OBSTETRICS

Frequency of spontaneous resolution of vasa previa with advancing gestational age

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BACKGROUND: Vasa previa is a serious obstetric complication that can result in fetal hemorrhage and death on spontaneous labor. Suggested management for vasa previa is elective hospitalization and cesarean delivery before spontaneous labor. There is little reported evidence of the rate of vasa previa resolution over the course of gestation. Identification of the resolution rate and of factors predictive of resolution potentially could improve clinical management and patient counseling.

OBJECTIVE: The purpose of this study was to identify the resolution rate of vasa previa across gestation and to determine clinical and sonographic factors that are associated with vasa previa resolution.

STUDY DESIGN: We conducted a retrospective cohort study of all women who were diagnosed with vasa previa in a single ultrasound unit between 2005 and 2018. Vasa previa was defined as a fetal vessel within 2 cm of the internal cervical os on transvaginal sonography. The primary outcome was vasa previa resolution, defined as migration of the vasa previa to >2 cm away from the internal os.

RESULTS: One hundred women with vasa previa that had been diagnosed at a mean gestational age of 22.8±4.9 weeks were included. Thirty-nine women (39.0%; 95% confidence interval, 30—49%) had resolution of vasa previa at a mean gestational age of 28.6—4.7 weeks. Factors that were associated with vasa previa resolution were an earlier gestational age at diagnosis (adjusted odds ratio, 6.10; 95% confidence interval,1.92—19.40), vasa previa did not cover the internal os at diagnosis (adjusted odds ratio, 8.29; 95% confidence interval, 2.79—24.62), and vasa previa was not the result of a resolved placenta previa (adjusted odds ratio, 2.85; 95% confidence interval, 1.01-—8.03). One woman with a dichorionic twin pregnancy and vasa previa resolution (at 31 weeks gestation; fetal vessels located 2.8 cm from the internal os) presented at 33 weeks with massive bleeding and fetal death of twin A. It was unclear whether the death was related to vasa previa or placental abruption.

CONCLUSION: Thirty-nine percent of vasa previas in our population resolved over the course of pregnancy. Earlier gestational age at diagnosis, vasa previa not covering the internal os, and not having a resolved placenta previa all are associated independently with an increased likelihood of vasa previa resolution. Women with vasa previa should be observed serially to assess for vasa previa resolution, because many will resolve in the third trimester.

Key words: placenta previa, ultrasound, migration, vasa previa screening, velamentous cord insertion

Vasa previa is a serious obstetric condition, with a reported incidence of 0.60 per 1000 pregnancies,[1] defined by the presence of fetal blood vessels overlying or close to the internal cervical os. Vasa previa vessels are unsupported by either the umbilical cord or placenta and are at risk for compression or rupture during labor. Although a standard criterion remains to be agreed on, a threshold of 2 cm has been proposed as the maximal vessel distance from the cervix that constitutes a vasa previa.[2]

On spontaneous labor and ruptured membranes, vasa previa is associated with a high fetal mortality rate. Fetal death is due mainly to fetal exsanguination. Additionally, if blood flow to the vasa previa vessels becomes restricted, fetal asphyxia can occur. Previous studies have shown transvaginal ultrasound with color Doppler to be accurate in diagnosing vasa previa prenatally, with a detection rate of 93% and specificity of 99.0%.[1] Thus, current guidelines recommend sonographic screening specifically with the use of transvaginal imaging with color and pulsed wave Dopplers in women with resolved placenta previa.[3] Additional indications for vasa previa screening include velamentous insertion of the cord in the lower uterine segment, placenta succenturiata in the lower uterine segment, and twin gestations. The advent of accurate prenatal sonographic diagnosis along with careful management, which includes timely performance of cesarean delivery before the onset of labor, has been shown to improve prognosis and fetal outcomes greatly, such that there remains a <10% chance of fetal death.[2,4]

The Society of for Maternal Fetal Medicine recently issued recommendations to facilitate the diagnosis and management of vasa previa. Within the recommendations, they note that vasa previa diagnosis made in the second trimester has a 20% resolution rate, based on 2 small series.[5] Initially, Lee et al[6] reported in a small series of 18 cases of prenatally diagnosed vasa previa in which 3 patients exhibited "normal third-trimester scans" that allowed for uncomplicated vaginal deliveries. In 2014, we reported a 17.2% resolution rate of vasa previa based on migration in 5 patients of a series of 29 cases.[4] Although it is well-documented that placenta previa that is diagnosed in the second trimester resolves in most patients,[7,8] a similar large cohort analysis for patients with vasa previa does not exist. We sought to highlight the importance of serial assessment of vasa previa across gestation once the diagnosis is made to avoid unnecessary interventions and allow for proper patient

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AJOG at a Glance

Why was this study conducted?

