

Incidence and causes of perinatal death in prenatally diagnosed vasa previa: a systematic review and meta-analysis



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OBJECTIVE: This study aimed to estimate the perinatal mortality associated with prenatally diagnosed vasa previa and to determine what proportion of those perinatal deaths are directly attributable to vasa previa.

DATA SOURCES: The following databases have been searched from January 1, 1987, to January 1, 2023: PubMed, Scopus, Web of Science, and Embase.

STUDY ELIGIBILITY CRITERIA: Our study included all studies (cohort studies and case series or reports) that had patients in which a prenatal diagnosis of vasa previa was made. Case series or reports were excluded from the meta-analysis. All cases in which prenatal diagnosis was not made were excluded from the study.

METHODS: The programming language software R (version 4.2.2) was used to conduct the meta-analysis. The data were logit transformed and pooled using the fixed effects model. The between-study heterogeneity was reported by I^2 . The publication bias was evaluated using a funnel plot and the Peters regression test. The Newcastle-Ottawa scale was used to assess the risk of bias.

RESULTS: Overall, 113 studies with a cumulative sample size of 1297 pregnant individuals were included. This study included 25 cohort studies with 1167 pregnancies and 88 case series or reports with 130 pregnancies. Moreover, 13 perinatal deaths occurred among these pregnancies, consisting of 2 stillbirths and 11 neonatal deaths. Among the cohort studies, the overall perinatal mortality was 0.94% (95% confidence interval, 0.52–1.70; $I^2=0.0\%$). The pooled perinatal mortality attributed to vasa previa was 0.51% (95% confidence interval, 0.23–1.14; $I^2=0.0\%$). Stillbirth and neonatal death were reported in 0.20% (95% confidence interval, 0.05–0.80; $I^2=0.0\%$) and 0.77% (95% confidence interval, 0.40–1.48; $I^2=0.0\%$) of pregnancies, respectively.

CONCLUSION: Perinatal death is uncommon after a prenatal diagnosis of vasa previa. Approximately half of the cases of perinatal mortality are not directly attributable to vasa previa. This information will help in guiding physicians in counseling and will provide reassurance to pregnant individuals with a prenatal diagnosis of vasa previa.

Key words: neonatal death, perinatal mortality, prenatal diagnosis, stillbirth, vasa previa

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AJOG at a Glance

Why was this study conducted?

The incidence and causes of perinatal mortality after a prenatal diagnosis of vasa previa have not been studied. In addition, it is not known what proportion of perinatal mortality in prenatally diagnosed vasa previa is directly attributable to vasa previa.

Key findings

Perinatal mortality after prenatal diagnosis of vasa previa is uncommon. Overall perinatal mortality was 0.94% (95% confidence interval [CI], 0.52–1.70; $I^2=0.0\%$). However, the pooled perinatal mortality directly attributable to vasa previa was only 0.51% (95% CI, 0.23–1.14; $I^2=0.0\%$).

What does this add to what is known?

Our study found that perinatal mortality directly attributable to vasa previa in prenatally diagnosed patients is low (0.51%). Approximately one-half of perinatal mortality is not directly due to vasa previa. Our study will help guide caregivers in counseling and will provide reassurance to pregnant individuals diagnosed with vasa previa.

Introduction

Vasa previa is a pregnancy complication in which unprotected fetal vessels flow through the amniotic membranes to the cervix.^{1–9} Vasa previa, when undiagnosed prenatally, is associated with extremely high perinatal mortality.^{1–12} When the membranes rupture either before or during labor, these vessels frequently rupture, leading to fetal blood loss or exsanguination and, in approximately 56% of cases, perinatal death.^{1,12} Thus, historically, in most cases, vasa previa was only diagnosed after the death of the neonate, and for the most part, vasa previa was considered a condition with a dismal outcome.

In 1987, Gianopoulos et al¹³ first described the ultrasound diagnosis of vasa previa. This made possible the prospect of prenatal diagnosis of the condition and then scheduled cesarean delivery before the membranes rupture, with the potential for preventing this high perinatal mortality. Since that original report, several studies have documented the accuracy of ultrasound in the prenatal diagnosis of vasa previa and documented the high sensitivity and specificity and the feasibility of prospective screening for vasa previa.^{14–24} These studies uniformly document a high perinatal survival when vasa previa is diagnosed prenatally. A recent

