






RESEARCH ARTICLE

Incidence and outcomes of vasa praevia in the United Kingdom [version 1; peer review: 2 approved, 1 approved with reservations, 1 not approved]

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Abstract

Background

Vasa praevia is an obstetric condition in which the fetal vessels run through the membrane over the internal cervical os, unprotected by the placenta or umbilical cord. It is associated with perinatal mortality if not diagnosed antenatally. We investigated the incidence and outcomes of vasa praevia in the UK.

Methods





We conducted a population-based descriptive study using the UK Obstetric Surveillance System (UKOSS). Cases were identified prospectively through monthly UKOSS submissions from all UK hospitals with obstetrician-led maternity units. All women diagnosed with vasa praevia who gave birth between 1st December 2014 and 30th November 2015 were included. The main outcome was incidence of vasa praevia with 95% confidence intervals, using 2015 maternities as the denominator.




Results

Fifty-one women met the case definition. The incidence of diagnosed

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vasa praevia was 6.64 per 100,000 maternities (95% CI 5.05-8.73). Of 198 units, 10 (5%) had a vasa praevia screening programme; one of these 10 units identified 25% of the antenatally diagnosed cases. Among women who had vasa praevia diagnosed or suspected antenatally (n=28, 55%), there were no perinatal deaths or hypoxic ischaemic encephalopathy (HIE). Twenty-four women with antenatal diagnosis were hospitalised at a median gestation of 32 weeks and caesarean section was scheduled at a median gestation of 36 weeks. When vasa praevia was diagnosed peripartum (n=23, 45%), the perinatal mortality rate was 37.5% and 47% of survivors developed HIE.

Conclusions

The incidence of diagnosed vasa praevia was lower than anticipated. There was high perinatal mortality and morbidity for cases not diagnosed antenatally. The incidence of antenatally identified cases was much higher in the few centres that actively screened for this condition, and the perinatal outcomes were better. However, this group were all delivered by caesarean section and may include women who would not have experienced any adverse perinatal outcome.

Plain Language Summary

Vasa praevia is a pregnancy complication in which the blood vessels that connect the mother and fetus run across the opening of the womb, without protection from the placenta or umbilical cord. During birth, the vessels can tear. This can result in rapid blood loss from the baby and in some cases, death of the baby. We investigated how common vasa praevia is in the UK, and how women with the condition and their babies fared.

The UK Obstetric Surveillance System (UKOSS) collects anonymous information from all maternity units in the UK about pregnant women who have certain medical conditions. UKOSS reporters provided information about all women with vasa praevia who gave birth between December 2014 and November 2015. We identified 51 women with vasa praevia, meaning vasa praevia was diagnosed less often in the UK than we had expected based on studies from other countries. Twenty-eight women were diagnosed during the antenatal period, while 23 were diagnosed during labour or after giving birth. Pregnant women in the UK are not screened for vasa praevia as standard, and some women may have had vasa praevia that was not diagnosed. A small number (5%) of maternity units in our study did offer screening for vasa praevia in their pregnant population. One of these units identified a quarter of all the women who had vasa praevia diagnosed during pregnancy.

Babies born to women whose vasa praevia was diagnosed during pregnancy had good outcomes. All of these women gave birth by

planned caesarean section, and they and their babies survived. Babies born to women whose vasa praevia was suspected or diagnosed during labour or after birth had worse outcomes. Around 40% were stillborn or died shortly after birth, and about half of those who survived had brain damage caused by lack of oxygen.

Keywords

Keywords: Vasa praevia, incidence, outcomes, perinatal mortality, velamentous cord insertion, pregnancy, surveillance, UK Obstetric Surveillance System

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Introduction

Vasa praevia is a rare obstetric complication which is defined as fetal vessels coursing through the membranes over the internal cervical os and below the fetal presenting part, unprotected by placental tissue or the umbilical cord¹. This can be secondary to a velamentous cord insertion (vasa praevia type 1) or to fetal vessels running between lobes of a placenta with one or more accessory lobes (vasa praevia type 2). Rupture of the vessels during labour can lead to rapid fetal exsanguination and fetal death.

Vasa praevia can be associated with high perinatal mortality if it is not diagnosed antenatally^{2,3}. Although antenatal screening is possible, a suspicion of vasa praevia usually leads to caesarean section before labour, avoiding the chance of fetal vessel rupture during birth. However, the rarity of the condition; the possibly high false positive rate of antenatal diagnosis; the potential harms of iatrogenic late preterm delivery, such as neurodevelopmental issues⁴; and the inability of antenatal diagnosis to predict which cases of vasa praevia will rupture and bleed during labour means that antenatal screening has the potential for greater harm than benefit. Consequently, routine screening for vasa praevia is not advised by Royal College of Obstetricians and Gynaecologists guidelines⁵ or the National Screening Committee (NSC)^{6,7}, although both organisations indicate a paucity of evidence on which to base a recommendation. Conversely, a recent international expert consensus statement supported routine screening because of the potential reduction in preventable perinatal mortality⁸.

A recent systematic review of 24 studies suggested a mean incidence of vasa praevia of 7.9 (95% CI 5.9–10.1) per 10,000 pregnancies⁹. The majority of the included studies were retrospective, single-centre investigations and ultrasound protocols for antenatal detection of vasa praevia varied between studies. Two included prospective studies were small (4 and 11 cases of vasa praevia) and each based in two institutions^{10,11}. Two large population-based studies were identified: a retrospective study of the California birth cohort from 2007 to 2012 found an incidence of 2 per 10,000 live singleton births¹², while a prospective study using the Australasian Maternity Outcomes Surveillance System (AMOSS) showed a similar incidence of 2.1 per 10,000 women giving birth¹.

