INTRODUCTION

Vasa previa remains a hidden, rare complication that occurs approximately in 1/2500 pregnancies.\(^1\) It was first described by Lobstein in 1801.\(^2\) Vasa previa is defined as the crossing of fetal vessels, unsupported by the placenta or the umbilical cord, between internal cervical os and the presenting part of the fetus. Injuries of these vessels can cause fetal bleeding and induce fetal blood loss to varying extents.\(^3\) Different types of vasa previa have been described with changing frequencies. Currently, the risk factors have been clearly described. In particular, risk factors for vasa previa include pregnancies after ART, low-lying placenta, placenta previa, bilobate placenta or succenturiate placenta, multiple gestation and velamentous cord insertion.\(^4\) In such cases, physicians should rule out vasa previa and, if confirmed, implement sufficient management to prevent mortal complications. Delivery before the onset of labor through an elective cesarean section is recommended at 34–35 weeks of pregnancy.\(^5\) Herein, we report on five cases with vasa previa that were prenatally detected and managed with different procedures without complications in our tertiary referral hospital during the past year, and a review of the literature based on especially diagnosis and management.

CASE SERIES

2.1 Case 1

The first case was a 35-year-old primiparous woman who achieved pregnancy after using assisted reproductive technology (intracytoplasmic sperm injection). She was referred to our tertiary center for birth planning at 34 weeks and 3 days of gestation. At the primary care provider, ultrasound indicated placenta previa with transverse presentation of the fetus during the 29th week of pregnancy. At the hospital, transabdominal and transvagal grayscale sonography showed a breech presentation and a low-lying placenta with bilobate placenta with lobes located on the anterior and posterior walls. The diagnosis of vasa previa was made transvaginally by adding the use of color-coded Doppler sonography (Figure 1). We initially planned a cesarean section at 36 weeks of gestation; however, at 34 weeks and 6 days, the membranes...
spontaneously ruptured. An uncomplicated emergency cesarean section was performed. At the time of surgery, the diagnosis of bilobate placenta and vasa previa was confirmed (Figure 2).

2.2 | Case 2

The second case was a 30-year-old woman, gravida 2, with a history of one interruption via dilation and curettage. At 30 weeks and 6 days, she was referred to our tertiary center by her specialist with preterm labor, which was suspicious for a SGA pregnancy and vasa previa type I in meanings of an insertio velamentosa causing the vasa previa. We performed a routine grayscale abdominal and vaginal sonography and color-coded Doppler ultrasound, to evaluate the pregnancy. We were able to confirm the vasa previa and SGA diagnosis (Figure 3). A cesarean section was planned at 35 weeks and 6 days of gestation, and our patient was discharged. We performed an elective cesarean section at 35 weeks and 6 days of gestation. During the cesarean section, insertio velamentosa with vasa previa was observed. We confirmed the diagnosis of an insertio velamentosa postnatally (Figure 4).
2.3 | Case 3

The third case was a 34-year-old woman, gravida 3 with a history of one ectopic pregnancy and one first-trimester abortion who achieved pregnancy after using assisted reproductive technology (intracytoplasmic sperm injection). The patient was transferred to our hospital at 25 weeks and 3 days with contractions and vaginal bleeding after sexual intercourse. At the time of admission, we diagnosed a bilobate placenta with previa presentation. The fetal vessels crossed near the cervix. Consecutive ultrasound examinations during outpatient management showed no further previa, but a bilobate placenta and vasa previa were still present. We planned readmission at 34 weeks and an elective cesarean section at 36 weeks of pregnancy. Emergency admission occurred at 30 weeks and 5 days due to vaginal bleeding. An emergency cesarean section was performed due to increased vaginal bleeding with contractions at 33 weeks and 3 days. We were able to intraoperatively confirm the diagnosis of bilobate placenta with vasa previa (Figure 5).