The purpose of this study was to determine the resolution rate of vasa previa and the factors that are associated with its resolution in a large cohort.

Key findings

Vasa previa resolved in 39% of the women in this study over the course of their pregnancies. Factors that were associated with vasa previa resolution were (1) earlier gestational age at diagnosis, (2) vasa previa did not cover the internal os at diagnosis, and (3) vasa previa was not the result of a resolved placenta previa. Factors that were not associated with vasa previa resolution were maternal age, parity, in vitro fertilization, number of fetuses, vessel type (artery, vein, or both), cervical length at diagnosis, velamentous cord insertion, 2-vessel umbilical cord, succenturiate lobe, uterine anomalies, and fibroid tumors.

What does this add to what is known?

Few studies report the extent of resolution of vasa previas, and only 1 previous study suggested that gestational age at diagnosis affected resolution rate. Our study attempts to review the resolution rate in 1 of the largest single center cohorts reported and to explore other factors that may be associated with resolution. These findings can be used in clinical counseling. Knowing the likelihood of resolution can better inform clinical treatment for patients who are diagnosed with vasa previa in the second trimester.

counseling. The primary objective of this study was to identify the resolution rate of prenatally diagnosed vasa previa across gestation in a large cohort of women and to determine clinical and sonographic factors that are predictive of vasa previa resolution.

Materials and Methods

After Biomedical Research Alliance of New York Institutional Review Board approval was obtained, the charts of all patients who were diagnosed with vasa previa in a single ultrasound unit between June 2005 and June 2018 were reviewed. Cases were identified by International Classification of Diseases−9 th revision codes and content search analysis of 2 ultrasound reporting systems (Sonultra Ultra 64; Sonultra Corporation, Beverly Hills, CA; and *AS*-OBGYN; AS Software Inc, Englewood Cliffs, NJ) with the use of the key words *vasa previa*. The data set obtained in this series included all of the previous cases in our initial analysis of vasa previas that has been published by our group.[4] *Vasa previa* was defined as any velamentous fetal vessel (arterial or venous) noted to be within 2 cm of the internal cervical os. We excluded funic presentation by requiring that vessels be followed from the placental edge either into another placental lobe or into the root of the umbilical cord itself. The imaging staff consisted of multiple registered diagnostic medical sonographers and 6 maternal fetal medicine specialists.

Our ultrasound unit has standardized policies and protocols for the evaluation of potential vasa previa. Initial screening is conducted at 16 weeks gestation. Screening for vasa previa with transvaginal ultrasound imaging with color flow mapping was performed routinely in the following clinical situations: resolved placenta previa, history of vasa previa in a previous pregnancy, velamentous insertion of the cord in the lower uterine segment, succenturiate placenta with implantation in the lower uterine segment, twin gestations, and any vasa previa that was suspected incidentally on transabdominal or transvaginal ultrasound imaging in women without risk factors. Once a vasa previa was suspected with gray scale and/or color flow, confirmation was performed with the use of pulsed Doppler to differentiate arterial and venous vessels. Use of 3- and 4-dimensional technology was performed in certain cases to enhance the diagnosis and mapping of the path of the vessel(s) across the lower uterine segment. A variety of ultrasound equipment was used that allowed for gray scale, color Doppler, power Doppler, and 3-/4-dimensional ultrasound capabilities (GE Voluson 730 Expert, Voluson E10, E8, E6, equipment; GE Healthcare, Chicago, IL; Medison XG Accuvix ultrasound equipment; Samsung Medison, Pangyo, Republic of Korea). Serial scans were used to characterize the natural history of vasa previa across gestation at 2−4 week intervals until delivery or resolution. Patients who were found to be negative on initial screen were not rescreened. The primary outcome for this study was vasa previa resolution, which was defined as fetal vessels noted to be >2 cm from the internal os.