Data from the UK are limited; a retrospective study of data from a prospective vasa praevia screening programme in a single UK fetal medicine unit estimated an incidence of 8 per 10,000 singleton pregnancies, in a study population of 26,830¹³, while a 5-year historical cohort study at a single UK hospital with a screening program estimated a similar incidence of 7.7 per 10,000 births¹⁴. However, no study has investigated the population incidence of vasa praevia in the UK prospectively or using nationwide data. We used the United Kingdom Obstetric Surveillance System (UKOSS) to investigate prospectively the incidence and outcomes of vasa praevia in the UK. We also

surveyed all UKOSS reporting centres about vasa praevia antenatal screening practices.

Methods

Patient and Public Involvement

Patients were not directly involved in the design of the study. Two members of the public were indirectly involved in the design of the study via representatives on the UKOSS Steering Committee, which reviews, comments on, and approves all studies to be run through UKOSS.

This is a population-based descriptive study using the UK Obstetric Surveillance System (UKOSS). UKOSS was established to study rare pregnancy disorders through routine monthly reporting from all UK maternity units. The UKOSS methodology has been previously described¹⁵. In summary, nominated reporting clinicians (midwives, obstetricians and/or obstetric anaesthetists) in each hospital were sent a card each month, which included a simple tick-box to indicate a case of vasa praevia (along with other conditions studied). When a case was reported, a data collection form was sent to the reporting clinician to collect details on demographics, pregnancy risk factors, ultrasound diagnosis, antenatal and intrapartum management, delivery and neonatal outcome. We asked about the following risk factors for vasa praevia: IVF conception, low lying placenta, marginal or velamentous cord insertion, and bilobed or succenturiate lobed placentation.

We used a robust case definition where each case was required to meet at least one clinical criterion and at least one postnatal confirmation criterion (Table 1). Cases were confirmed against the case definition. The woman's year of birth, hospital and estimated date of delivery were used to exclude duplicate cases.

We collected data for vasa praevia cases in births occurring between 1st December 2014 and 30th November 2015. To establish the existence of screening programmes for vasa praevia, we asked each reporting centre the following question: "Between the 1st of December 2014 and the 30th of November 2015 was there a formal screening programme for vasa praevia at your hospital/centre?"

Incidence with 95% confidence intervals was calculated using the number of maternities for 2015 as denominator, using published data from the Office for National Statistics (England and Wales)¹⁶, National Records of Scotland¹⁷ and the Northern Ireland Statistics and Research Agency¹⁸. For the purpose of the analyses, those cases diagnosed or suspected in the antenatal period were labelled as "antenatal". Those cases not suspected/diagnosed in the antenatal period, but identified either during labour/delivery or after birth we labelled as "peripartum".

We used chi-square test, Fisher exact test, t-test and Mann-Whitney U tests as appropriate for statistical comparisons. We

Table 1. Case definition.

Clinical criteria (at least one of)	Confirmation criteria (at least one of)
Suspected VP on antenatal ultrasound ≥ 18 weeks gestation, and confirmed on antenatal ultrasound ≥ 31 weeks gestation (if not delivered prior to 31 weeks)	Clinical examination of the placenta confirming intact or ruptured velamentous vessels. These may be a velamentous insertion of the umbilical cord or exposed fetal vessels between placental lobes
Palpation or visualisation of the fetal vessels during labour	Confirmation of VP on pathological examination of the placenta
Rupture of membranes with bleeding associated with fetal death/ exsanguination or severe neonatal anaemia	Torn umbilical cord or placenta (not able to provide placental examination)
Antenatal or intrapartum bleeding of fetal origin with pathological CTG and/or positive Apt test	
VP documented in medical records as reason for admission and caesarean section	

VP: vasa praevia; CTG: cardiotocography

used SPSS 22.0 (IBM Corp., Armonk, NY, USA) for statistical analyses.

Ethics

The UK Obstetric Surveillance System general methodology was approved by the London Multi-Centre Research Ethics Committee (04/ MRE02/45; 24 September 2004) and this study was approved by the Proportionate Review Sub-committee of the East Midlands-Derby NRES Committee (14/EM/1237; 10 November 2014). Consent was not required for the collection of anonymous routine data.

Results

Following exclusion of duplicates, 73 cases were reported to UKOSS. However, only 51 met the case definition (details of excluded cases are in [Figure 1](#)). Most excluded cases did not meet the placental confirmation criteria of our case definition: 10 cases had planned caesarean section for suspected vasa praevia but there was no documentation of the placenta being examined or sent to histopathology after birth, so there was no confirmation of vasa praevia; 7 cases did not have vasa praevia (2 had cord prolapse, 2 had placenta praevia, 3 others had suspected vasa praevia but no evidence of vasa praevia on postnatal examination of the placenta and membranes); and for 4 other cases vasa praevia was not confirmed on histopathology despite suspicious delivery events or outcomes.

The total number of maternities for 2015 was 768,161. Therefore, we calculated the incidence of vasa praevia in the UK as 6.64 per 100,000 maternities (95% CI 5.05–8.73). This equates to approximately 1 case for every 15,062 maternities.

