OBSTETRICS

Vasa previa: a multicenter retrospective cohort study

Hadi Erfani, MD, MPH; Sina Haeri, MD, MHSA; Scott A. Shainker, DO; Antonio F. Saad, MD; Rodrigo Ruano, MD, PhD; Timothy N. Dunn, MD; Atefeh Rezaei, MD; Soroush Aalipour, MD; Ahmed A. Nassr, MD; Amir A. Shamshirsaz, MD; Micah Vaughn, MD; William Lindsley, RDMS; Melissa H. Spiel, DO; Sherif A. Shazly, MD; Eniola R. Ibirogba, MD; Steven L. Clark, MD; George R. Saade, MD; Michael A. Belfort, MD, PhD; Alireza A. Shamshirsaz, MD

OBJECTIVE: The objective of the study was to describe the characteristics and outcomes of patients with antenatal diagnosis of vasa previa and evaluate the predictive factors of resolution in a contemporary large, multicenter data set.

STUDY DESIGN: This was a retrospective multicenter cohort study of all antenatally diagnosed cases of vasa previa, identified via ultrasound and electronic medical record, between January 2011 and July 2018 in 5 US centers. Records were abstracted to obtain variables at diagnosis, throughout pregnancy, and outcomes, including maternal and neonatal variables. Data were reported as median [range] or n (percentage). Descriptive statistics, receiver-operating characteristics, and logistic regression analysis were used as appropriate.

RESULTS: One hundred thirty-six cases of vasa previa were identified in 5 centers during the study period, 19 (14%) of which resolved spontaneously at median estimated gestational age of 27 weeks [19—34]. All subjects with unresolved vasa previa underwent cesarean delivery at a median estimated gestational age of 34 weeks [27—39] with the median estimated blood loss of 800 mL [250—2000]. Rates for vaginal bleeding, preterm labor, premature rupture of membrane, and need for blood product transfusion were not different between the resolved and unresolved group (P = NS). The odds ratio for resolution in those with the estimated gestational age of less than 24 weeks at the time of diagnosis was 7.9 (95% confidence interval, 2.1—29.4) after adjustment for confounding variables.

CONCLUSION: Our data suggest that outcomes in antenatally diagnosed cases of vasa previa are excellent. Furthermore, our data report a higher chance of resolution when the condition is diagnosed before 24 weeks of gestation.

Key words: contemporary multicenter study, estimated gestational age at diagnosis, fetal mortality, maternal morbidity, resolution, vasa previa

Vasa previa is defined as the presence of fetal vessels overlying the cervical internal os without protection of placenta tissue with the reporting incidence of 0.2—2.2 per 1000 pregnancies in various studies.[1,2] The condition has been associated with high fetal mortality because of fetal vessels tearing when the membranes rupture, in labor, or spontaneously. However, recent advance in ultrasound technology and improved antenatal diagnosis of vasa previa have led to decreased mortality because of early recognition and delivery prior to membranes rupture.[3,4]

In 2015, a systematic review of related studies identified different risk indicators and markers for vasa previa including the presence of second-trimester placenta previa, use of assisted reproductive technology, bilobed placenta, umbilical cord insertion in the lower third of the uterus in the first-trimester ultrasound, and velamentous cord insertion.[2] Earlier and improved antenatal diagnosis has been linked with improved outcomes, leading to an increased focus on optimizing risk factor identification and screening algorithms.[5—7]

Our aims in this study were as follows: (1) to describe characteristics and outcomes of patients with antenatal diagnosis of vasa previa in a contemporary large multicenter database and (2) to identify predictive factors for resolution of vasa previa prior to delivery.

Materials and Methods

We performed a retrospective chart review of all patients with confirmed vasa previa from 5 US referral institutions between January 2011 and July 2018. In all participating institutions, anatomic surveys between 18 and 22 weeks included universal cervical length screening. In addition to cases diagnosed during these routine surveys, other cases were diagnosed, always via transvaginal ultrasound, when a velamentous cord insertion along the lower uterine segment on transabdominal ultrasound raised suspicion for vasa previa, necessitating a transvaginal study.