2.4 | Case 4

The fourth case was a 32-year-old primiparous woman after spontaneous conception. She was referred to our hospital at 34 weeks and 4 days for birth planning. In the first trimester and during a routine ultrasound at 12 weeks of pregnancy, her obstetrician noted a lower insertion at lower uterine segment of the umbilical cord. Ultrasound screening in the second trimester at 21 weeks showed vasa previa with posterior placenta localization with velamentous cord insertion, whereby aberrant vessels were found to overlie the internal OS. We were also able to confirm the vasa previa diagnosis (Figure 6). One
day after the referral, we admitted the patient for inpatient observation and performed an elective C-section at 36 weeks and 4 days of pregnancy. At the time of surgery, we were able to detect velamentous insertion with vasa previa.

### 2.5 Case 5

The fifth case was a 32-year-old primiparous woman after spontaneous conception. She was referred to our hospital at 23 weeks and 3 days by her specialist with a suspected SGA fetus for further assessment. We performed routine grayscale abdominal and vaginal sonography, and color-coded Doppler ultrasound, to evaluate the pregnancy. The examination showed a bilobate placenta with connecting vessels presenting as vasa previa (Figure 7). Outpatient management was followed until we planned an admission at 32 weeks of gestation. Directly after admission, the patient received RDS prophylaxis. We performed an elective cesarean section at 34 weeks and 3 days of gestation. At the time of the C-section, we were able to detect a bilobate placenta with vasa previa (Figure 8).

### 3 DISCUSSION

Vasa previa is a rare obstetric condition with an uncertain incidence, and it is reported to occur in approximately 1/2500 pregnancies and in up to 1/135 twin pregnancies in relation to a highly selected group, especially after the rise of assisted reproductive technology.1,6

The term “vasa previa” derives from the Latin words “vasa,” meaning vessels, “pre” or “prae” meaning before and “via” meaning way. Vasa previa is defined as a condition in which the unprotected fetal vessels transverse the lower uterine segment between cervix and the fetal presenting part.1

Morbidity and mortality are caused by any kind of damage of these vessels, which typically occurs after spontaneous or artificial rupture of membranes and labor, leading to hemorrhage, exsanguination, and even death of the fetus. Fetal mortality rises up to 100%1 in prenatally undiagnosed cases but can be decreased to 0% if correct prenatal diagnosis and management are performed.7

Since the entire fetal blood volume is usually 100 ml/kg, clinically important bleeding can rapidly occur. Bleeding of even 100 ml is sufficient to cause fetal morbidity.3 In cases with prenatal diagnosis when regarding morbidity, only 3.4% of all newborn infants required a transfusion, compared with 58.5% in those infants without a correct prenatal diagnosis.8

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**FIGURE 4** Case 2: Placenta with velamentous inserted fetal vessels causing vasa previa (arrow)

**FIGURE 5** Case 3: Visualization of fetal vessels connecting two lobes of the placenta using color-coded Doppler ultrasound. (transabdominal)—bilobate placenta and the connecting vessel causing vasa previa (arrow)
3.1 Types, occurrence and risk factors

Two types of vasa previa were primarily defined by Catanzeirte et al. in 2001. Type I describes the condition when a velamentous cord insertion occurs and the vessels cross freely over the cervix or in close proximity to it. Type II describes the condition when the lobes of placenta in case of a placenta succenturiate or multilobata (typically bilobate) are connected via vessels, which cross over or near the cervix. The proportion of Type I is approximately at 25%–65% and Type II approximately at 35%–60%.8,9

In addition to frequently reported known types in the literature, there are also rare and uncharacteristic non-Type I/II vasa previa. A report of two cases with resolved placenta previa showed that vessels lying on the placental surface, which have an abnormal orbit, can also cross the cervix and cause a so-called “Type III” vasa previa.10

Known risk factors to cause concomitant vasa previa are low-lying placenta, placenta previa, bilobate placenta or succenturiate placenta, and a velamentous cord insertion.4

Two theories most likely explain the occurrence of vasa previa. The first theory is the “polarity theory,” which may occur when the embryo does not face the implantation base and the umbilical vessels extend between umbilical cord insertion and the placenta at the implantation base. The second theory that may be associated with vasa previa is the “trophotropism theory,” which explains the occurrence of these pathologies with low-lying placenta pathologies. This situation occurs when the early placenta migrates with advancing gestational age to ensure a better blood supply and to appropriately develop, thus resulting in either marginal or membranous insertion.11

