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The case for screening for vasa previa: time to implement a life-saving strategy

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Accepted Article

For the past half-century, obstetric ultrasound has played a pivotal role in improving perinatal outcomes. In middle- and high-income countries, many preventable complications are now routinely screened for during pregnancy, enabling appropriate interventions to ensure the best outcomes. Vasa previa (VP) remains a condition that is not routinely screened for, even though it has been possible to diagnose VP prenatally with ultrasound imaging for 35 years, and its diagnosis before birth is highly effective in preventing the corresponding perinatal morbidity and mortality.¹⁻

¹⁰In this opinion, we discuss the controversies and possible solutions for screening for VP.

VP and obstetric outcomes

VP refers to unprotected fetal vessels (arterial or venous) crossing the membranes overlying the cervix.¹⁻⁷ The reported prevalence of vasa previa in the international literature ranges between 1 in 365 to 1 in 5000 pregnancies.^{1,3,5,7,8} The condition is probably under-reported as only cases associated with perinatal complications tend to be recorded. When undiagnosed prenatally, the vessel(s) often rupture along with the membranes, leading to rapid fetal exsanguination and death.^{3,5,7} In 2004, a large study found a perinatal mortality rate of 56% in cases not diagnosed prenatally.¹⁰ Survivors had low Apgar scores, with median scores of 1 and 4 at 1 and 5 minutes, respectively.¹⁰ Conversely, survival was 97% in prenatally diagnosed cases.¹⁰ A recent systematic review and meta-analysis found that the risk of hypoxic morbidity is increased 50-fold in undiagnosed VP compared to those cases not diagnosed prenatally.¹¹ When VP is diagnosed prenatally, perinatal survival is almost 100%, with normal long-term outcomes.^{4,10,11}

Ultrasound screening for VP

Until the advent of ultrasound imaging, VP was essentially a post-delivery postmortem diagnosis.²⁻

⁴ Gianopoulos *et al.*¹² in 1987 first reported the prenatal diagnosis of a case of VP with ultrasound.

Subsequently, large cohort studies have demonstrated a very high sensitivity and specificity of ultrasound in diagnosing VP.¹³⁻²⁴ It was estimated in 2013 that around 150 fetuses had died at birth

that year due to VP.²⁵ However, the United Kingdom Screening Committee (UKSC) recommends against screening for VP, giving the following reasons:²⁶

1. There is not enough information about the number of babies affected by VP in the UK.
2. VP can be found by ultrasound but there is insufficient knowledge about the accuracy of the test.
3. A Cesarean section (CS) to deliver the baby early would usually be recommended to prevent the effects of VP. However, this can bring its own complications including iatrogenic premature delivery.
4. Some women may be advised to have an unnecessary and early CS.
5. Other women may be falsely reassured but have a problem during delivery anyway.
6. There is insufficient information on the case definition, natural history and epidemiology of VP. There is also uncertainty on the accuracy and practical application of the test and there is no agreed management pathway for those with confirmed VP and for those with some risk factors in the absence of VP.

We believe that the reasoning behind these points is fundamentally flawed for the following reasons:

1. The incidence of VP is underestimated

Epidemiologic data from different countries indicate that the prevalence of VP could be as high as 1:1,200.^{8,9,13-17,21} A UK prospective study of 26,830 pregnancies found 21 cases of VP confirmed at birth, corresponding to a rate of 1 in 1,278 pregnancies.²¹ These authors estimated that if no cases of VP had been diagnosed antenatally, 50% would have resulted in stillbirth and that antenatal screening would prevent around 10% of stillbirths from all causes.²¹ There are around 700,000 births/per year in the UK²⁷, and thus with a rate of 1 VP/1,278 pregnancies,²¹ approximately 550 pregnancies present with VP annually. As the perinatal mortality of undiagnosed VP is around 56%,¹⁰ there are over 300 preventable perinatal deaths from VP annually in the UK.

Significant health resources are dedicated to prenatal screening programs with the goals of detecting severe abnormalities, preventing stillbirths and improving perinatal outcomes. Many conditions routinely screened for are much rarer than VP. For example, spina bifida, anencephaly, omphalocele and encephalocele occur in approximately 1 in 1,724, 2,008, 3,846 and 7,299 births, respectively,^{28,29} and the corresponding screening value for these conditions has never been challenged. Furthermore, in most of these conditions prenatal diagnosis makes little impact on survival rates and long-term handicap.