Also, if there was a low-lying placenta, placenta previa, or any question of placenta distance from the cervix, a transvaginal ultrasound was performed and repeated when the patient was back for follow-up. All participating centers followed the practice protocol of early hospitalization at 30—32 weeks and elective delivery at 34 weeks' gestation. Institutional review board approval was obtained prior to data collection.

Cases of vasa previa were identified via ultrasound (diagnosis and key word) and electronic medical record (*Internation Classification of Diseases*, ninth and 10th editions, code) queries. Records were reviewed by physician researchers who were blind to the analysis, and data were abstracted to obtain baseline demographic information, antenatal variables at diagnosis and throughout pregnancy, and maternal-neonatal outcomes at delivery using previously designed information forms.

Cite this article as: Erfani H, Haeri S, Shainker SA, et al. Vasa previa: a multicenter retrospective cohort study. Am J Obstet Gynecol 2019;221:644.e1-5.

0002-9378/$36.00

https://doi.org/10.1016/j.ajog.2019.06.006

Related editorial, page 539.

AJOG at a Glance

Why was this study conducted?

To describe the characteristics and outcomes of patients with antenatal diagnosis of vasa previa and the predictive factors of resolution.

Key findings

One hundred thirty-six cases were included from 5 US centers. Rates for vaginal bleeding, preterm labor, premature rupture of membrane, and need for blood product transfusion were not different between the resolved and unresolved group.

What does this add to what is known?

Outcomes in antenatally diagnosed cases of vasa previa are excellent. The gestational age of less than 24 weeks at the time of diagnosis is a good predictor for resolution.

Ultrasound images were reevaluated by one of the authors, who also was blinded to the analysis, for the purpose of quality assurance. We compared clinical variables for women whose vasa previa resolved prior to delivery with those of patients whose vasa previa persisted until delivery. In all 5 centers, management protocols were based on the recommendations of Robinson and Grobman.[8]

Continuous variables were tested for normality using the Kolmogorov-Smirnov test. Data were reported as median [range] or number (percentage) and were compared between the study groups using a Mann-Whitney U test, a χ^2 test, or a Fisher exact test, as appropriate. The association between resolution and potential predictive factors was first evaluated using the univariate analysis. Then potential factors with a value of $P < .2$ on univariate analysis were included in the multivariate logistic regression model to identify the predictors for the resolution of vasa previa.

To evaluate the ability of estimated gestational age (EGA) at diagnosis to discriminate between women with and without resolution, a receiver-operating characteristics' curve (ROC) was constructed and performance measures were calculated using the optimal cutoff point. SPSS software (version 23.0; SPSS Inc, Chicago, IL) was used for the purpose of statistical analysis and a value of $P < .05$ was considered statistically significant.

Results

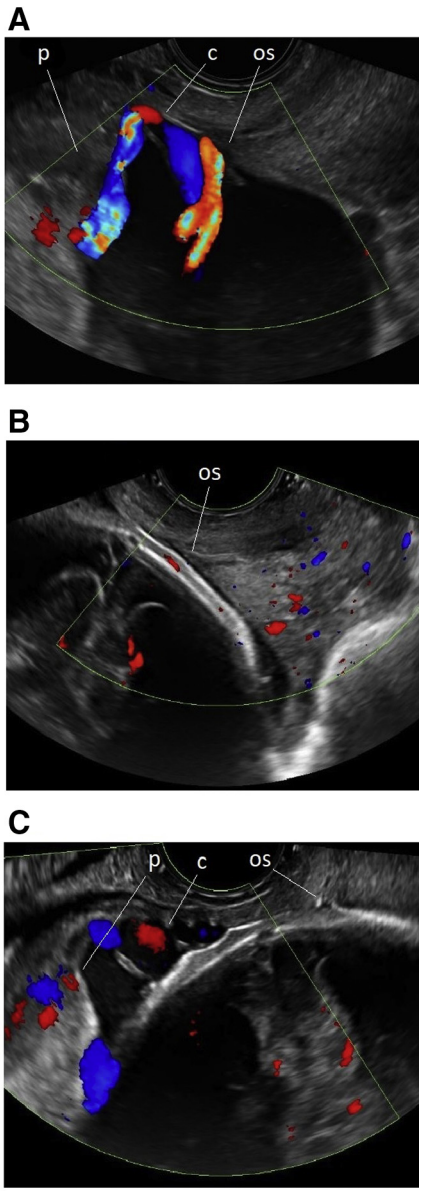
One hundred thirty-six cases of vasa previa were identified in 5 centers during the study period, 19 (14%) of which resolved spontaneously, with resolution diagnosed at a median estimated gestational age (EGA) of 27 weeks (range, 19–34); Figure 1 depicts color Doppler images of a subject with vasa previa at 20 weeks of gestation, which resolved by 30 weeks.

