | - |
| Age | 32.0 ± 5.0 | 30.1 ± 3.4 | 0.136 |
| \geq 35, <i>n</i> (%) | 32 (26.7) | 1 (6.3) | 0.139 |
| ART, n (%) | 16 (13.3) | 8 (50.0) | 0.001 |
| GA at diagnosis (wks), n (%) | 26.6 ± 4.9 | 24.4 ± 4.1 | 0.097 |
| Second trimester of pregnancy | 80 (66.7) | 13 (81.2) | 0.272 |
| Third trimester of pregnancy | 40 (33.3) | 3 (18.8) | |
| GA at admission (wks) | 34.1 ± 2.0 | 31.1 ± 2.6 | 0.000 |
| Irregular vaginal bleeding at early pregnancy, n (%) | 43 (35.8) | 5 (31.3) | 0.788 |
| Antenatal hospital LOS (day) | 8 (1-47) | 10 (2-52) | 0.029 |
| Indication for hospitalization, n (%) | | | |
| Asymptomatic | 83 (69.2) | 7 (43.8) | 0.004^{*} |
| Vaginal bleeding | 20 (16.7) | 1 (6.3) | |
| Premature rupture of membrane | 3 (2.5) | 0 (0.0) | |
| Threatened premature labor | 13 (10.8) | 6 (37.5) | |
| Abnormal fetal monitoring | 1 (0.8) | 2 (12.5) | |
| Corticosteroids for fetal lung maturity, n (%) | 104 (86.7) | 15 (93.8) | 0.687 |
| Tocolysis, n (%) | 32 (26.7) | 11 (68.8) | 0.001 |
| Length of tocolysis (days) | 3 (1-21) | 3 (2-14) | 0.945 |
| GA at delivery (wks), n (%) | 35.3 ± 1.5 | 33.4 ± 1.1 | 0.000 |
| 28-31 6/7 | 2 (1.7) | 1 (6.3) | 0.000^{*} |
| 32-33 6/7 | 9 (7.5) | 8 (50.0) | |
| 34-36 6/7 | 92 (76.7) | 7 (43.8) | |
| \geq 37 | 17 (14.2) | 0 (0.0) | |
| Planning cesarean, n (%) | 92 (76.7) | 10 (62.5) | 0.357 |
| Emergency cesarean, n (%) | 28 (23.3) | 6 (37.5) | |
| Live births | 120 | 29 | |
| Neonatal mortality, n (%) | 0 (0.0) | 2 (6.9) | 0.037^{*} |
| Preterm, n (%) | 103 (85.8) | 29 (100.0) | 0.068 |
| Birth weight (g) | $2,495.2 \pm 385.5$ | $1,909.5 \pm 331.8$ | 0.000 |
| Birth weight < 2500 g, n (%) | 63 (52.5) | 28 (96.6) | 0.000 |
| NICU, <i>n</i> (%) | 59 (49.2) | 23 (79.3) | 0.003 |

Table 3. Perinatal outcomes between singleton and twin pregnancies in antenatal diagnosed cases

ART: Assisted reproduction technology; GA: gestational age; LOS: Length of stay; NICU: neonatal intensive care unit. *Fisher's Exact Test.

3.5. Neonatal outcomes

Except for one twin death due to selected termination, sudden death and severe fetal growth retardation in twin pregnancies, there were 183 live births in 157 cases.

In prenatal diagnosis cases, there were 152 live births with mean birth weight $2,374.5 \pm 439.2g$ and 88.8% were preterm infants. Over half of neonates (55.9%) were transferred to NICU with length of stay about 8 days (1-49 days). Nineteen neonates had respiratory distress syndrome, twelve of them were treated with pulmonary surfactant; 19 neonates were diagnosed with anemia and nine of them required blood transfusions. The neonatal mortality was 1.3% (2/152). Perinatal outcomes between singleton and twin pregnancies in antenatal diagnosed cases are shown in detail in Table 3.

There were 31 live births in cases with no antenatal diagnosis, mean birth weight 2,380.7 \pm 665.6g and 54.8% were preterm infants. Eleven neonates (35.5%,) were transferred to NICU with length of stay about 6 days (5-50 days), 2 neonates were complicated with respiratory distress syndrome, and 3 (9.7%) with anemia. The neonatal mortality was 9.7% (3/31).