Of the 51 cases included, 28 cases (55%) were antenatal (diagnosed or suspected in the antenatal period). The remaining 23 cases (45%) were peripartum (not suspected/diagnosed in the antenatal period). All but one of these 23 cases were associated with bleeding during labour or during induction of labour.

Demographic data and pregnancy characteristics are summarised in [Table 2](#). A low placenta or a succenturiate lobe were more likely to have been identified in the antenatally diagnosed cases. Otherwise, there were no differences between the two groups. It is notable that all cases had at least one risk factor for vasa praevia.

The clinical presentation and management are summarised in [Table 3](#). Most peripartum-diagnosed cases presented with bleeding and this bleeding was at membrane rupture for 13 (57%) of these cases. Of the 23 women diagnosed peripartum, 22 (96%) delivered by caesarean section, of which 83% were category 1 surgeries; 15 women (65%) had general anaesthesia. There was one vaginal birth of a stillborn baby in this group. Of the 23 peripartum-diagnosed cases, 20 (87%) were born after 37 weeks and all after 36 weeks.

Only 14% (n=4) of antenatally diagnosed cases were not admitted to hospital prior to delivery. The cervical length was measured in 10 (36%) of the antenatally diagnosed cases but it was used as a factor in the decision to admit for only 3 (11%) cases. Fetal fibronectin was measured in only one case and it was not a factor in the decision to admit. The median gestation at diagnosis was 29 weeks, with the earliest at 17 and the latest at 36 weeks. The earliest admission for antenatally diagnosed vasa praevia was at 21 weeks. This woman had 4 admissions for a total of 73 days. Only 3 other women with an antenatal diagnosis of vasa praevia were admitted to hospital prior to 30 weeks (two of them because of vaginal bleeding). The median gestation at admission was 32.6 weeks with the latest admission at 36.5 weeks. The median duration of admission was 6 days (range 1–73). Seventeen (61%) women with antenatal diagnosis stayed in hospital for more than 10 days. The 4 women who were not admitted had planned caesarean sections at 38–39 weeks.

All antenatally diagnosed cases were scheduled for a caesarean section, with the majority scheduled between 36 and

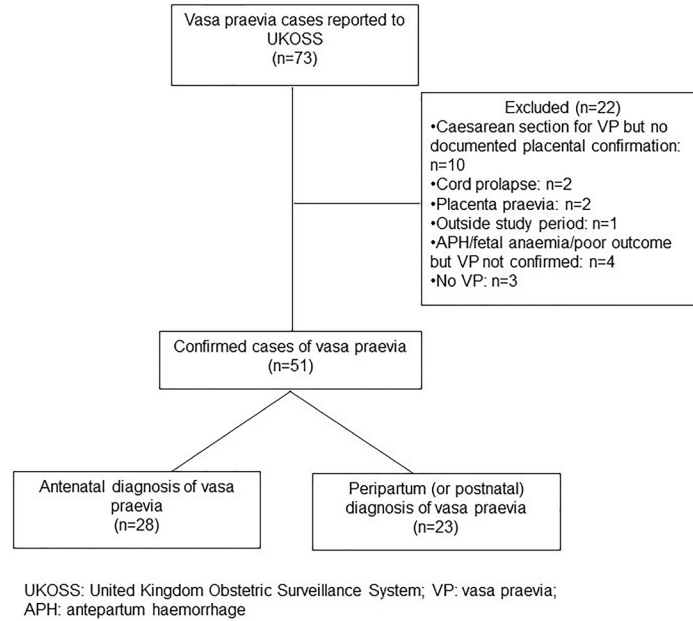


Figure 1. Reported and confirmed cases of vasa praevia during the study period.

Table 2. Maternal characteristics of vasa praevia cases.

Characteristics	Total (n=51)	Antenatal (n=28)	Peripartum (n=23)	p*
Maternal age (years)	32.7 (4.5)	33.3 (4.4)	31.9 (4.7)	0.29
Body Mass Index	25.2 (4.5)	24.4 (3.3)	26.0 (5.7)	0.22
Ethnic group				0.27
<i>Any white background</i>	41 (80)	20 (71)	21 (91)	
<i>Other</i>	10 (20)	8 (29)	2 (9)	
Nulliparous	25 (49)	16 (57)	9 (39)	0.34
Smoking during pregnancy	7 (14)	3 (11)	4 (17)	0.25
Risk factors for VP				
<i>Low lying placenta</i>	34 (67)	24 (86)	10 (43)	0.001
<i>Velamentous cord insertion</i>	25 (49)	15 (54)	10 (43)	0.26
<i>Bilobed placenta</i>	5 (10)	2 (7)	3 (13)	0.75
<i>Succenturiate lobe</i>	13 (25)	10 (36)	3 (13)	0.07
<i>Marginal cord insertion</i>	3 (6)	1 (4)	2 (9)	0.21
<i>IVF conception</i>	8 (16)	6 (21)	2 (9)	0.26
<i>At least one risk factor</i>	51 (100)	28 (100)	23 (100)	

Data are presented as mean (SD) or n (%).

* P-value for comparison between antenatal and peripartum diagnosis cases.