systematic review and meta-analysis by Zhang et al¹² found a 97.1% intact survival when vasa previa was diagnosed prenatally, compared with only a 28.1% intact survival in cases of vasa previa not diagnosed prenatally. Although vasa previa, when diagnosed prenatally, is associated with excellent outcomes, studies continue to report a small, but important, mortality among prenatally diagnosed patients with vasa previa.¹² When the diagnosis of vasa previa is made prenatally, it tends to cause considerable anxiety for the patient, who often spends the entire pregnancy in fear of the potential death of the neonate. This fear is often aggravated by physicians and other providers who often counsel the patient that there is a considerable risk that their neonate may not survive. However, our combined previous observation has been that although some very rare deaths have occurred after a prenatal diagnosis of vasa previa, these deaths are often the result of other pregnancy complications, such as congenital malformations, preterm birth, and fetal growth restriction (FGR), rather than from fetal exsanguination after rupture of the fetal vessels.

For this reason, we conducted a systematic review of the literature and meta-analysis to determine how often perinatal death occurred in the world

literature of prenatally diagnosed vasa previa and to assess what the causes of the perinatal mortality were in those cases in which there was a stillbirth or neonatal death after a prenatal diagnosis of vasa previa.

Objectives

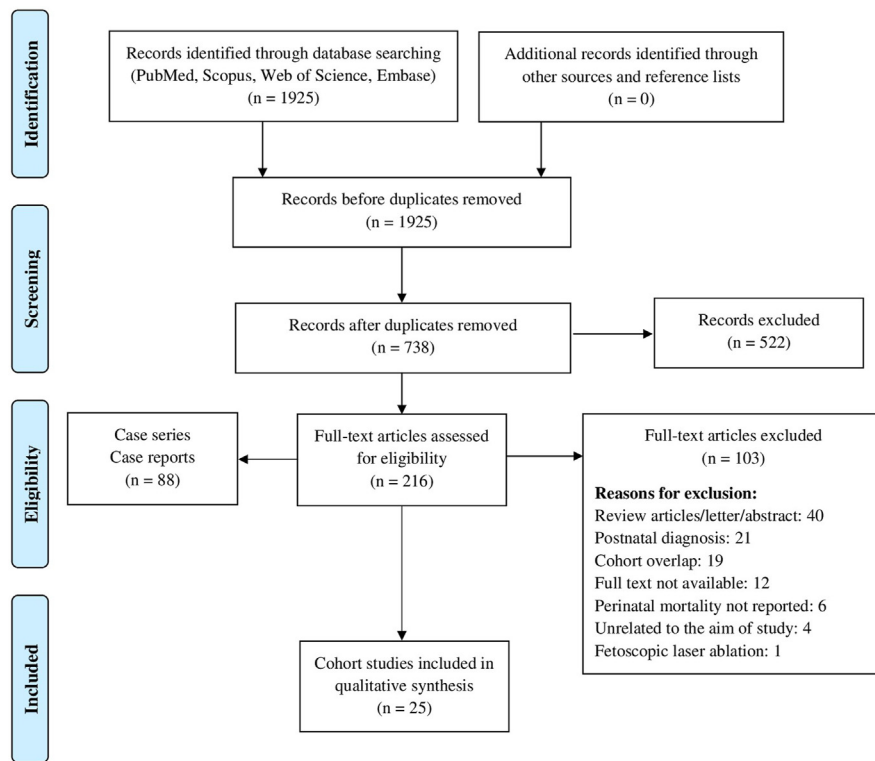
This study aimed to estimate the perinatal mortality associated with prenatally diagnosed vasa previa and to determine what proportion of these perinatal deaths are directly attributable to vasa previa and to assess causes of perinatal deaths not due to vasa previa.

Methods**Eligibility criteria, information sources, and search strategy**

The current study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 criteria and proposed reporting checklist for meta-analyses of observational studies.^{25,26}

The eligibility criteria were set based on the following framework: (P) population, patients with vasa previa who were diagnosed before labor; (I) intervention, none; (C) comparison, none or any; and (O) outcome, perinatal mortality rate and the cause of mortality. Studies were excluded if any of the following criteria were met: (1) conference abstracts, review articles, editorials, letters, and book chapters; (2) non-English, French, and Spanish; (3) perinatal survival (including in utero and neonatal death) was not reported; (4) the outcome of prenatally diagnosed patients was not reported separately (reported in conjunction with postnatally diagnosed patients); (5) full text not available; and (6) patients who underwent fetoscopic laser ablation for vasa previa, as this procedure significantly alters the natural course of the disease and could potentially be curative. We limited our study to include only publications from 1987 onward, as the first prenatal diagnosis of vasa previa was reported in 1987.¹³ Of note, 2 independent authors (M.J. and N.Z.) performed a systematic electronic search of the PubMed, Scopus, Web of Science, and Embase databases from January 1, 1987, to January 1, 2023. Our search strategy was based on the Medical

FIGURE
PRISMA flow diagram for the search and selection process



PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

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Subject Headings term “Vasa Previa,” which is shown in [Supplemental Table 1](#).