Compared with cases with prenatal diagnosis of VP, neonatal mortality was significantly higher in cases

with no prenatal diagnosis (9.7% vs. 1.3%, p = 0.035). There was no difference in neonatal respiratory distress syndrome between the prenatal diagnosis cases and no prenatal diagnosis cases (p = 0.513). Meanwhile, there was a significantly higher rate of NICU admission, premature infant and neonatal pneumonia in cases with prenatal diagnosis. All surviving newborns were followed up and in good health.

4. Discussion

VP is a rare and life-threatening condition for the fetus. The incidence in this study was higher due to our hospital being the regional tertiary referral center in west China.

In this study, 96.2% cases of VP had one or more identifiable placental and/or maternal risk indications, velamentous cord insertion (70.1%) and placenta previa or low-lying placenta (59.2%) are most prevalent among them, the same as published reports (3, 6, 7).

Some authors put forward that velamentous insertion of the cord is a prerequisite for VP (13). In this study, 4 cases were difficult to classify into either type1 or type2 VP, in which the umbilical cord showed no velamentous insertion and some vessel branches went out of the placental surface and subsequently returned to the

| Table 4. Perinata | l outcomes | between | typel | and | type 2 | 2 vasa previa |
|-------------------|------------|---------|-------|-----|--------|---------------|
|-------------------|------------|---------|-------|-----|--------|---------------|

| Variables | Type 1 | Type 2 | <i>p</i> value |
|--|---------------------|---------------------|----------------|
| Total | 141 | 12 | - |
| Age | 31.5 ± 4.8 | 33.8 ± 5.1 | 0.111 |
| \geq 35, <i>n</i> (%) | 32 (22.7) | 6 (50.0) | 0.079 |
| Singleton, n (%) | 116 (82.3) | 11 (91.7) | 0.666 |
| ART, n (%) | 28 (19.9) | 0 (0.0) | 0.187 |
| Prenatal diagnosis, n (%) | 121 (85.8) | 12 (100.0) | 0.340 |
| GA at diagnosis (wks), n (%) | 26.1 ± 4.8 | 27.5 ± 5.7 | 0.366 |
| Second trimester of pregnancy | 86 (71.1) | 6 (50.0) | 0.238 |
| Third trimester of pregnancy | 35 (28.9) | 6 (50.0) | |
| Antenatal hospital LOS (day) | 7 (1-52) | 6 (1-25) | 0.788 |
| GA at admission (wks) | 33.9 ± 2.6 | 33.7 ± 1.5 | 0.693 |
| Irregular vaginal bleeding at early pregnancy, n (%) | 44 (31.2) | 7 (58.3) | 0.111 |
| Indication for Hospitalization, n (%) | | | |
| Asymptomatic | 89 (63.1) | 7 (58.3) | 0.554^{*} |
| Vaginal bleeding | 18 (12.8) | 3 (25.0) | |
| Premature rupture of membrane | 7 (5.0) | 0 (0.0) | |
| Threatened premature labor | 4 (2.8) | 1 (8.3) | |
| Abnormal fetal monitoring | 20 (14.2) | 1 (8.3) | |
| Corticosteroids for fetal lung maturity, n (%) | 120 (85.1) | 8 (66.7) | 0.211 |
| Tocolysis, <i>n</i> (%) | 46 (32.9) | 3 (25.0) | 0.813 |
| GA at delivery (wks), n (%) | 35.2 ± 1.9 | 35.0 ± 1.6 | 0.693 |
| 28-31 6/7 | 5 (3.5) | 0 (0.0) | 0.725* |
| 32-33 6/7 | 16 (11.3) | 2 (16.7) | |
| 34-36 6/7 | 92 (65.2) | 9 (75.0) | |
| ≥ 37 | 28 (19.9) | 1 (8.3) | |
| Mode of delivery, n (%) | | | |
| Vaginal delivery | 3 (2.1) | 0 (0.0) | 1.000^{*} |
| Cesarean delivery | 138 (97.9) | 12 (100.0) | 11000 |
| Planning cesarean delivery | 100 (72.5) | 11 (91.7) | 0.187^{*} |
| Emergency cesarean delivery | 38 (27.5) | 1(8.3) | 0.107 |
| Neonatal outcomes | 20 (2712) | 1 (0.0) | |
| Live births, n | 166 | 13 | _ |
| 5 min Apgar < 7 , n (%) | 2 (1.2) | 2 (15.4) | 0.027^{*} |
| Premature infant, <i>n</i> (%) | 136 (81.9) | 12 (92.3) | 0.567 |
| Birth weight (g) | $2,355.4 \pm 488.4$ | $2,490.8 \pm 385.5$ | 0.331 |
| NICU, n (%) | 86 (51.8) | 9 (69.2) | 0.261 |
| NICU LOS (days) | 8 (1-50) | 7 (3-10) | 0.001 |
| Neonatal mortality, n (%) | 3 (1-30) | 2 (15.4) | 0.001 |
| RDS, n (%) | 19 (11.4) | 2 (15.4) | 0.653* |
| Pneumonia, n (%) | 5 (32.5) | 4 (30.8) | 1.000 |
| IVH, n (%) | 16 (9.6) | 4 (50.8) 0 (0.0) | 0.504 |
| Anemia, n (%) | 21 (12.7) | 1 (7.7) | 0.932 |