37 weeks. The earliest scheduled caesarean section was at 34 weeks (n=4) and the latest at 39 weeks (n=2). However, 9 (32%) of these women had a category 2 or 3 caesarean section earlier than planned. The earliest caesarean birth was at 31 weeks

(n=1) because of recurrent antepartum bleeding. Only one other woman was delivered before 34 weeks, because of threatened preterm labour. Of the prenatally diagnosed cases, 25 (89%) had regional anaesthesia.

Table 3. Clinical management and presentation.

	Antenatal diagnosis n=28	Peripartum diagnosis n=23	p
Number of scans after 17 weeks of gestation			0.03
1	0 (0)	4 (17)	
2	2 (7)	5 (22)	
3	5 (18)	10 (43)	
4	10 (36)	2 (9)	
5 or more	11 (39)	2 (9)	
Antenatal bleeding	0 (0)	10 (43)	<0.0001
Bleeding during labour	0 (0)	8 (35)	0.002
Bleeding at membrane rupture	0 (0)	13 (57)	<0.0001
Antenatal hospital admission	24 (86)	11 (48)	0.006
Cervical length measured	10 (36)	0 (0)	0.001
Cervical length used in decision to admit	3 (11)	0 (0)	0.006
Fetal fibronectin testing	1 (4)	0 (0)	
Fetal fibronectin used in decision to admit	0 (0)	0 (0)	
Antenatal steroids	25 (89)	2 (9)	<0.0001
CTG classification (where used)			<0.0001
Normal	7 (25)	4 (17)	
Suspicious	0 (0)	3 (13)	
Pathological	1 (4)	11 (48)	
Delivery by CS	28 (100)	22 (96)	0.45
Planned CS	28 (100)	3 (13)	<0.0001
Gestation of planned CS	36.7 (34.2–39.0)	37.7 (37.7–37.7) (1 case)	1.000
Gestation at delivery	36.4 (31.3–39.6)	38 (36.1 – 39.9)	<0.0001
Urgency category			<0.0001
Category 1	0 (0)	19 (83)	
Category 2	6 (21)	1 (4)	
Category 3	3 (11)	2 (9)	
Category 4	19 (68)	0 (0)	
Anaesthesia method			
Regional	25 (89)	7 (30)	<0.0001
General	3 (11)	15 (65)	<0.0001
PPH > 1000 ml	3 (11)	1 (4)	0.38
Placenta examined	28 (100)	21 (91)	0.28
Placenta to pathology	9 (32)	15 (65)	0.03

Data are presented as n (%) or median (range).

CTG: cardiotocography; CS, caesarean section; PPH, postpartum haemorrhage

The perinatal outcomes are summarised in Table 4. There was a multiple pregnancy in the peripartum diagnosis group, so the outcomes refer to 52 fetuses. There were 4 stillbirths and 5 neonatal deaths in the peripartum group, making the perinatal mortality rate 37.5% for this group. The overall perinatal mortality rate was 17%. Almost 50% (7 of 15) of the surviving babies in the peripartum group had hypoxic ischaemic encephalopathy (HIE). In the group with no antenatal diagnosis, 11 (46%) of babies had a blood transfusion for anaemia. There were no stillbirths, neonatal deaths or HIE cases in the antenatally diagnosed group but 2 babies in this group developed respiratory distress syndrome after delivery at 35–36 weeks.

Of the 198 reporting centres, 174 (88%) replied to our question: “Between the 1st of December 2014 and the 30th of November 2015 was there a formal screening programme for vasa praevia at your hospital/centre?”. Only 10 hospitals (6% of respondents) declared they had a formal screening programme for vasa praevia during the time of the study. Fifteen replies (9%) were “unknown”. One of the 10 hospitals with screening programmes reported 7 cases, all antenatally diagnosed (14% of all cases and 25% of all antenatally diagnosed cases). The other 9 hospitals did not report any cases. This difference in antenatally diagnosed cases between screening and non-screening hospitals was statistically significant (Table 5).

Discussion

This prospective population-based study showed a lower than anticipated incidence of vasa praevia in the UK: 6.64 per

100,000 maternities, or 1 case for every 15,062 maternities. There was high perinatal mortality and morbidity with peripartum diagnosis. The incidence of antenatally identified cases in the few centres that actively screened for this condition was much higher, and the perinatal outcomes were better. However, this group were all delivered by caesarean section and some infants had respiratory morbidity as a consequence of elective preterm delivery.

A significant strength of our study is its prospective population-based design, which does not rely on routinely coded data to ascertain cases. This is a national study, conducted at all obstetric units in the UK and therefore covering the whole of the pregnant population. UKOSS is a well-established and validated system for identifying cases of uncommon pregnancy complications and, because it covers all obstetric units, is not subject to the usual biases of single-centre studies. While we cannot exclude the possibility that there may have been a few cases that were diagnosed but not reported, we have no reason to suspect substantial under-ascertainment or bias in reporting. This study therefore represents a true snapshot of the current number of diagnosed cases in the UK pregnant population, with the caveat that only a small number of centres are actively screening for vasa praevia.

We used a robust case definition in order to accurately capture clinically diagnosed and confirmed cases. However, this strict definition was a potential weakness, as demonstrated by the 10 antenatally suspected cases who could not be included as there was no evidence of examination

Table 4. Perinatal outcomes.