Maternal medical records were reviewed for the following variables and outcomes: maternal age, parity, gestational age at delivery, mode of delivery, birthweight, and APGAR scores of the neonate. Ultrasound images in all cases were again reviewed before inclusion into the series by a single maternal fetal medicine specialist (A.R.) for accuracy of diagnosis. Confirmation of the ultrasound findings in unresolved vasa previa cases was based on the obstetrician's clinical operative findings at time of delivery. It was our standard practice to offer elective admission at 32−34 weeks gestation based on physician discretion/patient desire and elective delivery at 35−36 weeks gestation without amniocentesis for lung maturity based on our usual practice before published guidelines. We compared baseline characteristics between women whose vasa previa did and did not resolve. Univariate statistical analysis was performed with the use of nonparametric and parametric analysis as appropriate. We then performed a logistic regression analysis to assess the independent association between several risk factors and vasa previa resolution. All risk factors that were associated with vasa previa resolution in our univariate analysis with a probability value <.05 were included in the final

TABLE 1
Baseline characteristics, with comparison of unresolved and resolved vasa previa groups

Variable	Total (N=100)	Unresolved (n=61)	Resolved (n=39)	*P* value (unresolved vs resolved)
Maternal age, y[a]	35.96±6.17	35.79±5.33	35.80±7.02	.995
Parity, n (%)				.544
Nulliparous	63 (63)	37 (60.7)	26 (66.7)	
Multiparous	37 (37.0)	24 (39.3)	13 (33.3)	
In vitro fertilization, n (%)	32 (32.0)	17 (27.9)	15 (38.5)	.268
Fetuses, n (%)				.424
1	85 (85.0)	53 (86.9)	32 (82.1)	
2	14 (14.0)	8 (13.1)	6 (15.4)	
3	1 (1.0)	0 (0.0)	1 (2.6)	
Vessel type, n (%)				.513
Artery	38 (38.0)	20 (32.8)	18 (46.2)	
Vein	28 (28.0)	18 (29.5)	10 (25.6)	
Both	31 (31.0)	20 (32.8)	11 (28.2)	
Unknown	3 (3.0)	3 (4.9)	0 (0.0)	
Cervical length at diagnosis, cm[a]	4.01±0.78	3.99±0.89	4.04±0.66	.775
Velamentous cord insertion, n (%)	51 (51.0)	29 (47.5)	22 (56.4)	.387
Umbilical cord, n (%)				.747
2 Vessels	2 (2.0)	1 (1.6)	1 (2.6)	
3 Vessels	98 (98.0)	60 (98.4)	38 (97.4)	
Succenturiate lobe, n (%)	8 (8.0)	5 (8.2)	3 (7.7)	.928
Uterine anomalies, n (%)	3 (3.0)	2 (3.3)	1 (2.6)	.838
Uterine fibroid tumors, n (%)	13 (13.0)	6 (9.8)	7 (17.9)	.239
Gestational age at diagnosis, wk[a]	22.82±4.90	24.31±5.19	20.81±3.81	.000
Vasa previa covering os, n (%)	56 (56.0)	42 (68.9)	14 (35.9)	.001
Placenta previa, n (%)	70 (70.0)	48 (78.7)	22 (56.4)	.018

[a] Data presented mean±standard deviation.

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regression analysis. For the variable of gestational age at diagnosis, our regression model entered the binary variable of <24 vs ≥24 weeks gestation. Adjusted odds ratios and 95% confidence intervals were calculated (IBM SPSS for Windows version 22.0; IBM Corp, Armonk, NY).

Results

A total of 37,236 patients were referred to our units for fetal anatomic surveys over the study period. One hundred ten cases of vasa previa that were diagnosed prenatally by ultrasound imaging were identified by our database search strategies and amounted to a prevalence of 2.95 per 1000 pregnancies in our population. Of these, 10 pregnancies were excluded because no resolution data were available; 100 cases had full records available for analysis; 94% of patients who were diagnosed with vasa previa had at least 1 criteria for vasa previa screening in our protocol; 70% of the patients had a resolved placenta previa; 21% of the patients had a velamentous cord insertion; 1% of the patients had a succenturiate lobe, and 2% of the pregnancies were twin gestations. The remaining 6% of cases were found incidentally on either transabdominal or transvaginal imaging for other indications.