The UK Obstetric Surveillance System (UKOSS) collects population data from participating maternities about specific complications of pregnancy using anonymous questionnaires. UKOSS conducted a 12-month (December 2014–November 2015) study on the incidence of VP in the UK³⁰ which, to our knowledge, was never published nor were results available online as of 16th June 2022. The use of questionnaires is known to be associated with selection and recall bias. The

diagnosis of VP is usually made based on examination of the placenta after birth. A velamentous umbilical cord is more likely to detach from the placenta at delivery, making pathological confirmation potentially difficult, and not all placentas are sent for histopathology examination, thus underestimating the prevalence of VP.

2. Ultrasound imaging is efficient in screening and diagnosing VP

A 2015 systematic review by Ruiters *et al.* showed that transvaginal sonography (TVS) combined with color Doppler imaging (CDI) had a sensitivity of 100% with a specificity of 99.0–99.8% in identifying VP when performed by trained operators at 18-26 weeks.²⁴ Several new prospective studies have reported detection rates of $\geq 90\%$ with low false positive rates (Table 1)^{13-17,19-23} confirming the high performance of ultrasound imaging in screening for and diagnosing VP antenatally.

There are three main methods of screening for VP with ultrasound: routine examination for placental cord insertion (Figure 1), CDI sweep of the region over the cervix (Figure 2), and TVS/CDI (Figure 3). Routine identification of the placental cord insertion (Figure 1) during the mid-gestation fetal anatomy ultrasound examination is easy to perform.¹⁸ It adds no significant cost or time, nor does it require additional personnel or equipment.^{18,31,32} The Royal College of Obstetricians and Gynaecologists (RCOG) green-top guideline 27B states that “The performance of ultrasound in diagnosing VP at the time of the routine fetal anomaly scan has a high diagnostic accuracy with a low false-positive rate”.³³ The argument that “Some women may be reassured by false test results and may still have a problem during delivery” is flawed. Several studies have shown that false negatives are highly unlikely when TVS/CDI is used in the diagnosis of VP.

Furthermore, the rate is so low that it does not justify the argument of not screening for fear that rare cases may be missed.

3. Cesarean delivery is the only safe option for the management of VP

While there remain some controversies regarding the antenatal management of VP such as the need for prenatal hospitalization, administration of steroids, timing of delivery, and strategies for monitoring,^{1,33-42} there is widespread consensus that women diagnosed with VP should be delivered by CS prior to the onset of labor or of rupture of the membranes.^{1-7, 10-23} There are data dating back 100 years showing that undiagnosed VP at the time of birth is associated with an extremely high perinatal mortality and morbidity.^{3,4,43} Therefore, VP is one of the few conditions for which the benefit of CS clearly outweighs the risk even in the case of iatrogenic premature delivery. As 10-40% of cases of VP diagnosed at 20 weeks will resolve before 30-32 weeks, the diagnosis should be confirmed by TVS/CDI performed by experts at about 32 weeks.^{13,17} Within this context, it is highly unlikely that an unnecessary early CS will be performed.

The largest cohort study published so far comparing outcomes between cases that were and were not diagnosed prenatally found that fetuses diagnosed with VP prenatally had a 97% survival at a mean gestational age at delivery of 34.9 (± 2.5) weeks of gestation.¹⁰ A recent meta-analysis showed that the best perinatal outcomes were achieved when asymptomatic women with VP are delivered by CS at 36 weeks.^{41,42} Given this overwhelming evidence, it is surely not justifiable to recommend against screening, since there is a clear pathway to prevent avoidable perinatal mortality.

Current national guidelines

US consensus guidelines for imaging in pregnancy recommend routinely identification of the placental cord insertion “where feasible” and TVS/CDI in cases of low-lying placenta/placenta previa.⁴⁴ The Society of Obstetricians and Gynaecologists of Canada (SOGC) recommends to consider TVS for all women at high risk of VP.³⁴ The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) guidelines recommend against routine universal screening for VP, but do recommend TVS/CDI screening in patients with risk factors i.e. placenta previa, second trimester low-lying placentas, bilobed placentas or those with succenturiate lobes, multifetal gestations, and pregnancies resulting from in vitro fertilization.³⁷ Only the UK RCOG recommends against screening for VP in any circumstance.³³