	Antenatal diagnosis (n=28)	Peripartum diagnosis (n=24*)	p
Gender			0.58
<i>Male</i>	13 (46)	13 (54)	
<i>Female</i>	15 (54)	11 (46)	
Birthweight (g)	2685 (±488)	3126 (±378)	0.001
Stillbirth	0 (0)	4 (17)	0.04
Neonatal death	0 (0)	5 (21)	0.002
NICU admission	10 (36)	15 (62)	0.006
Anaemia	0 (0)	9 (37)	<0.0001
Blood transfusion	0 (0)	11 (46)	<0.0001
Hypoxic ischaemic encephalopathy	0 (0)	7 (29)	0.002
Seizures	0 (0)	6 (25)	0.007
Renal failure	0 (0)	4 (17)	0.04

Presented as mean (±SD) or n (%).

NICU: neonatal intensive care unit

* There was a multiple pregnancy in the peripartum diagnosis group, so the outcomes refer to 52 fetuses in total

Table 5. Cases diagnosed in centres with and without a formal antenatal screening program (n=51).

	Number of cases identified	Perinatal deaths	Denominator numbers of births	Incidence (95% CI) per 100,000 births*	Perinatal mortality (95% CI) per 100,000**
With screening programme	7	0	42,814	16.4 (6.6–33.7)	0 (0–8.6)
Without screening programme (or not known)	44	9	739,906	6.0 (4.3–8.0)	1.2 (0.6–2.3)

Birth data from MBRRACE-UK perinatal mortality report

* $p=0.021$ when comparing screened to unscreened (Fisher's exact test)

** $p=1.0$ when comparing screened to unscreened (Fisher's exact test)

CI: confidence interval

(histopathological or not) of the placenta after birth. Although we had multiple reporters in each hospital, we cannot be certain all cases were identified. In particular, the diagnosis may never have been considered as there is a possibility that ruptured vasa praevia mimics other conditions (e.g., abruption) and there is no “gold” standard to confirm the diagnosis after birth if the vessels are not ruptured.

There are guidelines about the diagnosis and management of vasa praevia in the UK, USA, Canada and Australia highlighting the importance of the condition. These were compared in a recent publication¹⁹. All guidelines agree that colour and pulsed Doppler transvaginal ultrasound should be used in mid-trimester to diagnose the condition, but third trimester confirmation is also needed. Universal screening is not recommended but rather a targeted screening for women with risk factors, such as low placenta, is advocated. Antenatal steroids are to be considered from 28–32 weeks and hospitalisation from 30–32 weeks. All four guidelines agree the optimal timing of birth is unknown, but they recommend birth by caesarean section at 34–37 weeks. A recent expert consensus statement recommended caesarean birth at 35–37 weeks, but advocated second-trimester screening as routine for all pregnancies, via transabdominal ultrasound with colour Doppler sweep over the cervix, followed by third-trimester confirmation of the diagnosis by transvaginal ultrasound⁸.

Our study demonstrates that vasa praevia diagnosis in the UK is less common than anticipated, with a lower incidence of vasa praevia than found in previous studies^{1,9,12}. Even if the 10 planned caesarean sections with no postnatal confirmation were included, the estimated incidence would still be relatively low at 7.94 per 100,000 maternities (1 case for every 12,593 maternities). Although our strict case definition may be partially responsible, the AMOSS study in Australia demonstrated about 2–3 times higher incidence (21 per 100,000) using an almost identical case definition. However, in the Australian study, 92% of cases were identified antenatally with only 5 cases being identified peripartum. Peripartum cases might be considered to represent the true incidence of ruptured vasa praevia; the incidence of peripartum vasa praevia in Australia was 1.7 per 100,000, and in the

UK it was 3 per 100,000. The differing thresholds and screening protocols for detecting vasa praevia antenatally are likely to explain these apparent differences in the overall incidence between the two countries.

Other possible reasons include cases not being reported or not recognised during the study period; women with undiagnosed vasa praevia having pre-labour caesarean section for other indications (especially low lying placenta); and some cases with poor outcome could have been attributed to other causes, such as abruption, or ruptured fetal vessels on placental histopathology being attributed to “snapped” cord during continuous cord traction at delivery, which is more likely to occur with velamentous cord insertion.

Our study found very different outcomes in those cases that were identified antenatally compared with those diagnosed intrapartum or postnatally. In cases not diagnosed antenatally there was an almost 40% perinatal mortality. This high perinatal mortality is remarkably similar to that observed in a retrospective study (44%)² and in the prospective AMOSS study (40%)¹ and confirms the high fatality rate of vasa praevia when it is not suspected or diagnosed before labour. Our study also found that almost half of the survivors in cases with no antenatal diagnosis had hypoxic ischaemic encephalopathy, although the grade and consequences of this are unknown; in contrast, none of the infants in cases with antenatal diagnosis had hypoxic ischaemic encephalopathy. This is in keeping with the findings of a recent systematic review, which found that 58% of surviving neonates in cases of vasa praevia without antenatal diagnosis displayed hypoxic morbidity, compared with only 2.7% in cases with antenatal diagnosis³.

Most previous studies²⁰ demonstrated the presence of risk factors in most vasa praevia cases; in our study all cases had at least one risk factor. This might suggest that targeted screening for cases with risk factors, particularly low placenta and velamentous cord insertion, might be useful as one or both of these were present in almost half of the cases in our study.