Study selection

All the records were imported into Rayyan, an online platform for study selection, upon conducting the systematic reviews.²⁷ Of note, 2 independent reviewers (N.Z. and M.J.) screened the records first by title and abstract and then by full text. In the entire screening process, conflicts were resolved by the third reviewer (A.J.).

Data extraction

In this study, the following items were extracted from the articles:

1. Study characteristics: first author, publication year, institute, and country
2. Demographic features: total number of patients, number of twin or multiple pregnancies, and number of

- pregnancies conceived through assisted reproductive technology
3. Perinatal outcome: stillbirth, neonatal death, and cause of death

Data extraction was performed by 2 independent reviewers (N.Z. and M.J.), and the conflicts were resolved by the third reviewer (A.J.). To eliminate overlapping studies, records from each institute were checked, and the most recent article or the one with the highest number of cases was included. When there was an overlapping study period for different studies from a single center, the authors were contacted to determine which of their articles were more comprehensive and eligible to be included. In cases in which the details of the perinatal deaths were not clear, the authors were contacted to provide details. The French studies were evaluated by one of the authors who is professionally fluent in French (A.J.), and the

Spanish articles were translated by a Spanish-speaking medical practitioner (see Acknowledgments).

Assessment of risk of bias

In the current study, the Newcastle-Ottawa Scale (NOS) was used to assess the risk of bias in retrospective, prospective, observational, and cohort studies.²⁸ In studies in which the “nonexposed cohort” was lacking, question 2 of the selection domain and the comparability domain was not answered, and the overall score was calculated out of 6. All processes were performed independently by 2 reviewers (N.Z. and M.J.), and conflicts were resolved by a third reviewer (A.J.).

Data synthesis

In this study, the programming language software R (version 4.2.2) was used to conduct the meta-analysis.²⁹ The following packages were used for the analysis: “meta,” “dmetar,” and “tidyverse.” Only the data from cohort studies were included in the analysis. To calculate the pooled proportion of perinatal mortality and survival, we used the “metaprop” R function. We pooled the data using the generalized linear mixed-effects model and logit-transformed proportions using the fixed effects model. Between-study heterogeneity was assessed using the chi-square test of heterogeneity and reported by I^2 . The publication bias was assessed using a funnel plot and the Peters regression test using “funnel.meta” and “metabias” R functions, respectively.

Results

Study selection

As shown in the [Figure](#), a total of 1925 studies were identified through the search, of which 1187 were duplicates. After screening 738 titles and abstracts, 216 studies were identified as potentially relevant and included in the full-text screening process. After a full-text assessment, 113 studies met the inclusion criteria.

Study characteristics

A total of 113 studies with a cumulative sample size of 1297 pregnant women were evaluated in this review. Among

them, 25 studies were cohorts with 1167 pregnancies, and 88 were case series or reports with 130 pregnancies, as presented in [Table 1](#) and [Supplemental Table 2](#), respectively. Among the cohort studies, 122 pregnancies (10.45%) were multifetal pregnancies, and 284 pregnancies (24.33%) were conceived through assisted reproductive technologies. All diagnoses were confirmed at the time of delivery.

Of note, 13 perinatal deaths occurred among these pregnancies, consisting of 2 stillbirths and 11 neonatal deaths ([Table 2](#)). The noteworthy aspect of these deaths is that 6 deaths were attributed to vasa previa and the other deaths occurred because of other factors. Of the 6 reports of perinatal death attributable to vasa previa, 3 occurred in dichorionic diamniotic twin pregnancies. The first patient had an emergency cesarean delivery at 27 weeks of gestation because of bleeding and an abnormal fetal heart rate tracing. Twin A died at 3 days of life from complications of blood loss, whereas twin B survived.⁴² In the second patient, there was a short cervix at 28 weeks of gestation. The patient underwent an emergency cesarean delivery at 31 weeks of gestation because of bleeding and an abnormal fetal heart rate. Twin A was stillborn, whereas twin B survived.⁴² In the third case, a stillbirth occurred in twin A in a dichorionic twin pregnancy after rupture of membranes and bleeding at 33 weeks of gestation. In that case, the fetal vessel was 2.8 cm from the internal os, and in addition, there was a short cervix of 1.4 cm.¹⁵