In each participating center, all cases confirmed at the time of delivery had been diagnosed prior to delivery. Median EGA at diagnosis were 26 weeks (range, 14–40) and 21 weeks (range, 17–30) in the groups with unresolved and resolved vasa previa, respectively ($P = .002$). Table 1 depicts the demographics and antepartum characteristics of the study population.

All patients with unresolved vasa previa underwent cesarean delivery at a median EGA of 34 weeks (range, 27–39) with a median estimated blood loss of 800 mL (range, 250–2000). Rates of vaginal bleeding, preterm labor, premature rupture of membrane, and need for blood product transfusions were not different between the resolved and unresolved vasa previa groups. Table 2 demonstrates the details of delivery and neonatal outcomes of both groups.

Table 3 depicts the analysis of potential predictive factors of resolution in the study subjects. According to the

FIGURE 1
Color Doppler images of a subject with vasa previa



A, Velamentous umbilical cord insertion identified via color Doppler is seen overlying the internal cervical os by transvaginal ultrasound at 20 weeks' gestation. **B,** Fetal cranium seen presenting at the internal cervical os at 30 weeks' gestation. The umbilical cord and velamentous insertion are not identified near the os. **C,** Anterior angulation of the transvaginal ultrasound probe allow for visualization of the umbilical cord and placental edge in relation to the internal cervical os. This view confirms resolution of the vasa previa at 30 weeks' gestation.

c, umblical cord; *os*, internal cervical os; *p*, placental edge.

Erfani et al. Contemporary outcomes of vasa previa. Am J Obstet Gynecol 2019.

TABLE 1
Demographics and characteristics of the study participants (n = 136)

Variables	Unresolved VP (N = 117)	Resolved VP (N = 19)	*P* value
Maternal age, y, median [range]	31 [20–44]	31 [17–42]	.777
Race/ethnicity, n %			.974
Non-Hispanic white	39 (33.3)	7 (36.8)	
Non-Hispanic black	7 (6.0)	1 (5.3)	
Hispanic	13 (11.1)	2 (10.5)	
Others/not identified	58 (49.6)	9 (47.4)	
Gravidity, median [range]	2 [1–8]	3 [1–7]	.015[a]
Parity, median [IQR]	1 [0–7]	2 [0–6]	.232
Number of prior CDs, median [range]	0 [0–2]	0 [0–1]	.380
EGA at diagnosis, wks, median [range]	26 [14–40]	21 [17–30]	.002[a]
EGA at resolution, wks, median [range]	N/A	27 [19–34]	—

Values are presented as median [range] and n (percentage). *P* values are calculated using a Mann-Whitney *U* test, χ^2/Fisher exact tests as appropriate.

ART, assisted reproductive technology; *CD*, cesarean delivery; *EGA*, estimated gestational age; *VP*, vasa previa.

[a] Statistically significant.