Of the 100 vasa previa cases included for analysis, 39 of them (39%; 95% confidence interval [CI], 30–49%) resolved at a mean gestational age of 28.6±4.7 weeks, and 61 of them had unresolved or persistent vasa previa at the time of delivery. Table 1 summarizes some pertinent clinical and sonographic characteristics for the 2 groups. Of note, the mean maternal age for the whole group was 36.0 years, with 55 women considered to be at advanced

TABLE 2
Likelihood of vasa previa resolution, based on gestational age at diagnosis and location of the vasa previa on initial presentation

Variable	Gestational age at diagnosis of vasa previa, %				*P* value
	<20 Weeks	20–24 Weeks	24–28 Weeks	>28 Weeks	
All women with vasa previa (N=100)	66.7 (n=21)	40.5 (n=41)	26.3 (n=19)	16.7 (n=18)	.001
Vasa previa 0–2 cm from internal cervical os (n=44)	100 (n=6)	64.7 (n=17)	55.6 (n=9)	25.0 (n=12)	.002
Vasa previa covering internal cervical os (n=56)	53.3 (n=15)	24.0 (n=25)	0 (n=10)	0 (n=6)	.001

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maternal age (≥35 years old at time of delivery). The following factors did not differ between the 2 groups and were not associated with vasa previa resolution: maternal age, parity, in vitro fertilization, number of fetuses, vessel type, cervical length at time of diagnosis, velamentous cord insertion, a 2-vessel umbilical cord, a succenturiate lobe, uterine anomalies, and uterine fibroid tumors.

The gestational age at time of diagnosis differed between the 2 groups: 24.31 (standard deviation, 5.19) weeks in the unresolved group vs 20.81 (standard deviation, 3.81) in the resolved group. Of the unresolved cases, 68.9% had vessels that were covering the internal os (distance=0 cm) at the time of diagnosis compared with 35.9% of resolved cases (*P*=.001). Additionally, 78.7% of unresolved vasa previa resulted from resolved placenta previas, compared with 56.4% of resolved cases (*P*=.018).

Table 2 shows the likelihood of vasa previa resolution in all women, based on gestational age at diagnosis and on the location of the vasa previa on initial presentation. The earlier the gestational age at initial diagnosis, the more likely the vasa previa was to be resolved by the time of delivery. For the whole group, the resolution rates by the time of delivery were 66.7%, 40.5%, 26.3%, and 16.7% when diagnosed at <20, 20–24, 24–28, and >28 weeks, respectively. Furthermore, in each diagnostic period, vessels that covered the os at diagnosis were less likely to resolve than adjacent vasa previa vessels. Additionally, the vasa previas that were between 0–2 cm from the internal os at time of initial diagnosis resolved quicker than those that were covering the os. In the women who were <20 weeks gestation at time of initial diagnosis (n=21), the mean time to resolution in vasa previa 0–2 cm from os was 5.34±2.49 weeks, compared with mean time to resolution in vasa previa covering os of 11.37±3.85 weeks (*P*=.004).

Three variables were associated with vasa previa regression on univariate analysis (Table 1). Logistic regression analysis showed that all 3 variables were associated independently with vasa previa resolution: (1) gestational age at diagnosis of <24 weeks (adjusted odds ratio, 6.10; 95% CI, 1.92–19.40), (2) vasa previa not covering the internal os at diagnosis (adjusted odds ratio, 8.29; 95% CI, 2.79–24.62), and (3) vasa previa not being the result of a resolved placenta previa (adjusted odds ratio, 2.85; 95% CI, 1.01–8.03).