The remaining 3 perinatal deaths occurred in singleton pregnancies; in the fourth patient, perinatal death, bleeding, and an abnormal fetal heart rate tracing led to an emergency cesarean delivery at 31 weeks of gestation. The neonate died at 1 day of life because of complications from blood loss.⁴² In the fifth patient, the mother had type 1 diabetes mellitus, complicated by polyhydramnios, a large-for-gestational-age neonate, and a short cervix at 33 weeks of gestation. Admission was recommended but declined because of social reasons. At 33 1/7 weeks of gestation, bleeding and an abnormal fetal heart rate tracing

occurred, necessitating an emergency cesarean delivery. The neonate had a 1-minute Apgar score of 2 and an umbilical artery pH of 6.9 and died 2 days after birth from complications of blood loss.²¹ The sixth stillbirth occurred in the study by Klahr et al¹⁵ at 22 weeks of gestation after rupture of membranes and bleeding.

Risk of bias of included studies

This systematic review assessed the methodological quality of the included studies using the NOS. The results are shown in [Supplemental Table 3](#).

Synthesis of results

The pooled perinatal survival rate among cohort studies was 99.06% (95% confidence interval [CI], 98.30–99.48; $I^2=0.0\%$). The perinatal mortality was 0.94% (95% CI, 0.52–1.70; $I^2=0.0\%$). However, the pooled perinatal mortality attributed to vasa previa was 0.51% (95% CI, 0.23–1.14; $I^2=0.0\%$). Stillbirth and neonatal death were reported in 0.20% (95% CI, 0.05–0.80; $I^2=0.0\%$) and 0.77% (95% CI, 0.40–1.48; $I^2=0.0\%$), respectively. The Peters regression test was not significant ($t=1.81$; $P=.13$), indicating no funnel plot asymmetry and no publication bias.

Comment

Principal findings

Our study indicated that, at least based on published cohort studies, perinatal mortality after prenatal diagnosis of vasa previa is uncommon, occurring in approximately 0.5% of cases. This was only a fraction of the previously described mortality of 56% when vasa previa was not diagnosed prenatally. We found in our meta-analysis of cohort studies that the pooled perinatal mortality in prenatally diagnosed cases was 0.94% (95% CI, 0.52–1.70; $I^2=0.0\%$). Furthermore, our study indicated that when perinatal mortality did occur, only 0.51% (95% CI, 0.23–1.14; $I^2=0.0\%$) of cases of perinatal mortality were directly attributable to ruptured vasa previa. Over half of the cases of perinatal mortality were the result of congenital malformations or prematurity and, therefore, were not the direct result of

vasa previa. This finding provides reassurance to pregnant persons who may be diagnosed prenatally with vasa previa and gives doctors and midwives some data on which to counsel their patients.

Comparison with existing literature

To the best of our knowledge, no study to date has attempted to determine how often perinatal mortality occurs in the presence of prenatally diagnosed vasa previa and to determine the causes of the few deaths that do occur. Most studies have reported perinatal deaths without assessing which of those deaths were the direct result of vasa previa. Studies to date have examined survival rather than perinatal death in prenatally diagnosed vasa previa.

Importantly, half (3/6) of the perinatal mortality attributable to vasa previa in our study occurred in patients with twin pregnancies.^{15,42} In addition, in 2 of 3 of these patients with twin pregnancies, there was a short cervix. This suggests that twin pregnancies should be considered at a higher risk of perinatal death. Another neonatal death attributable to vasa previa occurred in a patient who was known to have a shortened cervix and polyhydramnios and, thus, was potentially preventable.²¹ In 1 neonatal death in a patient with twin pregnancies, the vasa previa was considered resolved in twin A because the vessel was 2.8 cm from the internal os.¹⁵ In addition, there was a short cervix, measuring 1.4 cm in length. In this patient, there was rupture of membranes and bleeding with fetal bradycardia for which an emergent cesarean delivery was performed. This case illustrated the potential hazard of considering vasa previa resolved when the vessels are at a distance of >2 cm from the internal os. Although some have defined vasa previa as vessels within 2 cm of the internal os, there has never been any evidence to support the use of that distance. Given that the cervix dilates to 10 cm, any vessels within a 5-cm radius of the internal os are potentially at risk, and we suggest that any exposed vessels within this distance from the internal os be considered as concerning. In summary, in 4 of 6 patients with perinatal death

TABLE 1

Study characteristics of cohort studies on patients with vasa previa who were diagnosed prenatally