Erfani et al. Contemporary outcomes of vasa previa. Am J Obstet Gynecol 2019.

final regression model, the odds of resolution is 7.9 times higher (95% confidence interval, 2.1–29.4) if the condition is diagnosed earlier than 24 weeks of gestation (Table 3); Figure 2 demonstrates the ROC curve showing the discriminating power of EGA at diagnosis. Based on the ROC analysis, Table 4 shows the performance of various indices in predicting resolution; the ROC analysis suggests that EGA of less than 24 weeks at the time of diagnosis is the best cutoff point estimate.

Comment

Principal findings

Our data suggest that outcomes in antenatally diagnosed cases of vasa previa are generally excellent, regardless of whether the condition resolves prior to delivery. These outcomes are based on

TABLE 2
Delivery and neonatal outcomes of the study participants (n = 136)

Variables	Unresolved VP (n = 117)	Resolved VP (n = 19)	*P* value
EGA at admission, wks, median [range]	32 [24–40]	39 [23–41]	< .001[a]
EGA at delivery, wks, median [range]	34 [27–39]	39 [27–41]	< .001[a]
Vaginal bleeding, n, %	20 (17.4)	4 (21.1)	.748
Preterm labor, n, %	10 (8.5)	2 (10.5)	.675
Premature ROM, n, %	3 (2.6)	0 (0)	.999
Cesarean delivery, n, %	117 (100)	13 (68.4)	< .001[a]
EBL, mL, median [range]	800 [250–2000]	400 [200–2000]	.001[a]
RBC transfusion, n, %	4 (3.5)	1 (5.3)	.202
Platelet transfusion, n, %	0 (0)	0 (0)	—
5 min Apgar <7, n, %	4 (3.4%)	0 (0)	.999
NICU LOS, d, median [range]	11 [0, 75]	0 [0, 0]	< .001[a]
Neonatal mortality, n, %	0 (0)	0 (0)	—

Values are presented as median [range] and n (percentage). *P* values are calculated using a Mann-Whitney *U* test, χ^2/Fisher exact tests as appropriate.

EBL, estimated blood loss; *EGA*, estimated gestational age; *LOS*, length of stay; *NICU*, neonatal intensive care unit; *RBC*, red blood cell; *ROM*, rupture of membranes; *VP*, vasa previa.

[a] Statistically significant.

Erfani et al. Contemporary outcomes of vasa previa. Am J Obstet Gynecol 2019.

TABLE 3
Analysis of potential predictive factors of resolution in the study participants (n = 136)

Variables	Unresolved VP (n = 117) n, %	Resolved VP (n = 19) n, %	Univariate analysis Crude OR (95% CI)	*P* value	Logistic regression analysis Adjusted OR (95% CI)	*P* value
Placenta previa	52 (44.4)	5 (26.3)	0.4 (0.1–1.3)	.145	0.6 (0.2–1.9)	.368
Velamentous cord	57 (50.0)	11 (57.9)	1.4 (0.5–3.7)	.525	–	
ART	15 (13.6)	2 (12.5)	0.9 (0.2–4.4)	.901	–	
Multiple gestation	7 (6.0)	4 (21.1)	4.2 (1.1–16.0)	.036[a]	4.2 (0.9–18.5)	.061
EGA at diagnosis <24 wks	44 (37.6)	16 (84.2)	8.5 (2.3–30.8)	.001[a]	7.9 (2.1–29.4)	.002[a]

Potential risk factors with $P < .2$ on univariate analysis were included in the multivariate logistic regression model.

ART, assisted reproductive technology; *CI*, confidence interval; *EGA*, estimated gestational age; *OR*, odds ratio; *VP*, vasa previa.

[a] Statistically significant.

Erfani et al. Contemporary outcomes of vasa previa. Am J Obstet Gynecol 2019.