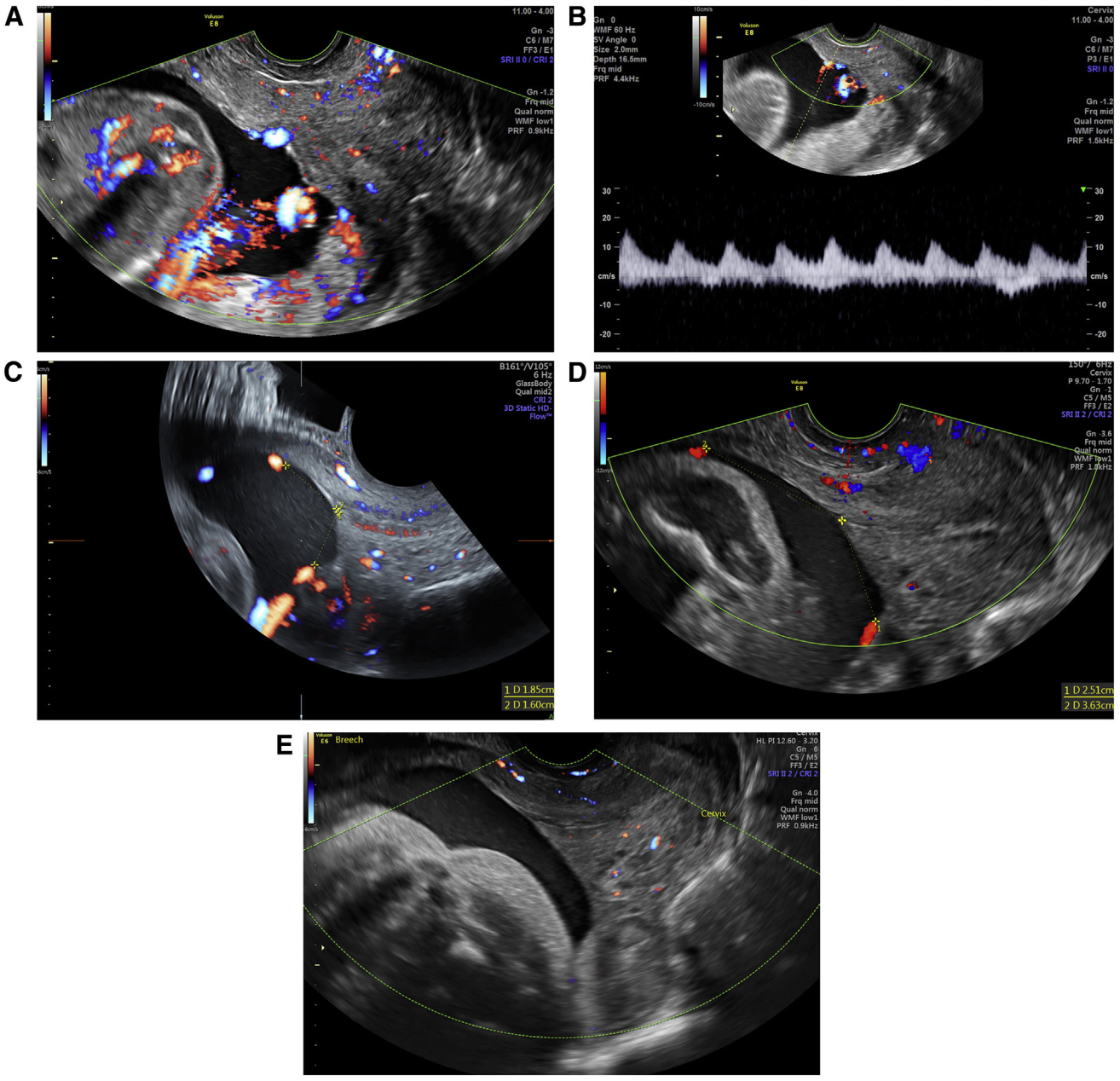
Delivery data were available for 98 cases. Among the 61 unresolved cases, there was a 98% (95% CI, 92–100%) survival of infants with a median length of gestation of 35 weeks. The fetal death involved a previable fetus that died on preterm premature rupture of membranes at 22 weeks gestation. Two of the 39 resolved cases did not have delivery data available. Among the 37 resolved cases that were analyzed, 19 women delivered vaginally, and 18 women delivered via cesarean section; 1 fetal death occurred. In this case, the patient had a dichorionic twin gestation, and vasa previa resolution was noted at 31 weeks gestation; the aberrant fetal vessels measured 2.8 cm from the internal os. At 33 weeks gestation, she presented to Labor and Delivery at a different institution with preterm premature rupture of membranes and vaginal bleeding. Earlier that day, she was evaluated for a short cervix (1.4 cm) and identified to have a viable twin gestation with biophysical profile scores of 8 of 8 for each fetus. At presentation, she was noted to be 4–5 cm dilated; 500 cc of clots were noted in the vagina, and a slow fetal heart rate of twin A was at <60 beats per minute. Emergent cesarean delivery was performed. On delivery, fetus A appeared pale and limp with Apgar scores of 0, 0, and 1. The infant was emergently transfused with 30 mL of O-negative blood at delivery with full intubation and resuscitation. Supportive care was withdrawn 12 hours after birth because of multiorgan failure. It is unclear if the death was related to vasa previa or placental abruption.