Study	Year	Institute	Total	IVF ART	MP	Stillbirth	Neonatal death
Green et al ³⁰	2022	Atlantic Maternal Fetal Medicine, Morristown, NJ	57	—	2	0	0
La et al ³¹	2021	Westmead Hospital, Sydney, New South Wales, Australia	19	4	2	0	0
Gross et al ³²	2021	Ambulatorium für Fetalmedizin, Feldkirch, Austria	21	5	5	0	0
Liu et al ³³	2021	West China Second University Hospital, Sichuan University; Chengdu, China	137	22	17	0	2
Sutera et al ³⁴	2021	Sant'Anna Hospital, Turin, Italy	20	5	0	0	0
Tachibana et al ³⁵	2021	Osaka City University Hospital, Osaka, Japan	43 ^a	26	3	0	0
Zhang et al ²¹	2020	Fetal Medicine Unit, Medway Maritime Hospital, Gillingham, United Kingdom	21	4	0	0	1
Westcott et al ³⁶	2020	NYU Langone Health (Manhattan and Brooklyn campuses), Mount Sinai Hospital, Mount Sinai West, Maimonides Medical Center, Montefiore, Medical Center, NewYork-Presbyterian Columbia campus, and NewYork Presbyterian Cornell campus, United States	122	29	15	0	1
Furuya et al ³⁷	2020	Department of Obstetrics and Gynecology, St. Marianna University School of Medicine, Kanagawa, Japan	30	—	—	0	0
Klahr et al ¹⁵	2019	Department of Obstetrics, Gynecology, and Reproductive Science, Icahn School of Medicine at Mount Sinai, New York, NY	62	17	8	1	1 ^b
Bartal et al ³⁸	2019	Sheba Medical Center, Israel	109	65	6	0	1
Erfani et al ¹⁴	2019	Division of Maternal-Fetal Medicine, Baylor College of Medicine Texas Children's Fetal Center, Houston, TX; Department of Women's Health, Dell Medical School, University of Texas at Austin, Austin, TX; Department of Obstetrics and Gynecology, Beth Israel Deaconess Medical Center, Boston, MA; Department of Obstetrics and Gynecology, The University of Texas Medical Branch, Galveston, TX; Department of Obstetrics and Gynecology, Mayo Clinic College of Medicine, Rochester, MN	117	15	7	0	0
Yerlikaya et al ³⁹	2019	Division of Obstetrics and Fetal-Maternal Medicine, Vienna, Austria	19	6	4	0	0
Melcer et al ¹⁹	2018	Assaf Harofeh Medical Center, Zerifin, Israel	38	20	7	0	0
Sullivan et al ²⁴	2017	Australasian Maternity Outcomes Surveillance System, multicentric national study, Australia	58	11	2	0	0
Nohuz et al ²⁰	2017	Department of Obstetrics and Gynecology, University Hospital Estaing, Clermont-Ferrand, France	8	1	2	0	0
Swank et al ¹⁸	2016	University of California, Irvine Medical Center, Orange, CA; Mednax/Pediatrix Medical Group, Sunrise, FL; Das Consulting, San Francisco, CA; Obstetrix Medical Group, Phoenix, AZ; Obstetrix Medical Group, California, San Jose, CA; Obstetrix Medical Group, Denver, CO; Obstetrix Medical Group, Seattle, WA; Obstetrix Medical Group, Southern California, Long Beach, CA; Obstetrix Medical Group, Southern California, Laguna Hills, CA; University of South Alabama, Mobile, AL; Obstetrix Medical Group, Center for Research Education & Quality, Mednax, Inc, Sunrise, FL	47	8	5	0	0

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(continued)

TABLE 1

Study characteristics of cohort studies on patients with vasa previa who were diagnosed prenatally (continued)

Study	Year	Institute	Total	IVF ART	MP	Stillbirth	Neonatal death
Catanzarite et al ¹⁷	2016	Sharp Mary Birch Hospital for Women & Newborns, San Diego, CA	96	22	19	0	1
López-Ramón et al ⁴⁰	2016	University Hospital of Vigo, Spain	20	10	9	0	0
Hasegawa et al ⁴¹	2015	Department of Obstetrics and Gynecology, Showa University School of Medicine, Tokyo, Japan	21	—	—	0	0
Bronsteen et al ⁴²	2013	William Beaumont Hospital, Royal Oak, MI	56	—	7	1	2
Golic et al ⁴³	2013	Klinik für Geburtsmedizin, Campus Virchow-Klinikum, Charité — Universitätsmedizin Berlin, Germany	18	6	0	—	0
Kanda et al ⁴⁴	2011	Kagoshima City Hospital, Kagoshima, Japan	9	4	0	0	0
Baulies et al ⁴⁵	2007	Department of Obstetrics, Gynaecology, and Human Reproduction, Institut Universitari Dexeus, Barcelona, Spain	9	4	2	0	0
Catanzarite et al ⁴⁶	2001	Sharp Mary Birch Hospital for Women & Newborns, San Diego, CA	10	—	0	0	0

ART, assisted reproductive technology, IVF, in vitro fertilization, MP, multiple pregnancy.