A systematic review that classified the risk factors in detail reported that women with a placenta previa in the second trimester have a common odds ratio (OR) for the development of vasa previa (VP) of 19 (95% CI 6.1–58) compared to women with a normal placental localization. Women with velamentous insertion of the umbilical cord showed an increased risk for developing vasa previa compared to women with a normal placental cord insertion (common OR 672; 95% CI 112–4034). Women with a bilobed or succenturiate placenta had an increased risk for VP compared to women with a normal placenta (common OR 71; 95% CI 14–349). Compared to singleton gestations, multiple gestations have been reported as risk factors in this review; however, multiple gestations were not an independent risk factor for vasa previa in this review, with common ORs of 2.66 (95% CI 0.80–8.8) and 2.8 (95% CI 0.9–8.3) in a study by Gross et al.4,12
3.2 | Assisted reproductive technology as a risk factor

In addition to assisted reproductive technology (ART), which is known as a risk factor for various complications that have been previously mentioned, pregnancies due to ART are also often complicated with vasa previa (VP). The higher incidence of umbilical cord anomalies, such as vasa previa after ART, was related to the inadequate orientation of the blastocyst at the time of implantation. It has been reported that 80% of all embryos implant in the area of transfer by ARTs, which is not the most favorable location.

Although it is unclear how this may affect the implantation process, artificial induction of ovulation can also lead to a higher incidence of cord anomalies in twin pregnancies than in naturally conceived twins. This finding was rather associated with high levels of estrogen and progesterone, which resulted in a thicker endometrium. Pregnancies after IVF cycles, wherein the estradiol (>10,000 pmol/L) level has been shown to be higher, were more associated with abnormal placentation.

All of these factors seem to play a role in the development of placental-umbilical cord pathologies, such as vasa previa. Although maternal serum estradiol was not measured, one investigation showed that an embryo cryo-transfer, wherein the hormone levels are relatively physiological, showed a decrease in the placental complication rates.

3.3 | Diagnosis and screening

The most important variable of vasa previa influencing fetal–neonatal outcome is early prenatal diagnosis. A review by Oyelese et al. containing 155 cases found that prenatal diagnosis reduced late fetal and neonatal mortality by approximately 95%.

The first description of ruptured vasa previa was done by Lobstein in 1801. Until the first ultrasound...
description of vasa previa was performed by Gianopoulou\textit{et al.}, the diagnosis was often made too late and after the occurrence of membrane rupture, painless vaginal bleeding (fetal bleeding, which is known as Benckiser’s hemorrhage) and fetal distress or death.\textsuperscript{18} Historically, Nelson et al. reported the first use of color flow Doppler to diagnose vasa previa.\textsuperscript{19}

The detection rate of vasa previa with the use of combined ultrasound is over 93%, and the specificity is between 99% and 100%. The detection of vasa previa is more likely to be accomplished in the second trimester.\textsuperscript{20}

According to some authors, an accurate diagnosis should first be ensured after the opening of the uterine isthmus as the amniotic sac expands towards the cervix because of the opposite migration of velamentous vessels to the direction of migration of the placenta in the lower uterine segment.\textsuperscript{21}

In addition, physicians should be attentive to hints and risk factors that can be observed in the first trimester. Pregnancies with cord insertions located in the lower third of the uterine cavity in the first trimester were more likely to be found with abnormal placental forms and with complications such as placenta previa, velamentous cord insertion, and vasa previa.\textsuperscript{22}

However, differentiating between maternal and fetal vessels can be challenging in some cases. Heart rate measurement may help to differentiate maternal vessels from fetal arterial vessels. Rates between 120 and 180 bpm are likely to represent fetal vessels, and rates between 70 and 90 bpm will most likely represent maternal vessels. It can be more difficult to differentiate venous vessels. Some authors have suggested using Valsalva maneuver to differentiate between arterial and venous vessels. In particular, a fetal vein would display no change in phasicity with the Valsalva maneuver.\textsuperscript{23}