Comment

Principal findings

Our findings in a large retrospective cohort study suggest that prenatally diagnosed vasa previa has an overall 39% resolution rate. Our data suggest that the likelihood of resolution of a vasa previa is dependent on the gestational age and vessel distance from the internal os at the time of diagnosis and a history of a placenta previa in the index pregnancy.

FIGURE
Vasa previa migration across the gestation



A, Color flow Doppler imaging: At 20 weeks gestation, the vasa previa is overlying the internal cervical os. **B,** Pulsed wave Doppler imaging: At 20 weeks gestation, confirmation of fetal cardiac rate in a fetal artery. **C,** Color flow Doppler imaging: At ≥27 weeks gestation, indication of migration of both fetal vessels. **D,** Color flow Doppler imaging: At ≥30 weeks gestation, indication of further migration of both fetal vessels. **E,** Color flow Doppler imaging: At ≥35 weeks gestation, complete resolution of vasa previa from the lower uterine segment can be seen.

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Results

Vasa previa is a serious complication of pregancy in which fetal vessels are aberrantly overlying the cervical os. The prevalence of vasa previa in our cohort was 2.95 per 1000 pregnancies.[1–6,9–11] Our group is a referral center that primarily treats high-risk patients. This value exceeds the incidence previously published by Society of Maternal Fetal Medicine of 1 per 2500 pregnancies (737.5% greater). Given the demographics of our population therefore, our cited prevalence may be overestimated compared with the general population.

With the exception of several small series, little evidence exists to identify

the resolution rate of vasa previa and factors that are predictive of resolution in large cohorts. The first description of ultrasonographic vasa previa resolution was noted in a series of 18 prenatally diagnosed cases, of which 3 cases appeared to have resolved across gestation for a 16.6% resolution rate. The authors cited that vasa previa migration is likely due to the growth of the lower uterine segment in the later trimester.[6]

The 39% resolution rate in our cohort of 100 women (Figure) is greater than the aforementioned 16.6% resolution rate,[6] than the 8.6% rate reported by Oyelese et al[10] in a cohort of 35 patients, and than the 17.2% resolution rate we previously reported in a smaller series of 29 patients.[4] In contrast to our previous study, we noted a 16.7% resolution for cases that were diagnosed even after 28 weeks gestation. Our results mimic those of Eichelberger et al,[8] which indicate that gestational age at diagnosis of placenta previa and placental distance from the internal os at diagnosis are associated significantly with placenta previa resolution. Therefore, we believe that similar mechanisms may be involved in the resolution of these pathologic states; we found that a vasa previa was less likely to resolve when it resulted from a resolved placenta previa.

We saw a 98% survival rate in persistent vasa previa cases with 1 very preterm previable fetal death that was thought to be due to vasa previa rupture secondary to preterm labor. In the setting of vasa previa resolution, we also noted a late preterm death of a co-twin presenting with fetal distress and vaginal bleeding after preterm premature rupture of the membranes of the presenting twin. Analysis of this case indicates that, given the volume of blood transfused (ie, 30 mL), with an initial hematocrit level that was obtained only after transfusion of 35.9%, we can estimate a pretransfusion hematocrit level of 25−30%, based on the fetus's weight. Given the fetus's gestational age, this represents an initial presenting fetus who has probably lost one-half of its blood volume before delivery. Although the pathology report did not identify the cause clearly, the differential includes vasa previa rupture, despite an ultrasonographic distance of 2.8 cm from the internal os vs a placental abruption. Because the total blood volume of this infant would be estimated to be 150 mL (given approximately, 80 mL/kg), it is likely, given the finding of 500 cc of blood clots in the vagina, that a placental abruption was the primary cause for the event.