Ten maternity units declared they had a formal screening programme for vasa praevia. Of these, only one centre reported

any cases of antenatally detected vasa praevia during the study period. Table 5 illustrates that the number of reported cases of vasa praevia was substantially higher if there was antenatal screening. Large, well-designed prospective screening studies may elucidate this observation further; our study was not designed to evaluate screening efficiency or accuracy. A historical cohort study of a screening program in a single UK institution reported 100% sensitivity and 99.78% specificity, but a perinatal mortality of 5% (one death in 19 confirmed cases of vasa praevia)¹⁴.

Evaluation of accuracy of screening methods for vasa praevia is difficult because of the absence of a diagnostic “gold standard”. Once the placenta is delivered, velamentous cord insertion or bilobed placenta can be confirmed but it is impossible to know what the proximity of the vasa praevia to the cervix was. Inspection during the caesarean section is often difficult because of bleeding from the uterine incision and the placental bed. In addition, there is no clear definition of vasa praevia as there is no evidence about a “safe” distance from the internal os. A distance of 2 cm between the fetal vessels and the internal os has been proposed^{21,22} but it is not based on robust evidence. It is likely that many clinicians would find it difficult to recommend expectant management and normal birth to a woman with fetal vessels at e.g. 2.3 cm from the cervix. Indeed, a recent expert consensus process failed to reach agreement on the fetal vessel-internal os distance that should be used to define vasa praevia, but concluded that it should not be limited to 2 cm⁸, and a recently registered clinical trial of fetoscopic laser photocoagulation in management of vasa praevia (<https://clinicaltrials.gov/study/NCT06290232>) will use a 5-cm threshold for diagnosis. A UK single-institution study of a two-stage screening strategy for vasa praevia used a diagnostic threshold of 5 cm and estimated an incidence of 8 per 10,000 singleton pregnancies¹³. If reporting centres in our study were using more restrictive criteria, this may go some way to explaining the much lower incidence that we observed.

The Royal College of Obstetricians and Gynaecologists⁵ recommends consideration of prophylactic hospitalisation for confirmed vasa praevia after 30–32 weeks. Our study showed a wide variation in practice with most women with an antenatal diagnosis of vasa praevia being admitted after 30 weeks, at a median gestation of 32–33 weeks. Although most women spent up to 18 days in hospital in the antenatal period, there were 2 women who were admitted for over 2 months. The 4 women who did not have antenatal hospital admission had later planned caesarean sections at 38–39 weeks, suggesting the absence of any episodes of antepartum bleeding, no risk factors for early labour or even perhaps maternal preference.

Our data showed that most caesarean sections for the antenatally diagnosed cases were scheduled for 36–37 weeks and some up to 39 weeks. In about one third of these cases the caesarean section had to be brought forward, usually because of episodes of bleeding or threatened preterm labour. Only 2 caesarean sections (7%) were performed before 34

weeks. Within the antenatally diagnosed group there were only 2 cases of respiratory distress syndrome but 10 (36%) babies were admitted to a neonatal unit. Given the recently recognised additional risks of late preterm birth^{4,23}, it would seem sensible to aim for delivery at 36–37 weeks and perform earlier caesarean sections for cases with episodes of vaginal bleeding or other risk factors. Clinicians can also consider using cervical length and/or fetal fibronectin or other cervicovaginal biochemical swab tests to stratify further the risk of preterm labour before 35 weeks of gestation although there is no current evidence to support this approach²⁴. Of course, maternal anxiety cannot be underestimated in these circumstances²⁵ and can be a significant factor in birth timing.

Conclusion

This prospective national study showed a lower than anticipated incidence of vasa praevia, and a very low population incidence of poor perinatal outcome after vasa praevia. However, peripartum diagnosis was associated with an almost 40% perinatal mortality and about 50% risk of HIE in the surviving neonates. Antenatal diagnosis led to planned caesarean section for the majority of infants at 36–37 weeks with no observed deaths or cases of HIE, but some infants had respiratory morbidity. Our study could not address screening efficacy or the optimal screening method, but showed that a screening programme was associated with an increased number of vasa praevia diagnoses and no perinatal deaths, although the difference on the latter metric between maternity units with and without a screening program did not reach statistical significance.

Data availability

Underlying data

Data cannot be shared because of confidentiality issues and potential identifiability of sensitive data as identified in the Research Ethics Committee approval. Requests to access the data can be made by contacting the National Perinatal Epidemiology Unit data access committee via general@npeu.ox.ac.uk. The estimated response time for requests is 4 weeks. Data sharing outside the UK or the European Union may require consultation with the UK Health Research Authority. For more information, please refer to the National Perinatal Epidemiology Unit Data Sharing Policy available at:

https://www.npeu.ox.ac.uk/assets/downloads/npeu/policies/Data_Sharing_Policy.pdf

Acknowledgements

The authors would like to thank the UK Obstetric Surveillance System (UKOSS) reporting clinicians who notified cases and completed the data-collection forms. They would also like to thank the UKOSS staff who enable these studies to be completed.

Preliminary study results were presented at the British Maternal and Fetal Medicine Society meeting in Amsterdam, March 2017.

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Cristina Trilla

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Attilakos and co-authors present a comprehensive study on the incidence of vasa previa in the UK. From their results, it is clear that a prenatal diagnosis is critical for a good neonatal outcome. The authors used a prospective, population-based study design using the UK Obstetric Surveillance System (UKOSS), which should ensure a correct national representation. However, I am concerned by the very low incidence of vasa previa the authors report and by the potential impact this may have on local policies regarding screening and management of the condition. This is why I would recommend a more cautious discussion on their findings.