Three-dimensional sonography can also be an additional part of diagnostics. 3D ultrasound allows for more scanning planes and can map out the course of the fetal vessels, which can subsequently guide the surgical pathway. 3D ultrasound also provides additional information compared to conventional 2D-Ultrasound.\textsuperscript{24} Additionally, magnetic resonance imaging has been used to confirm vasa previa in a few obscure cases.\textsuperscript{25}

In cases wherein vasa previa is suspected, repeated ultrasound assessments should be performed in the third trimester, due to the fact that up to 39% of apparent vasa previa will resolve by the late third trimester.\textsuperscript{26}

When regarding screening for vasa previa, some authors have established targeted screening strategies. The two-stage strategy encloses as screening group the pregnancies with risk factors regarding ultrasonic findings, such as low-lying placenta in the 20–22-week scan and velamentous cord insertion in the 11–13-week scan. These prospective screening data were retrospectively analyzed; however, the authors did not include any screening strategy for either multiple pregnancies or other risk groups in regards to pregnancies after ART.\textsuperscript{27}

Another retrospective study on prospectively examined pregnancies defined the one-stage screening strategy for vasa previa at the 20-week anomaly scan. Transvaginal sonography was performed during the same examination in cases with marginal or velamentous umbilical cord insertion, placental anomalies, such as succenturiate or bilobate placentas and placenta previa.\textsuperscript{12} Both of the authors reported targeted screening strategies for vasa previa as being feasible; however, due to the retrospective nature of these studies, a recommendation for universal screening on the basis of this situation is not possible.

In their decision-analytic model, Sinkey et al. demonstrated that a second-trimester ultrasound examination combined with Doppler ultrasound was considered to be useful and cost-effective for detecting pregnancies with risk factors for vasa previa; additionally, they demonstrated that it was then beneficial to perform targeted vasa previa screening with the combination of a transvaginal ultrasound.\textsuperscript{28} The authors only utilized the singleton pregnancies in their study and did not define any screening

\textbf{Figure 8} Case 5: Bilobate placenta and the connecting vessels between lobes causing vasa previa (arrows)
model for multiple gestations. Furthermore, in their decision-analytic model, Cipriano et al. demonstrated that, although not being an independent risk factor for vasa previa, universal screening, such as by the existence of other risk factors for vasa previa for twin pregnancies, is very likely to be useful regarding cost-effectiveness.

Ranzini et al. addressed necessary steps in screening vasa previa, such as evaluating the umbilical cord insertion site into the placenta, ruling out a bilobed or succenturiate placenta, and re-evaluating the lower uterine segment in all cases of resolving low-lying placenta or placenta previa.

### 3.4 Management

For all cases with vasa previa, which were prenatally diagnosed, an elective cesarean section should be performed to avoid fetal morbidity and mortality. Based on current knowledge, there is still no clear consensus with strong evidence concerning the management strategy including the need for antepartum hospitalization, the need for the administration of corticosteroids, and the timing of delivery. Although some authors recommend to manage inpatient, systemic antepartum hospitalization even from 28 to 32 weeks of gestation for the administration of corticosteroids and to allow closer surveillance for signs of labor and then a more timely performance of cesarean delivery to avoid membrane rupture.

A study showed no difference in perinatal outcomes between cases of vasa previa that were prenatally diagnosed when managed as outpatient or inpatient procedure. However, the study showed that women in the inpatient group were more likely to receive antenatal steroids (57.3% vs. 26.4%, \( p = 0.002 \)) and advantageously were less likely to have an urgent cesarean section (34.6% vs. 58.8%, respectively, \( p < 0.001 \)), but the gestational age at delivery did not differ significantly between the groups significantly (\( p = 0.01 \)).

A population-based study showed that pregnancies complicated with vasa previa tend to deliver preterm and face a higher prematurity risk than those without vasa previa. Nonetheless, the authors did not report the indications for cesarean sections. However, the available data and another systematic review and meta-analysis also confirmed that the patients with vasa previa tend to deliver preterm, and rates can even increase by up to 81.9%. 5,7,36

Data from a decision analysis study comparing 11 strategies for the timing of delivery reported that delivery between 34–36 weeks balances the risk of premature rupture of the membranes and subsequent fetal hemorrhage and death versus the risks of prematurity. This study did not differentiate between singleton and twin pregnancies.