Clinical implications

Before the introduction of sonographic detection of vasa previa in 1987 by Gianopoulos et al,[11] vasa previa was considered an undetectable and unavoidable tragedy. Prenatal diagnosis has markedly increased the fetal survival rate in vasa previa cases, with 1 study claiming a 97% survival rate for cases that were diagnosed before delivery compared with 56% for undiagnosed cases.[12] Despite these strides, vasa previa remains a threatening diagnosis that must be managed meticulously, including possible hospitalization. Current society recommendations include hospitalization between 32−34 weeks gestation and elective delivery at 35−36 weeks gestation. Little detail is given about the need for serial assessment and the possibility of resolution once the diagnosis is made in these practice guidelines. Additionally, little evidence-based literature exists to define a safe distance from the internal os of fetal vessels coursing along the fetal membranes in the lower uterine segment. We found that, for nearly 40% of women with vasa previa, these interventions (ie, hospitalization and cesaran delivery) may be unnecessary if serial assessment is performed. Moreover, clinicians can use our findings to estimate the likelihood of resolution at the intial time of diagnosis for a given patient based on her risk factors, as noted in Table 2.

Recent studies suggest the use of certain risk-based criteria for vasa previa screening, such as in vitro fertilization status,[13] to identify patients in a cost-effective manner. Our data suggest that >1 in every 20 vasa previa cases would be missed if only a risk factor−based approach is adopted. Given the mortality rate of undiagnosed vasa previa, we agree with the Society of Maternal Fetal Medicine guidelines that all pregnancies should be evaluated for possible vasa previa, with close transabdominal and/or transvaginal imaging of structures at the level of the internal os.[5]

Successful cases of intrauterine laser photocoagulation of vasa previa have been reported in the literature.[14−17] Although we believe this form of intervention will be limited both in scope and availability, the accurate prenatal diagnosis and projection of persistence vs resolution may be helpful to select candidates who may be eligible for laser treatment. Future prospective studies are warranted to assess safety and efficacy of this approach, given the morbidity of vasa previa if preterm premature rupture of membranes were to occur in these cases.

Strengths and limitations

Our series is 1 of the largest series conducted by a single center with a standarized approach that allowed for an analysis of the natural history of vasa previa across gestation. Other strengths of our study include its uniform screening protocol that uses transvaginal ultrasound imaging in at-risk populations with standard confirmation of vessel presence with the use of pulsed wave and color flow Doppler modalities. We are not aware of any missed cases during the study period. The accuracy of vasa previa detection in our series was assured further by retrospective review of all cases.

One limitation of our study is its retrospective design. We were unable to obtain delivery outcome data on all patients who were diagnosed with vasa previa at our ultrasound unit because some patients delivered at unaffiliated facilities. Our experience is that adverse fetal outcomes would be reported to us by the referring obstetricians, who, for the most part, deliver in 1 of 5 Manhattan (NY) hospitals. Additionally, the study's design prohibited us from

controlling for all potential confounding variables.

Research implications

Our findings support the use of serial ultrasound assessment after initial vasa previa diagnosis to inform optimal management both to prevent the rupture of vessels in persistent cases and to prevent unnecessary interventions in resolved cases. However, future research should be performed to better delineate the appropriate interval of serial ultrasound assessment. Additionally, future research should attempt to better define safe resolution distance of the fetal vessels from the interal os in these unique circumstances.

Conclusion

In conclusion, nearly 40% of the vasa previa cases that are diagnosed during the second trimester will be resolved at the time of delivery. The earlier the gestational age is when the diagnosis is made, the more likely the vasa previa is to resolve. Additionally, vasa previas that are not covering the cervical os at diagnosis or are not the result of a resolved placenta previa are more likely to resolve than their counterparts. ■

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