ART: Assisted reproduction technology; GA: gestational age; LOS: Length of stay; NICU: neonatal intensive care unit; RDS: Respiratory distress syndrome; IVH: Intraventricular hemorrhage. *Fisher's Exact Test.

placental cotyledons. Kanda *et al.* (14) and Suekane *et al.* (9) reported the same conditions and Suekane highlighted this new type as Type3. We agreed with the suggestion and classified the four cases as Type 3 VP. Based on these data, careful observation of fetal vessels running around the internal cervix by color Doppler imaging should be performed whether cases had velamentous cord insertion or not. At present, there is no evidence to prove that different forms of VP have different perinatal outcomes. The essence of VP classification is based on the variation of fetal blood vessels. It has no clear clinical significance in the current classification without considering the mechanism of developmental biology.

The ultrasonic signs of VP could be described as linear or tubular structures in front of the cervix inner

os, and pulsed wave color Doppler demonstrates the fetus's umbilical artery blood flow and a rate consistent with the fetal heart rate (10). VP should be confirmed by examining the placenta membrane during labor and postpartum (15).

Transvaginal ultrasound using colour and pulse-wave Doppler to evaluate the internal os and lower uterine segment is the most accurate means to diagnose VP (16). Prenatal diagnosis of VP was made most frequently during the second trimester of pregnancy. Although two prospective studies showed that the sensitivity of VP detection was 100% with a specificity of 99-99.8%, the prenatal detection rate of VP varied from 53% to 100% in retrospective studies (17). It should be known that not all cases of VP can be diagnosed antenatally (18). In published guidelines, universal screening for VP in singleton pregnancies by ultrasound is not recommended. However, targeted screening should be considered in high risk pregnant women during the midtrimester scan using a transvaginal ultrasound probe with color and pulsed Doppler (3, 16, 17, 20), which can reduce perinatal loss. Whereas, screening all twin pregnancies for VP with transvaginal ultrasound is cost-effective (20).

Some VP may be undiagnosed. The American Institute of Ultrasound in Medicine (AIUM) and Society for Maternal-Fetal Medicine (SMFM) recommend that the "placental position, appearance and relationship with the cervix" should be used as part of the standard parameters for routine ultrasound evaluation in obstetrics (21,22). Furthermore, the multiplanar imaging capability of magnetic resonance imaging (MRI) is more useful to identify the exact position of placenta and the area adjacent to the internal cervix os (23,24). In this study, five VP were diagnosed antenatally using MRI, one case with central placenta previa and bilobed placentas, three cases with placental implantation abnormality, and one case with marginal placental previa. It should be noted that MRI cannot be used in most obstetric practices due to its expensiveness and applicable conditions.

Hospitalization of VP was suggested at 30-32 gestational weeks by RCOG, SOGC and RANZCOG (11,16,19), 30-34 weeks by SMFM (22). Administration of corticosteroids in patients with VP was recommended at 28-32 weeks by SOGC and SMFM (19,22), around 30-32 weeks by RANZCOG (16), and at 32 weeks by RCOG (11).

To minimize the impact of prematurity and adverse outcomes due to VP, optimal gestational age at delivery is of vital importance. Gestational age at delivery was proposed to be 34-36 weeks by RCOG and RANZCOG(11,16), 34-37 weeks by SMFM (22), and the guidelines recommend that emergency cesarean delivery should be performed if bleeding or rupture of membranes occurs in cases with suspected VP (11,16,19,22). Swank (25) suggested elective delivery at 33-34 weeks. A decision analysis suggested that delivery at 34-35 weeks may balance the risk of perinatal death, risks related to prematurity as respiratory distress syndrome, mental retardation, and cerebral palsy (26).

Based on our findings, we concur with the delivery timing recommendations in singletons with antepartum VP at 34-36 weeks, and corticosteroids administration at 28-32 weeks. Whether advanced admission should be a combination of kinds of factors, including multiple pregnancy, prenatal bleeding and premature birth risk (11,27).