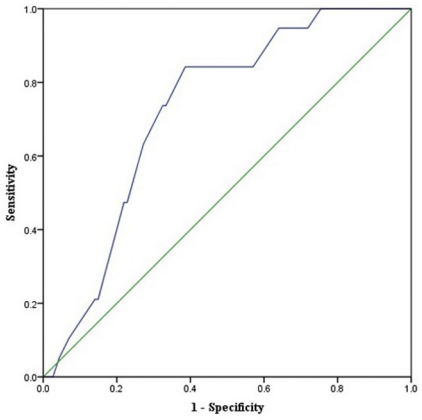
the widely adopted practice pattern of early hospitalization at 30–32 weeks followed by elective delivery at 34 weeks' gestation.[8] Because preterm cesarean delivery was an integral part of this management approach, a higher rate of cesarean delivery and preterm delivery would be expected.

Existing literature

In 2004, Oyelese et al[5] reported a 36% overall perinatal mortality rate associated with vasa previa, with a reported survival rate of 97% for pregnancies in which the diagnosis was made antenatally. In 2010, a 20 year retrospective review of cases demonstrated an increased antenatal diagnosis rate (25% to 60%) and a decreased perinatal mortality rate (25% to 0%) over the study period.[9] Finally, Rebarber et al[10] have suggested that standardization of perinatal management also reduces perinatal mortality. In addition, 25% of their studied subjects with second-trimester diagnosis of vasa previa had complete resolution by the third trimester. These findings have been most recently demonstrated in the literature.[11,12]

It is generally believed that the resolution of vasa previa is caused by the by migration secondary to differential growth between the placenta and the lower uterine segment, emphasizing the importance of confirming the diagnosis in the third trimester despite a second-trimester diagnosis.[10,13] Our observation that early diagnosis (<24 weeks' gestation) is associated with vasa previa resolution is an innovative and interesting observation that needs further investigation.

FIGURE 2
Receiver-operating characteristics curve for gestational age at the diagnosis for prediction of resolution



Receiver-operating characteristics curve shows the ability of estimated gestational age at the diagnosis of vasa previa to predict resolution.

Erfani et al. Contemporary outcomes of vasa previa. Am J Obstet Gynecol 2019.

Clinical implications

We believe our data reflect the current management and outcomes of vasa previa in the United States based on a large multicenter cohort. Our data support the finding that outcomes in antenatally diagnosed cases of vasa previa with the current management protocol are excellent. Additionally, early diagnosis of vasa previa is associated with resolution prior to delivery. Because this is a multicenter experience, these data are generalizable across centers for better counseling of patients with antenatal diagnosis of vasa previa.

Research implications

Further prospective and longitudinal multicenter studies are necessary to evaluate and better predict vasa previa resolutoin. Moreover, such studies could shed more light on the mechanisms of vasa previa resolution.

Strengths and limitations

This is the largest available study of antenatally diagnosed vasa previa. The contemporary study period, involving

TABLE 4
Performance measures of EGA at diagnosis of vasa previa for prediction of resolution

Variables	Point estimate	95% CI
Area under curve, %	72.4	62.2–82.7
Sensitivity, %	84.2	60.4–96.6
Specificity, %	62.4	53.0–71.2
Positive predictive value, %	26.7	21.2–33.0
Negative predictive value, %	96.0	89.5–98.6
Positive likelihood ratio	2.24	1.6–3.0
Negative likelihood ratio	0.25	0.1–0.7

Optimal point for EGA (EGA at diagnosis <24 weeks) was defined per receiver-operating characteristics analysis.

CI, confidence interval; *EGA*, estimated gestational age.

Erfani et al. Contemporary outcomes of vasa previa. Am J Obstet Gynecol 2019.

significant changes in both diagnosis and management from earlier decades, is an additional strength of this investigation. A limitation of our study is the retrospective nature of the study design. Despite our best efforts, undiagnosed cases may have been missed during our query, and some variables were not available for abstraction if not recorded during clinical visits.

Conclusions

In conclusion, our data suggest that with appropriate imaging techniques, the vast majority of cases of vasa previa may be accurately diagnosed prenatally, although fetal position or maternal habitus will certainly continue to preclude such diagnosis in a small number of cases. Outcomes of antenatally diagnosed cases of vasa previa with our current management plan of intensive monitoring and prelabor cesarean delivery in referral centers are excellent. Furthermore, the diagnosis of vasa previa earlier than 24 weeks of gestation is associated with reasonably good odds of resolution prior to delivery. ■

References

1. Oyelese KO, Turner M, Lees C, Campbell S. Vasa previa: an avoidable obstetric tragedy. Obstetrical & Gynecological Survey 1999;54:138–45.