Routine screening versus targeted screening for VP

Routine identification of the placental cord insertion at the mid-trimester transabdominal anomaly scan⁴⁴ as is recommended by the US guidelines, together with a CDI sweep of the region over the cervix is a highly effective strategic approach for universal VP screening.^{14,18} Targeted screening is better than no screening at all.^{38,45-47} Around 85% of cases of VP have one or more identifiable risk factors.⁴⁵⁻⁴⁷ Screening for VP using TVS/CDI at about 32 weeks in patients with second-trimester low-lying placentas/placenta previa would detect approximately 2/3 of cases of VP with a very low false positive rate. Screening with CDI can also be performed in patients who routinely have TVS in pregnancy such as those with risk factors for preterm delivery and those with multifetal pregnancies. A cost-effectiveness analysis comparing targeted and universal screening strategies found that “the use of colour Doppler at all transabdominal ultrasound examinations of singleton pregnancies and targeted use of TVS for IVF pregnancies or when the placenta has been

found to be associated with one or more risk factors is cost-effective.”⁴⁷ A rapid review approach used by the United Kingdom National Screening Committee stated “Most cases of VP are associated with VCI; however, only a minority of pregnancies affected by VCI are also affected by VP, and detection of VCI as part of a VP screening program would represent a departure from the current approach in UK practice with the potential for over-detection”.⁴⁸ We feel this view misses the point. In most screening programs, most patients are unaffected. For instance, most women with abnormal Pap smears do not develop cervical cancer. This same argument would not be used for cervical cancer screening.

Conclusions

Ultrasound resources and personnel differ from country to country and region to region. Some screening strategies discussed here may not be universally achievable and need to be adapted to local resources. However, given the high mortality when VP is undiagnosed prenatally, the high accuracy of ultrasound screening for VP, and the almost universal survival when prenatally diagnosed cases are delivered by Cesarean, there is a strong case for introducing widespread VP screening. A qualitative survey of women who had VP diagnosed at delivery demonstrated that women want antenatal diagnosis with ultrasound, and felt it was a failure of the medical system when VP was not diagnosed prenatally.⁴⁹ A survey of obstetricians in Australia found that most of those who responded supported targeted screening for VP.⁵⁰ Screening for VP reduces adverse perinatal outcomes including stillbirth and neonatal death, as well as long-term neurodevelopmental impairment from VP and the corresponding devastating psychosocial trauma for parents. There are no other conditions in which prenatal diagnosis makes such a profound difference between survival and death. It is time to implement widespread screening for VP.

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Figure legends

Figure 1. Transabdominal ultrasound showing a normal placental cord insertion.

Figure 2. Transabdominal ultrasound with color Doppler sweep of lower uterine segment showing a velamentous cord insertion with exposed vessels running over the cervix (cx) into the posterior placenta (pl). Bladder (bl).

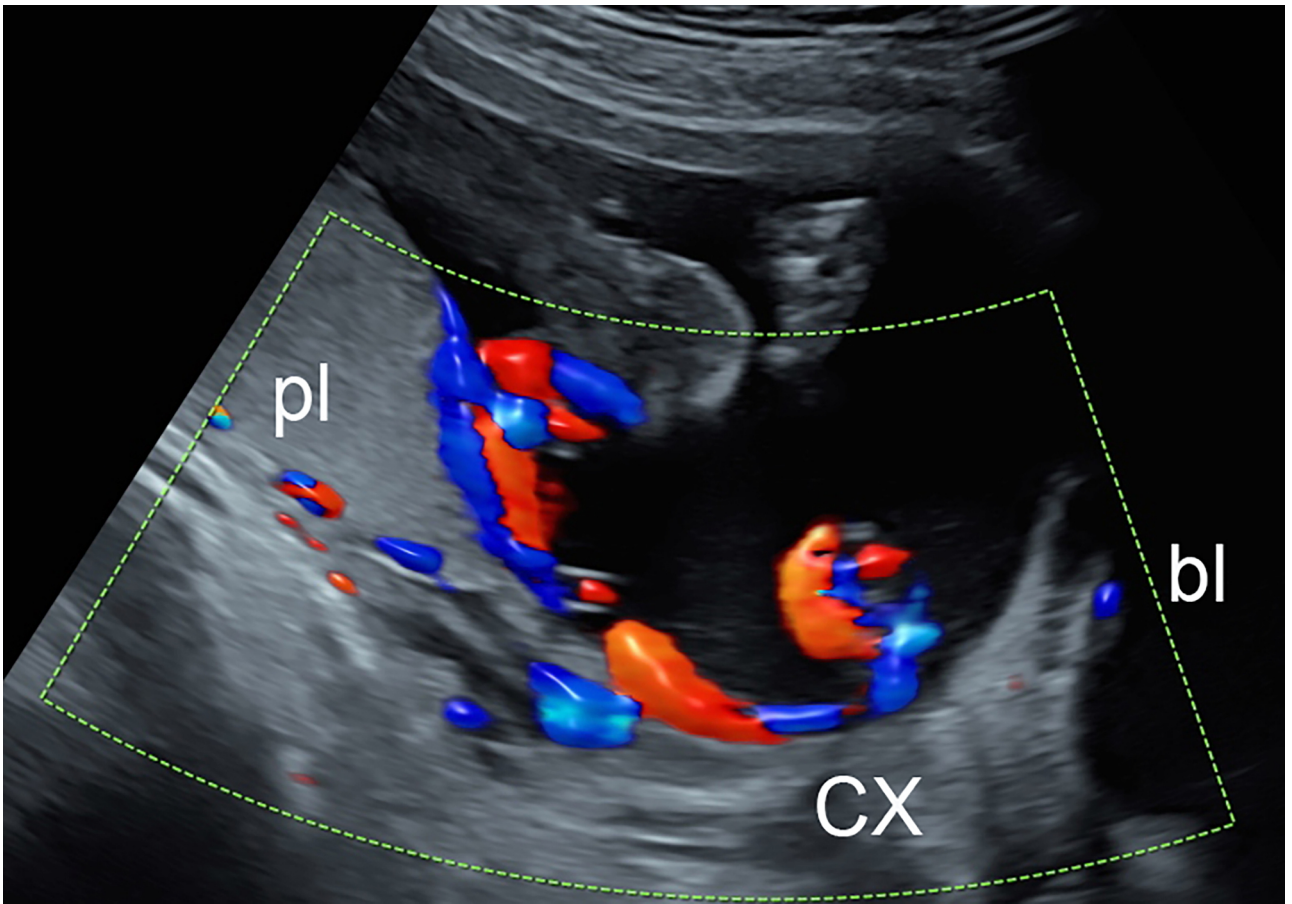
Figure 3. (a) Grayscale transvaginal ultrasound of the same patient in Figure 2, showing the cord inserting into the membranes over the cervix (cx), from where unprotected vessels run into the posterior placenta (pl) confirming vasa previa. (b) TVS/CDI of same patient.