^a In 12 of 55 patients (21.81%), vasa previa was resolved during pregnancy; ^b Neonatal death was reported in a patient who had resolved vasa previa (not included among 61 patients with unresolved vasa previa).

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attributable to vasa previa, there were risk factors that preceded the bleeding or rupture of membranes, and perhaps identification of these patients at risk may further lower the perinatal mortality. However, to the best of our knowledge, in 2 patients, no risk factor preceded the perinatal death. In 1 patient, there was rupture of membranes at 22 weeks of gestation, whereas the other patient in which rupture of membranes at 28 weeks of gestation resulted in neonatal death had no preceding risk factor.^{15,42} These 2 cases suggest that perinatal death, although rare, may still occur despite prenatal diagnosis and without any risk factors.

Strengths and limitations

Our study has several strengths. We have conducted a review of all relevant contemporary published cases of vasa previa diagnosed prenatally. In several of these cohorts, there were systematic approaches to screening for vasa previa and all outcomes, whether survival or death attributable to vasa previa was recorded. In addition, we have contacted the authors in cases of perinatal death to ensure that, as far as possible,

we correctly identified the causes of perinatal death. We excluded case reports, thus removing the likelihood that individual cases of vasa previa with perinatal death may have not been reported. However, in the large cohorts, both survival and death were reported.

Our study has some important limitations. Studies had differing methodologies. Importantly, the definitions of vasa previa varied between the studies. Some defined vasa previa as fetal vessels within 2 cm, some within 3 cm, and some within 5, and others defined it as fetal vessels over or close to the cervix. There is no consistent definition of vasa previa based on distance, and there is no consensus. Although the authors reported that they were aware of all cases of vasa previa—related mortality and reported them all, there will always be the potential that a few cases may not have been identified. In addition, we did not evaluate the effect of such interventions as hospitalization and timing of delivery. For instance, in several studies, patients were delivered as early as 33 to 34 weeks of gestation. It is unknown whether if some of those pregnancies had been

allowed to carry on to 36–37 weeks, some cases of ruptured vessels and perinatal death may have occurred. However, a recent systematic review and meta-analysis found that the lowest risks of adverse perinatal outcomes occurred when pregnancies with prenatally diagnosed vasa previa were delivered between 36 and 37 weeks of gestation. Furthermore, there was no perinatal death occurring at those gestational ages, adding support to our finding that perinatal death attributable to prenatally diagnosed vasa previa is exceedingly low.⁴⁸

Conclusions and implications

Our results indicated that, based on published studies, the risk of perinatal death directly attributable to vasa previa after prenatal diagnosis is approximately 0.5% and provides good data for counseling patients. This will provide reassurance to both patients and their physicians. Prenatal diagnosis of vasa previa was associated with a negative psychological effect in patients, which may lead to detrimental pregnancy experiences and poor maternal-fetal bonding and negative effect on

TABLE 2

Review of patients with vasa previa who died after being diagnosed prenatally

Study	GA at death	Cause of death	Death attributed to vasa previa?
Liu et al ³³	28 6/7 wk	Unclear	No
	27 wk	Severe fetal growth restriction	No
Zhang et al ²¹	Delivered at 33 1/7 wk Died at 2 d of life	Spontaneous preterm labor Antepartum hemorrhage	Yes
Klahr et al ¹⁵	22 wk	Vasa previa rupture secondary to preterm labor	Yes
	33 wk	Preterm premature rupture of membranes Antepartum hemorrhage	Yes
Bartal et al ³⁸	—	Severe fetal growth restriction	No
Westcott et al ³⁶	—	Prematurity complications	No
Bronsteen et al ⁴²	Delivered at 27 wk Died at 3 d of life	Antepartum hemorrhage	Yes
	31 wk	Antepartum hemorrhage	Yes
	31 wk	Antepartum hemorrhage	Yes
Catanzarite et al ¹⁷	Died 28 d after cardiac surgery	Complex heart defect (hypoplastic left heart syndrome + arterial septal defect)	No
Oyelese et al ³	Delivered at 25 wk Died at 7 d of life	Prematurity and sepsis	No
Wiafe et al ⁴⁷	Delivered at 37 2/7 wk Died within 24 h	Unclear (respiratory failure)	Unclear

GA, gestational age.