2. Ruiter L, Kok N, Limpens J, et al. Incidence of and risk indicators for vasa praevia: a systematic review. BJOG 2016;123:1278–87.

3. Swank ML, Garite TJ, Maurel K, et al. Vasa previa: diagnosis and management. Am J Obstet Gynecol 2016;215:223.e1–6.

4. Oyelese Y, Smulian JC. Placenta previa, placenta accreta, and vasa previa. Obstet Gynecol 2006;107:927–41.

5. Oyelese Y, Catanzarite V, Prefumo F, et al. Vasa previa: the impact of prenatal diagnosis on outcomes. Obstet Gynecol 2004;103(5 Pt 1):937–42.

6. Kulkarni A, Powel J, Aziz M, et al. Vasa previa: prenatal diagnosis and outcomes: thirty-five cases from a single maternal-fetal medicine practice. J Ultrasound Med 2018;37:1017–24.

7. Cipriano LE, Barth WH Jr, Zaric GS. The cost-effectiveness of targeted or universal screening for vasa praevia at 18-20 weeks of gestation in Ontario. BJOG 2010;117:1108–18.

8. Robinson BK, Grobman WA. Effectiveness of timing strategies for delivery of individuals with vasa previa. Obstet Gynecol 2011;117:542–9.

9. Smorgick N, Tovbin Y, Ushakov F, et al. Is neonatal risk from vasa previa preventable? The 20-year experience from a single medical center. J Clin Ultrasound 2010;38:118–22.

10. Rebarber A, Dolin C, Fox NS, Klauser CK, Saltzman DH, Roman AS. Natural history of vasa previa across gestation using a screening protocol. J Ultrasound Med 2014;33:141–7.

11. Melcer Y, Jauniaux E, Maymon S, et al. Impact of targeted scanning protocols on perinatal outcomes in pregnancies at risk of placenta accreta spectrum or vasa previa. Am J Obstet Gynecol 2018;218:443.e1–8.

12. Sullivan EA, Javid N, Duncombe G, et al. Vasa previa diagnosis, clinical practice, and outcomes in Australia. Obstet Gynecol 2017;130:591–8.

13. Lee W, Lee VL, Kirk JS, Sloan CT, Smith RS, Comstock CH. Vasa previa: prenatal diagnosis, natural evolution, and clinical outcome. Obstet Gynecol 2000;95:572–6.

Author and article information

From the Department of Obstetrics and Gynecology, Baylor College of Medicine and Texas Children's Hospital, Houston, TX (Drs Erfani, Rezaei, Aalipour, Nassr, Amir Shamshirsaz, Clark, Belfort, and Alireza Shamshirsaz); the Department of Women's Health, Dell Medical School, University of Texas at Austin (Dr Haeri), and Austin Maternal-Fetal Medicine (Drs Haeri and Lindsley), Austin, TX; the Department of Obstetrics and Gynecology, Beth Israel Deaconess Medical Center, Boston, MA (Drs Shainker and Spiel); the Department of Obstetrics and Gynecology, University of Texas Medical Branch, Galveston, TX (Drs Saad, Vaughn, and Saade); the Department of Obstetrics and Gynecology, Mayo Clinic College of Medicine, Rochester, MN (Drs Ruano, Shazly, and Ibirogba); and the Department of Obstetrics and Gynecology, University of Alabama—Birmingham, Birmingham, AL (Dr Dunn).

Received Feb. 26, 2019; revised May 15, 2019; accepted June 5, 2019.

All authors contributed to the present study.

The authors report no conflicts of interest.

Corresponding author: Alireza A. Shamshirsaz, MD. alirezashamshirsaz@yahoo.com or shamshir@bcm.edu