Although the perinatal mortality in VP is reduced with improved prenatal diagnosis, catastrophes also still happen (7). In Oyelese's report, prenatal diagnosed VP had a higher infant survival rate than cases with no prenatal diagnosis (97% vs. 44%) (2). In this study the neonatal mortality in cases without prenatal diagnosis was significantly higher (9.7% vs. 1.3%).

Because of fear of stillbirth, preterm delivery in VP is high. In this study, the rate of preterm delivery in prenatal diagnosis cases was significantly higher than that with no prenatal diagnosis cases (87.6% vs. 40%). The neonatal complications are always related to iatrogenic preterm birth and a good perinatal outcome can be obtained after treatment (28).

In published papers, there are few cases of VP in multiple pregnancies. Rupture of the vessels in VP can cause acute hemorrhage and acute fetal exsanguination, which occur in the corresponding twin in dichorionic twin pregnancy, and in both fetuses in monochorionic twin pregnancy.

No consensus suggested delivery age for twins with VP. In Jauniaux's systematic review of VP diagnosed prenatally in twin pregnancies, delivery age was 32+6 (3+5) weeks (29). Catanzarite suggests timing of elective delivery for singletons at 34-35 weeks and delivery at 32-34 weeks in twins may be risk-beneficial (30). Based on our findings, we think that in twin pregnancies with antepartum VP, optimal delivery timing is at 32-34 weeks.

The strengths of this study are that perinatal outcomes were compared in VP cases with prenatal diagnosis and with no prenatal diagnosis; there is a larger number of DC and MC twin pregnancy; and the perinatal outcomes between singleton and twin pregnancies in antenatal diagnosed cases were investigated. The limitation in this study lies in the retrospective study. Definitely, a prospective study in VP is not feasible due to its rarity.

5. Conclusion

Prenatal diagnosis of VP should be highlighted. Our results confirm that the fetal and neonatal outcomes either in singletons or in twins are better in cases with VP diagnosed antenatally. Early hospitalization of VP in the third trimester may be reasonable. The timing of elective delivery at 34-36 weeks in singletons and at 32-34 weeks in twins may be suitable. It should be emphasized to make a corresponding optimal delivery time according to individual differences for the women, especially in twin pregnancy.

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References

- 1. Oyelese Y, Smulian JC. Placenta previa, placenta accreta, and vasa previa. Obstet Gynecol. 2006; 107:927-941.
- Oyelese Y, Catanzarite V, Prefumo F, Lashley S, Schachter M, Tovbin Y, Goldstein V, Smulian JC. Vasa previa: the impact of prenatal diagnosis on outcomes. Obstet Gynecol. 2004; 103:937-942.
- Ruiter L, Kok N, Limpens J, Derks JB, de Graaf IM, Mol B, Pajkrt E. Incidence of and risk indicators for vasa praevia: a systematic review. BJOG. 2016; 123:1278-1287.
- Silver RM. Abnormal placentation: placenta previa, vasa previa, and placenta accreta. Obstet Gynecol. 2015; 126: 654-668.
- Jauniaux E, Savvidou MD. Vasa praevia: more than 100 years in preventing unnecessary fetal deaths. BJOG. 2016; 123:1287.
- Pirtea LC, Grigoraş D, Sas I, Ilie AC, Stana LG, Motoc AG, Jianu AM, Mazilu O. *In vitro* fertilization represents a risk factor for vasa praevia. Rom J Morphol Embryol. 2016; 57:627-632.
- Tsakiridis I, Mamopoulos A, Athanasiadis A, Dagklis T. Diagnosis and management of vasa previa: a comparison of 4 national guidelines. Obstet Gynecol Surv. 2019; 74:436-442.
- Catanzarite V, Maida C, Thomas W, Mendoza A, Stanco L, Piacquadio KM. Prenatal sonographic diagnosis of vasa previa: ultrasound findings and obstetric outcome in ten cases. Ultrasound Obstet Gynecol. 2001; 18:109-115.
- Suekane T, Tachibana D, Pooh RK, Misugi T, Koyama M. Type-3 vasa previa: normal umbilical cord insertion is not enough to exclude vasa previa in cases with abnormal placental location. Ultrasound Obstet Gynecol. 2020; 55:556-557.
- D'Antonio F, Bhide A. Ultrasound in placental disorders. Best Pract Res Clin Obstet Gynaecol. 2014; 28:429-442.
- Jauniaux E, Alfirevic Z, Bhide AG, Burton GJ, Collins SL, Silver R, Royal College of Obstetricians and Gynaecologists. Vasa praevia: diagnosis and management. Green-top Guideline No. 27b. BJOG. 2019; 126:e49-e61.
- Kelley BP, KlochkoCL, Atkinson S, Hillman D, Craig BM, Sandberg SA, Gaba AR, Halabi SS. Sonographic diagnosis of velamentous and marginal placental cord insertion. Ultrasound Q. 2020; 36:247-254.
- Stafford IP, Neumann DE, Jarrell H. Abnormal placental structure and vasa previa: confirmation of the relationship. J Ultrasound Med. 2004; 23:1521-1522.
- Kanda E, Matsuda Y, Kamitomo M, Maeda T, Mihara K, Hatae M. Prenatal diagnosis and management of vasa previa: a 6-year review. J Obstet Gynaecol Res. 2011; 37:1391-1396.
- 15. Derbala Y, Grochal F, Jeanty P. Vasa previa. J Prenat Med. 2007; 1: 2-13.
- 16. The Royal Australian and New Zealand College of Obstetricians and Gynaecologists Excellence in Women's Health. Vasa Praevia (C-Obs-47). https:// ranzcog.edu.au/RANZCOG_SITE/media/RANZCOG-MEDIA/Women%27s%20Health/Statement%20and%20 guidelines/Clinical-Obstetrics/Vasa-Praevia-(C-Obs-47). pdf?ext=.pdf (accessed November 30, 2020)
- Ruiter L, Kok N, Limpens J, Derks JB, de Graaf IM, Mol BWJ, Pajkrt E. Systematic review of accuracy of