Table 1. Studies with prospective screening protocols for VP since 2016.

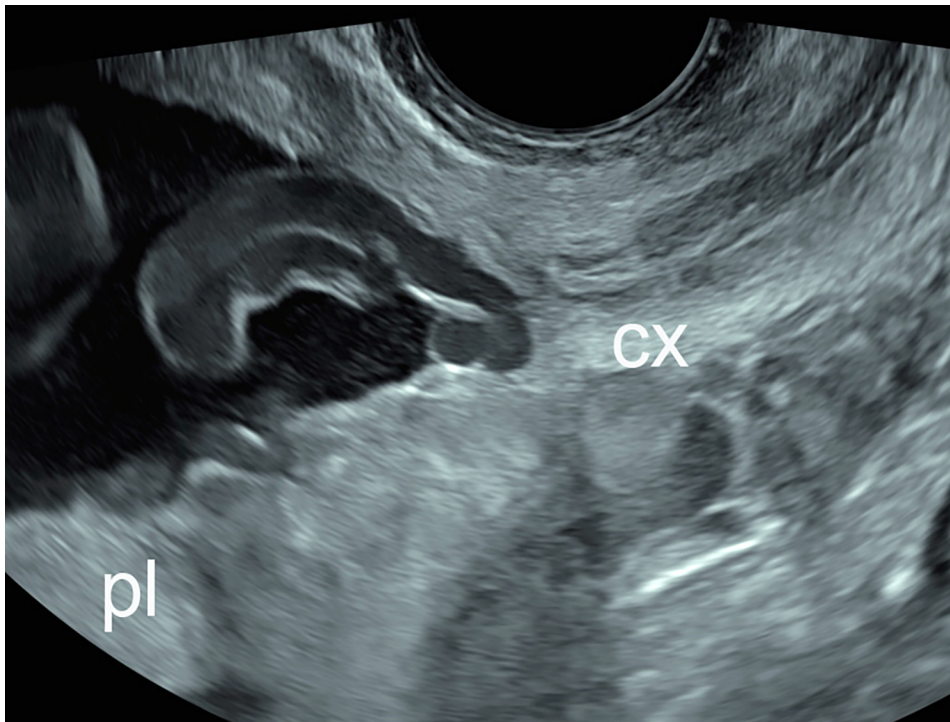
Author	Year	Number of pregnancies	Number of VP at delivery	Incidence at delivery	False positives	False negatives	Survival (%)	Percent detected
Melcer ¹⁹	2018	68,750	33	2,083	Not stated	3	96.9	87.9
Kulkarni ¹⁴	2018	56,000	33	1:1600	1	0	100	100
Catanzarite ¹⁵	2016	100,481	96	1:1272	4	0	98.95	100
Nohuz ²⁰	2017	18152	8	1:2269	0	0	100	100
Khlar ¹³	2019	37236	61	1:610	0	0	98.3	100
Zhang ²¹	2019	26830	21	1:1278	0	0	95.2	100
Gross ²²	2021	5905	21	1:250	0	0	100	100
Kamijo ²³	2021	8723	14	1:625	0	0	100	100