My main concerns are presented below:

1. Methods: the authors describe a screening program for vasa previa in some of the institutions involved in this survey. Please, provide more accurate information on these screening programs (universal? Risk-based?), as this could significantly affect prenatal diagnosis.
2. The definition criteria and confirmation criteria for vasa previa was very strict. Sometimes vasa previa is difficult to diagnose post-partum, even with a careful examination of the placenta and the cord. This could explain the unexpected low rate of vasa previa in the study. The authors have included this as a limitation of the study, but I would ask the authors to elaborate more regarding the added value of this research considering this limitation. I understand that the aim of the study was to provide accurate information on vasa previa incidence in the UK, but these results are not concordant with previous research on the topic in other countries, and there is no clear explanation for this very low incidence in the UK. In any case, vasa previa incidence should be increasing, mainly due to the increase of ART among other risk factors. This should be mentioned and discussed more clearly in the manuscript, as such data may impact management policies for the condition if the incidence is really this low.
3. Many cases were excluded (22 out of 73, which represents 30% of the suspected cases). I do not clearly understand the exclusion criteria for these, and I would suggest revising this, as I

- believe it has greatly affected the final numbers. Examination of the placenta was apparently a requirement for diagnosis, but how often is this really performed?
4. Please, provide accurate definition for urgency categories for CS in methods.
 5. If I understand correctly, 2015 maternity centers participated in the study. As such, many maternity centers did not report any cases of vasa previa. Did the number of deliveries per maternity center correlate with the number of vasa previa diagnosed (either antenatally or postnatally)? Please, provide more data regarding the number the deliveries per center and the number of cases diagnosed.
 6. I believe one of the main conclusions should be that a more clear definition of vasa previa and its diagnosis is needed, rather than that its incidence in the UK is lower than in other countries.

My minor concerns are presented below:

1. Introduction: the authors are only referring to vasa previa type 1 and 2, but a third type has been described. This should be mentioned in the introduction
2. Underreporting of vasa previa: They state there is no reason to believe there were any underreported cases, but this is impossible to ascertain and should be listed as a limitation for the study.
3. Minor spelling error in the Methods section of the abstract: "form" should be spelled "from". I did not find any other spelling concerns.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Partly

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Prenatal diagnosis, placenta previa and vasa previa. Pregnancy loss.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 30 September 2024

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Paolo Ivo Cavoretto 

Vita-Salute San Raffaele University, Milan, Italy

This is a very good study from a known research group in the UK, presenting a compelling study topic and aim, adequate rationale and methodology and acceptable conclusions. I have few remarks and recommendations to improve this interesting paper:

1. Type III vasa previa was not considered enough by the authors and this is an important reticence to be corrected. Type III vasa previa is a rare form of VP, not necessarily associated with other placental or vascular anomalies, in which aberrant vessels run from the placenta to the amniotic membranes, near the internal cervical os, before returning to the placenta. It was object of a recent systematic review published in UOG that should be considered by the authors (ref 1).

Were type III VP accounted for? Were they excluded from the study? This is very interesting to be added for readers. A wide dissemination on knowledge around type III vasa previa is required as this is not yet a well-known topic.

2. The authors state that in 10 cases "no documentation of the placenta being examined or sent to histopathology after birth, so there was no confirmation of vasa praevia". However I am afraid that anatomopatological diagnosis simply cannot rule out or rule in vasa previa, as the relationship with the uterine structures is only available as an intraoperative surgical macroscopic diagnosis. This diagnosis can be documented with pictures and videos or with clinical diagnosis during delivery. Anatomopatologists can only diagnose velamentous cord insertion, bilobate/succenturiate or type III extraplacental aberrant vessels as well as placental structural or morphological aberrations associated (but not pathognomonic) to vasa previa. This comment is not against the authors findings but instead it may be useful to reinforce their message (there is an extent of wrong prenatal diagnosis but this risk in expert hands is very low).

3. Methods. Among risk factors for VP multiple pregnancies should be included.

4. The issue of cervical screening for cervical length, to be used to screen also for vasa previa screening may be considered and mentioned with pros and cons.
I congratulate with the authors for this brilliant work.

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Is the work clearly and accurately presented and does it cite the current literature?

Partly

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: I am expert in maternal fetal medicine and obstetrics and I did previous research on the topic. I feel comfortable in providing a review on the paper. in object.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

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Neha Agarwal

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Attilakos et al are presenting a population based prospective study of vasa previa in UK to demonstrate registered incidence of vasa previa and its outcomes. The study confirms the well-known knowledge of antenatal diagnosis is critical in reducing perinatal mortality and morbidity of vasa previa. It also reflects upon the effect of lack of screening policy for vasa previa and its impact on the perinatal outcomes.