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relationships.⁴⁹ Our findings may help alleviate that. The fear of death may lead to an increase in iatrogenic preterm delivery with its attendant negative consequences. Perhaps knowledge of favorable outcomes may lead to a reduction in delivery before 35 weeks of gestation in stable asymptomatic patients, improving neonatal outcomes.

Although the deaths attributable to vasa previa are typically those that result from vessel rupture and fetal exsanguination, velamentous cord insertion may lead to FGR, fetal heart rate abnormalities, and cord compression, which may result in fetal death. However, in our study, we only found 2 deaths from FGR and none from other causes. It is uncertain whether vasa previa may have contributed to the growth restriction.

Prenatal diagnosis of vasa previa was associated with a low risk of perinatal death, and the few deaths that did occur were even more rarely attributable to vasa previa. Patients and physicians need

to be aware of this low risk, which will reduce stress for pregnant individuals and families with a prenatal diagnosis of vasa previa. ■

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REFERENCES

- Oyelese KO, Turner M, Lees C, Campbell S. Vasa previa: an avoidable obstetric tragedy. *Obstet Gynecol Surv* 1999;54:138–45.
- 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;213:615–9.
- Oyelese KO, Schwärzler P, Coates S, Sanusi FA, Hamid R, Campbell S. A strategy for reducing the mortality rate from vasa previa

using transvaginal sonography with color Doppler. *Ultrasound Obstet Gynecol* 1998;12:434–8.

- Jauniaux E, Savidou MD. Vasa praevia: more than 100 years in preventing unnecessary fetal deaths. *BJOG* 2016;123:1287.
- Oyelese Y, Smulian JC. Placenta previa, placenta accreta, and vasa previa. *Obstet Gynecol* 2006;107:927–41.
- Silver RM. Abnormal placentation: placenta previa, vasa previa, and placenta accreta. *Obstet Gynecol* 2015;126:654–68.
- Gagnon R. No. 231-guidelines for the management of vasa previa. *J Obstet Gynaecol Can* 2017;39:e415–21.
- Jauniaux E, Alfirevic Z, Bhide AG, et al. Vasa praevia: diagnosis and management: Green-top Guideline No. 27b. *BJOG* 2019;126:e49–61.
- Oyelese Y. Vasa previa: time to make a difference. *Am J Obstet Gynecol* 2019;221:539–41.
- Evans GM. Vasa praevia. *Br Med J* 1952;2:1243.
- Oyelese Y, Catanzarite V, Prefumo F, et al. Vasa previa: the impact of prenatal diagnosis on outcomes. *Obstet Gynecol* 2004;103:937–42.
- Zhang W, Geris S, Al-Emara N, Ramadan G, Sotiriadis A, Akolekar R. Perinatal outcome of pregnancies with prenatal diagnosis of vasa

previa: systematic review and meta-analysis. *Ultrasound Obstet Gynecol* 2021;57:710–9.

13. Gianopoulos J, Carver T, Tomich PG, Karlman R, Gadwood K. Diagnosis of vasa previa with ultrasonography. *Obstet Gynecol* 1987;69:488–91.

14. Erfani H, Haeri S, Shainker SA, et al. Vasa previa: a multicenter retrospective cohort study. *Am J Obstet Gynecol* 2019;221:644.e1–5.

15. Klahr R, Fox NS, Zafman K, Hill MB, Connolly CT, Rebarber A. Frequency of spontaneous resolution of vasa previa with advancing gestational age. *Am J Obstet Gynecol* 2019;221:646.e1–7.

16. 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.

17. Catanzarite V, Cousins L, Daneshmand S, et al. Prenatally diagnosed vasa previa: a single-institution series of 96 cases. *Obstet Gynecol* 2016;128:1153–61.

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

19. 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.

20. Nohuz E, Boulay E, Gallot D, Lemery D, Vendittelli F. Can we perform a prenatal diagnosis of vasa previa to improve its obstetrical and neonatal outcomes? *J Gynecol Obstet Hum Reprod* 2017;46:373–7.

21. Zhang W, Geris S, Beta J, Ramadan G, Nicolaides KH, Akolekar R. Prevention of stillbirth: impact of two-stage screening for vasa previa. *Ultrasound Obstet Gynecol* 2020;55:605–12.

22. Kamijo K, Miyamoto T, Ando H, et al. Clinical characteristics of a novel “type 3” vasa previa: case series at a single center. *J Matern Fetal Neonatal Med* 2022;35:7730–6.