ultrasound in the diagnosis of vasa previa. Ultrasound Obstet Gynecol. 2015; 45:516-522.

- Nishtar A, Wood PL. Is it time to actively look for vasa praevia? J Obstet Gynaecol. 2012; 32:413-418.
- Gagnon R. No. 231-guidelines for the management of vasa previa. J Obstet Gynaecol Can. 2017; 39: e415-e421.
- Cipriano LE, Barth WH Jr, Zaric GS. The costeffectiveness of targeted or universal screening for vasa praevia at 18-20 weeks of gestation in Ontario. BJOG. 2010; 117:1108-1118.
- 21. American Institute of Ultrasound in Medicine. AIUM practice guideline for the performance of obstetric ultrasound examinations. J Ultrasound Med. 2013; 32:1083-1101.
- Society of Maternal-Fetal (SMFM) Publications Committee, Sinkey RG, Odibo AO, Dashe JS. #37: Diagnosis and management of vasa previa. Am J Obstet Gynecol. 2015; 213: 615-619.
- Kikuchi A, Uemura R, Serikawa T, Takakuwa K, Tanaka K. Clinical significances of magnetic resonance imaging in prenatal diagnosis of vasa previa in a woman with bilobed placentas. J Obstet Gynaecol Res. 2011; 37:75-78.
- Oppenheimer DC, Mazaheri P, Ballard DH, Yano M, Fowler KJ. Magnetic resonance imaging of the placenta and gravid uterus: a pictorial essay. Abdom Radiol (NY). 2019; 44:669-684.
- Swank ML, Garite TJ, Maurel K, Das A, Perlow JH, Combs CA, Fishman S, Vanderhoeven J, Nageotte M, Bush M, Lewis D. Vasa previa: diagnosis and management. Am J Obstet Gynecol. 2016; 215:223.e1-e6.
- Robinson BK, Grobman WA. Effectiveness of timing strategies for delivery of individuals with vasa previa. Obstet Gynecol. 2011; 117:542-549.
- Yerlikaya-Schatten G, Chalubinski KM, Pils S, Springer S, Ott J. Risk-adapted management for vasa praevia: a retrospective study about individualized timing of caesarean section. Arch Gynecol Obstet. 2019; 299:1545-1550.
- Sullivan EA, Javid N, Duncombe G, Li Z, Safi N, Cincotta R, Homer CSE, Halliday L, Oyelese Y. Vasa previa diagnosis, clinical practice, and outcomes in Australia. Obstet Gynecol. 2017; 130:591-598.
- Jauniaux E, Melcer Y, Maymon R. Prenatal diagnosis and management of vasa previa in twin pregnancies: a case series and systematic review. Am J Obstet Gynecol. 2017; 21:568-575.
- Catanzarite V, Cousins L, Daneshmand S, Schwendemann W, Casele H, Adamczak J, Tith T, Patel A. Prenatally diagnosed vasa previa: a single-institution series of 96 cases. Obstet Gynecol. 2016; 128:1153-1161.

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