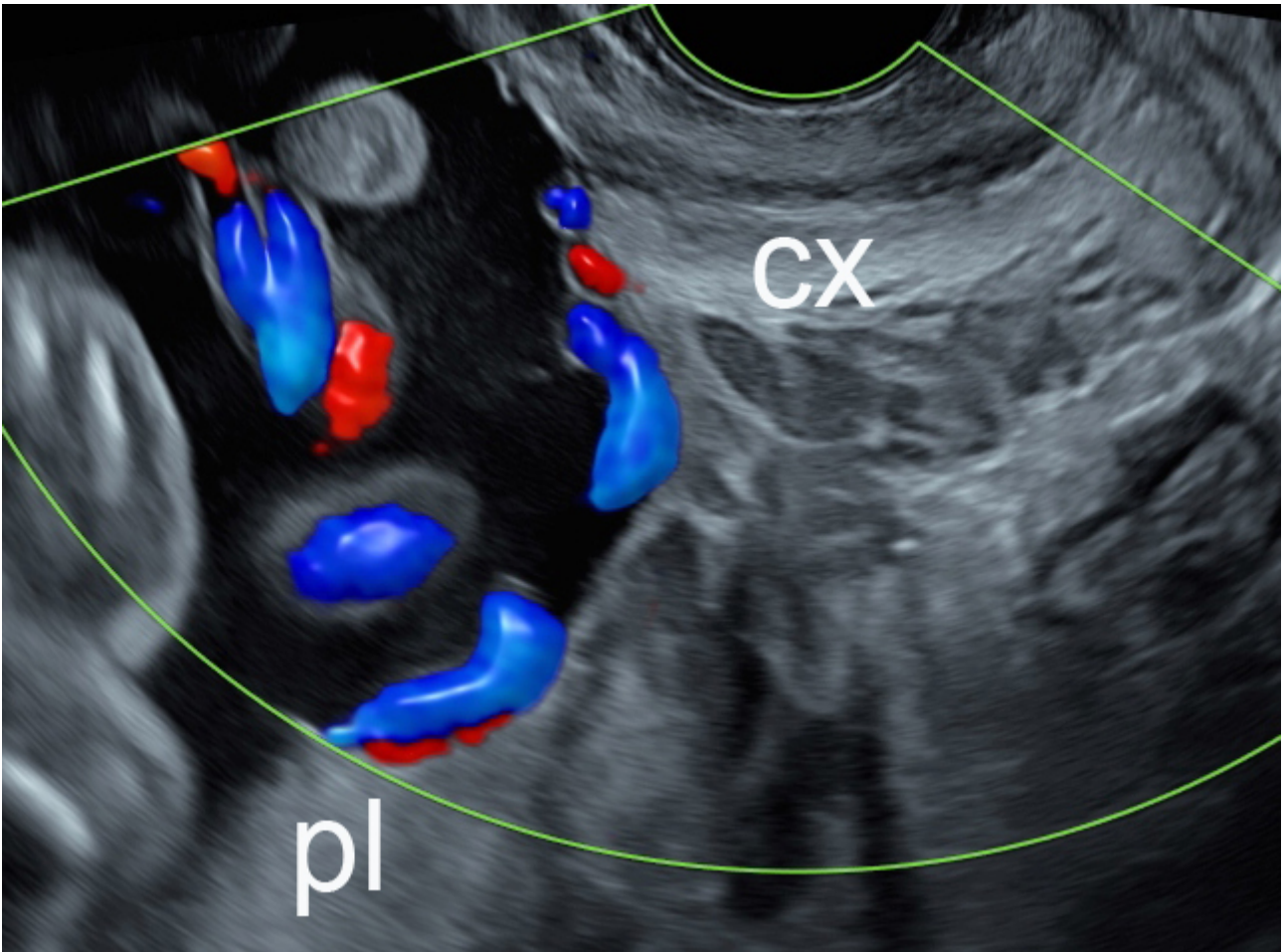
UOG_26085_Fig1CordinsertionUOG.jpg



UOG_26085_Fig2VPScreenUOG.jpg



UOG_26085_Figure3AUOGScreen.jpg



UOG_26085_Figure3bScreenUOG.jpg