23. Ruiters L, Kok N, Limpens J, et al. Systematic review of accuracy of ultrasound in the diagnosis of vasa previa. *Ultrasound Obstet Gynecol* 2015;45:516–22.

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

25. Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-

analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA* 2000;283:2008–12.

26. Page MJ, Moher D, Bossuyt PM, et al. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. *BMJ* 2021;372:n160.

27. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—a web and mobile app for systematic reviews. *Syst Rev* 2016;5:210.

28. Wells GA, Shea B, O’Connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Oxford; 2000. Available at: https://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.

29. Harrer M, Cuijpers P, Furukawa TA, Ebert DD. Doing meta-analysis with R: a hands-on guide. Boca Raton, FL: Chapman & Hall/CRC Press; 2021.

30. Green A, Chiu S, Manor E, Smith L, Oyelese Y. The association of gestational age at delivery with neonatal outcomes in prenatally diagnosed vasa previa. *J Matern Fetal Neonatal Med* 2022;35:10162–7.

31. La S, Melov SJ, Nayyar R. Are we over-diagnosing vasa praevia? The experience and lessons learned in a tertiary centre. *Aust N Z J Obstet Gynaecol* 2021;61:217–22.

32. Gross A, Markota Ajd B, Specht C, Scheier M. Systematic screening for vasa previa at the 20-week anomaly scan. *Acta Obstet Gynecol Scand* 2021;100:1694–9.

33. Liu N, Hu Q, Liao H, Wang X, Yu H. Vasa previa: perinatal outcomes in singleton and multiple pregnancies. *BioSci Trends* 2021;15:118–25.

34. Suter M, Garofalo A, Pilloni E, et al. Vasa previa: when antenatal diagnosis can change fetal prognosis. *J Perinat Med* 2021;49:915–22.

35. Tachibana D, Misugi T, Pooh RK, et al. Placental types and effective perinatal management of vasa previa: lessons from 55 cases in a single institution. *Diagnostics (Basel)* 2021;11:1369.

36. Westcott JM, Simpson S, Chasen S, et al. Prenatally diagnosed vasa previa: association with adverse obstetrical and neonatal outcomes. *Am J Obstet Gynecol MFM* 2020;2:100206.

37. Furuya N, Sasaki T, Homma C, Hasegawa J, Suzuki N. Ultrasound screening and management of vasa previa in Japan. *J Obstet Gynaecol Res* 2020;46:1084–9.

38. Fishel Bartal M, Sibai BM, Ilan H, et al. Prenatal diagnosis of vasa previa: outpatient versus inpatient management. *Am J Perinatol* 2019;36:422–7.

39. 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;299:1545–50.

40. López-Ramón, Cajal C, Cordeiro-Vidal G, Valladares-Bajo Z, Cerviño-Gómez E. Vasa previa: diagnostic algorithm (cases series). *Ginecol Obstet Mex* 2016;84:730–6.

41. Hasegawa J, Arakaki T, Ichizuka K, Sekizawa A. Management of vasa previa during pregnancy. *J Perinat Med* 2015;43:783–4.

42. Bronsteen R, Whitten A, Balasubramanian M, et al. Vasa previa: clinical presentations, outcomes, and implications for management. *Obstet Gynecol* 2013;122:352–7.

43. Golic M, Hinkson L, Bamberg C, et al. Vasa praevia: risk-adapted modification of the conventional management—a retrospective study. *Ultraschall Med* 2013;34:368–76.

44. 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;37:1391–6.

45. Baulies S, Maiz N, Muñoz A, Torrents M, Echevarría M, Serra B. Prenatal ultrasound diagnosis of vasa praevia and analysis of risk factors. *Prenat Diagn* 2007;27:595–9.

46. 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;18:109–15.

47. Wiafe YA, Adu-Bredu TK, Appiah-Denkyira K, Senaya CM. Antenatal diagnosis of vasa previa: report of three cases in an African setting. *Pan Afr Med J* 2020;37:24.

48. Mitchell SJ, Ngo G, Maurel KA, et al. Timing of birth and adverse pregnancy outcomes in cases of prenatally diagnosed vasa previa: a systematic review and meta-analysis. *Am J Obstet Gynecol* 2022;227:173–81.e24.

49. Javid N, Sullivan EA, Halliday LE, Duncombe G, Homer CS. “Wrapping myself in cotton wool”: Australian women’s experience of being diagnosed with vasa praevia. *BMC Pregnancy Childbirth* 2014;14:318.