In agreement with this recommendation, Oyelese et al. also reported that delivery should be performed at 35–36 weeks of pregnancy.

Regarding multiple gestations, some authors have reported an increase in the indicated deliveries with vasa previa at 32 weeks of gestation. In this study, the indication among 13 of 19 women with twin pregnancies included preterm contractions or labor, including two cases with a dilated cervix (1.5 and 3 cm). However, the authors did not describe the indication for the deliveries before 32nd week in twin pregnancies separately.

Except for singleton pregnancies, there are only a few reports that have focused on multiple gestations with vasa previa. Velamentous cord insertion and vasa previa, especially type I, are more common in multiple pregnancies. Some reports have suggested that monochorionicity doubles the risk for VCI compared to dichorionicity.

Due to the lack of strong evidence for multiple pregnancies with vasa previa, the recommendation for the timing of delivery refers to the decision analysis study, which does not differentiate between singleton and multiple pregnancies.

A combined strategy with cervical length screening can be effective in predicting the risk group, which would show a higher tendency to deliver earlier would allow the patients to be managed in inpatient settings.

Our clinic is a tertiary university center wherein no primary care is performed due to German health care. German health care routinely considers three ultrasound examinations in pregnancy between 9 and 12 weeks, 19 and 22 weeks, and 29 and 32 weeks. Screening between 19 and 22 weeks also includes screenings for placenta and fetal organs. Considering the fact that our facility is a tertiary center, the referred cases to our center are often highly selected and possess obstetrical risk factors and often established or suspected diagnoses. We guess that fact is a reason for the higher incidence in regard to the approximately 1/400 cases of vasa previa that have been reported at the time for this 5 case reports.

Our approach includes targeted screening of every referred pregnancy for vasa previa at presentation in the second trimester if risk factors are present. Furthermore, we suggest the documentation of umbilical cord insertion during every routine mid-trimester fetal ultrasound scan. The timing of delivery, and the method of management (outpatient versus inpatient), should be planned individually depending on other risk factors (e.g., cervical length, preterm contractions, or the presence of bleeding). We deliver pregnancies with vasa previa at 34–35 weeks of pregnancy through an elective cesarean section. From our point of view and based on the available evidence, a prolongation after 36 weeks does not seem to be acceptable.
3.5 Conclusions

It is important to note that in 85%–90% of cases of vasa previa, a risk factor is present. Some authors have ethically suggested screening for vasa previa as a complication with high mortality and morbidity in all undetected pregnancies. However, regarding cost-effectiveness is targeted screening for vasa previa compared with universal screening more acceptable. It is also difficult to conduct a randomized controlled trial in this field, which would not be ethical. Targeted screening strategies for vasa previa seem to be feasible to screen and detect such mortal complication.

A national survey conducted in 2006 among obstetric and fetomaternal consultants showed that only approximately 70% of the respondents were able to identify any risk factor for such a dangerous obstetric complication, “vasa previa” and most of them would even offer and perform a cesarean section at 38 weeks of gestation. Prospective studies, such as cohort studies and RCTs are needed to strengthen the available evidence. Increasing rates of vasa previa should motivate physicians to actively inform themselves about this condition. As studies have shown, an improved awareness of vasa previa and its risk factors can prevent complications and minimize perinatal deaths.

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CONFLICT OF INTEREST

The authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest, or nonfinancial interest in the subject matter or materials discussed in this manuscript.

AUTHOR CONTRIBUTIONS

YD¹ reviewed the literature and wrote the manuscript; YD¹ and AH² made substantial contributions to the conception and design; DM¹ made substantial contributions to the acquisition of data; JS¹ and AH² were involved in drafting the manuscript; JS¹, DM¹, and AH¹ were involved in revising the manuscript critically for important intellectual content.

ETHICAL APPROVAL

None.

CONSENT

Written informed consent was obtained from the patients to publish this report in accordance with the journal’s patient consent policy.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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