Below are the major concerns of the article:

1. Limited Scope of Screening Analysis: While the article mentions that only 5% of obstetric units in the UK had screening programs for vasa previa, it does not provide sufficient detail about the methods or criteria used for these screenings. Although there are significant differences in outcomes between hospitals with and without screening programs, the study lacks a detailed exploration of the specific screening strategies that could help reduce perinatal mortality and morbidity. A more in-depth investigation into the screening protocols used by the 10 units with programs would be beneficial. This additional detail could help inform future recommendations for the implementation of nationwide screening programs.
2. Exclusion of cases in antepartum vs postpartum: Need this distinction made to help improve the clarity of case selection. Of those 22 excluded cases are from antenatal diagnosis group, due to lack of sufficient details, it would help to make a better determination of the incidence.
3. Underestimation of the vasa previa. As authors acknowledge in the weakness of the study, there is high probability of underestimation of vasa previa due to nature of reporting in this large-scale study. There is lack of rigorous methods to determine the true incidence of vasa previa. Consider avoiding "incidence" in the title, objective, and use "estimates".
4. Confirmation of vasa previa: Lack of details in the diagnosis of vasa previa including exposed fetal vessels on clinical examination. How often is clinical examination performed of the placenta? Is this universal? Are there standard protocols that require post-delivery placental evaluation to ensure optimal case capture?
5. Confirmation of pathologic examination of the placenta" How many in this cohort? How can you confirm that without information on placental orientation within the uterine environment?
6. It is recommended that for the authors to estimates of effect of universal screening for vasa previa similar to 6% of hospitals on the obstetrical outcomes- number of c-sections to prevent one perinatal death and hypoxic ischemic encephalopathy. Does this justify the national guidelines for universal screening for vasa previa.

Below are the minor concerns of the article:

1. In the Methods section of the abstract, there is a spelling error in line 3. The word "form" should be corrected to "from."
2. 48% of the cases of peripartum identification had an antepartum admission. What were the indications for admission? Was this preterm labor? Vaginal bleeding? Unrelated medical indications (e.g., preeclampsia)?
3. Irrespective of universal screening recommendation, are there recommendations for screening among those with risk factors considering 43% of the cases with peripartum identification had low-lying placenta and/or velamentous cord insertion and 100% had at least 1 risk factor.
4. In the 7th paragraph of the Results section, why term "no antenatal diagnosis" rather than "peripartum" as is otherwise used throughout the article?

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

No

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Partly

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Vasa previa, placenta accreta and fetal surgery

We confirm that we have read this submission and believe that we have an appropriate level of expertise to state that we do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Reviewer Report 18 September 2024

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Antonios Siargkas 

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"Incidence and Outcomes of Vasa Praevia in the United Kingdom" by Attilakos et al. is an excellent and comprehensive study that sheds light on the rare but critical obstetric condition of vasa praevia. The authors have executed a robust, prospective, population-based study using the UK Obstetric Surveillance System (UKOSS), ensuring a sound methodology and national representation. They provided a clear definition of vasa praevia and meticulously described the case reporting process by nominated clinicians across all UK hospitals with obstetrician-led maternity units. This approach ensured that specific risk factors—such as IVF conception, low-lying placenta, marginal or velamentous cord insertion, and bilobed or succenturiate lobed placentation—were thoroughly reported and analyzed.

The statistical analysis was appropriately conducted and clearly presented, offering valuable insights into this rare pathological entity. The results were particularly interesting, revealing an incidence of diagnosed vasa praevia at 6.64 per 100,000 maternities, which is lower than

anticipated. This equates to approximately one case per 15,062 maternities. The study highlighted significant differences in outcomes between antenatally diagnosed cases and those diagnosed peripartum.

In the peripartum diagnosis group, there were four stillbirths and five neonatal deaths, resulting in a perinatal mortality rate of 37.5% for this group. The overall perinatal mortality rate was 17%. Moreover, almost 50% (seven out of 15) of the surviving babies in this group developed hypoxic ischaemic encephalopathy (HIE), and 46% required blood transfusions due to anaemia. In stark contrast, the antenatal diagnosis group reported no severe adverse outcomes, aside from a 36% admission rate to the neonatal intensive care unit (NICU), likely due to preterm delivery from planned caesarean sections.

The discussion was highly informative and thoroughly covered the key points of the study. One of the main findings was the high perinatal mortality and morbidity associated with peripartum diagnosis of vasa praevia. The authors used a robust case definition to accurately capture clinically diagnosed and confirmed cases. However, they acknowledged that this strict definition might have been a potential weakness, as it excluded ten antenatally suspected cases without postnatal confirmation due to the lack of examination of the placenta after birth. This exclusion could have led to an underestimation of the true incidence, but the authors transparently discussed this limitation and provided relevant data.

The study also reviewed relevant guidelines, noting that routine screening for vasa praevia is not currently advised. However, given that all cases in their study had at least one risk factor, the authors proposed that targeted screening for pregnancies with specific risk factors—particularly low-lying placenta and velamentous cord insertion—might be beneficial. This suggestion is compelling, as one or both of these risk factors were present in almost half of the cases. Such targeted screening could improve early detection without the drawbacks associated with universal screening.

Interestingly, only ten hospitals (6% of respondents) had a formal screening programme for vasa praevia during the study period. One of these hospitals identified 25% of the antenatally diagnosed cases, indicating that formal screening programmes in high-risk populations can significantly enhance detection rates and improve outcomes.

In conclusion, this study offers valuable insights into the incidence and outcomes of vasa praevia in the UK, highlighting the critical importance of antenatal diagnosis in improving perinatal outcomes. The authors have provided a well-structured and detailed analysis, with sound methodology and comprehensive reporting. Their proposal for targeted screening based on specific risk factors is particularly noteworthy and could inform future guidelines and clinical practice. Overall, this research represents a significant contribution to obstetric literature and has important implications for the management of pregnancies at risk of vasa praevia.

Upon carefully reading the article, I found no mistakes or issues that require correction.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Maternal Fetal Medicine, placenta, umbilical cord, high risk pregnancies

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.
