



**UK National  
Screening Committee**

# **Vasa praevia and placenta praevia screening in pregnancy**

External review against programme appraisal criteria  
for the UK National Screening Committee (UK NSC)

Version: One

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The UK NSC advises Ministers and the NHS in all four UK countries about all aspects of screening policy. Its policies are reviewed on a 3 yearly cycle. Current policies can be found in the policy database at <http://www.screening.nhs.uk/policies> and the policy review process is described in detail at <http://www.screening.nhs.uk/policyreview>

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### **Vasa Praevia and Placenta Praevia Screening – Update 2008-2012**

This review updates a previous review of the literature on screening for vasa praevia and placenta praevia submitted to the National Screening Committee in November 2008.

A literature search for vasa praevia publications was carried out covering the period January 2008 – November 2012. The search retrieved 103 publications of which 43 were considered relevant. 19 were case reports and 12 were conference abstracts. The search strategy is included as an appendix (to be added).

The previous review focused on vasa praevia and this is also the focus of the current review.

### **Conclusions - November 2008**

#### Vasa Praevia(VP)

- VP occurs when fetal vessels cross or run within the membranes between the amnion and chorion in close proximity to the internal cervical os and has been variously reported as occurring in 0.015-0.04% of all pregnancies and has a high perinatal mortality.
- Complications arising from VP are reported to be an ongoing cause of perinatal mortality and morbidity. Similarly both the perinatal loss rate and the incidence of neonatal transfusion are reported to be significantly reduced if the diagnosis is known before delivery.
- Antenatal diagnosis is currently seldom made but when such a prenatal diagnosis is made, delivery by caesarean section is recommended to avoid fetal haemorrhage.
- The risk of VP can be recognised prenatally using ultrasound by identifying a velamentous insertion of the umbilical cord followed up by visualisation of the vessels lying over the cervical os.
- Velamentous insertion is estimated to occur in approximately 1% of singleton pregnancies. Of these just 2% will be identified as having VP.
- Reports suggest that placental cord insertion and velamentous cord insertion can be consistently identified with the help of transabdominal colour flow Doppler imaging at the time of the mid trimester fetal anomaly scan.
- The condition is seen more commonly in other clinical circumstances such as multiple pregnancies, low-lying placentas, placental anomalies and pregnancies arising from in vitro fertilisation.
- If an ultrasound scan raises the possibility of VP then this should be reported in order to guide any additional ultrasound examinations in the third trimester.
- There was no agreed pathway for the obstetric management of prenatally diagnosed VP.
- Failure to exclude a velamentous cord insertion or VP as part of a screening programme should not result in a presumptive diagnosis of VP and the pregnancy should be managed as normal.
- The main system for screening (routine mid-trimester fetal anomaly ultrasound scans) is in place. Relatively little extra scanning time might be required in the vast majority of women, but some would require additional vaginal scans where none would otherwise have been indicated. Such resources need to be evaluated in the context of a wider approach to screening and factored into the overall costs of any universal screening programme. Potential staff education and training needs are yet to be identified and defined as necessary.
- At face value universal screening for VP is an attractive and desirable option in order to reduce perinatal mortality. Published evidence in relation to the wider ramifications of adopting this approach is limited.

- There was insufficient evidence to determine whether this might be a useful tool to incorporate into the fetal anomaly scan.
- There was insufficient evidence to base a decision to implement universal screening for velamentous insertion of the umbilical cord and VP on cost-effectiveness. However the human aspects of the problem, the sensitivity of the test, its relative rarity, the potential ease of diagnosis and the avoidance of preventable perinatal morbidity and mortality of otherwise healthy infants all needed to be taken into consideration.
- The potential effects on maternal anxiety, preterm delivery rates and incidence of caesarean section had not been evaluated and are important in the context of a universal screening programme.
- In the absence of a universal screening programme, selective examination of cases with an increased risk of VP could be a useful mechanism to evaluate the screening process further and allow for prenatal diagnosis. Initial selective scanning would also allow for the introduction and dissemination of wider education and training. Outstanding issues relating to a wider programme screening could then be explored in greater detail prior to potential universal adoption.
- Cases suitable for selective screening are those with a low-lying placenta in early pregnancy, succenturiate lobes, bilobed or multilobed placentas, multiple pregnancies and pregnancies that arise as a consequence of in vitro fertilisation.
- Consideration could be given to inclusion of VP within the reporting framework of the UKOSS (United Kingdom Obstetric Surveillance System) as a mechanism of expanding the available data surrounding this condition.
- There would appear to be a need to be a greater general awareness of the condition and of the potential for successful prenatal diagnosis.

#### Review of Evidence against NSC Criteria – 2008-12

### **1 Importance of Health Problem**

The main aim of antenatal screening for VP is to prevent perinatal death from exsanguination leading to asphyxiation. Cipriano et al (2010) reiterated how despite its relatively low incidence, VP remains an important health-related issue because the consequences of the condition can be so severe.

A conference abstract summarising a population-based review of 246,525 deliveries (Weintraub et al, 2012) described 0.1% of the pregnancies as being complicated by VP and this was an independent risk factor for perinatal mortality. RCOG Guidelines published in 2011 refer to a reported incidence of 1:2000-6000 pregnancies but accept that the condition may be under-reported, and this probably has remained the case. This rate would translate into between 117 – 350 cases / year on the basis of 723,913 live births in England and Wales in 2011 (Office of National Statistics). This does not include the number of stillbirths at a time when there is an increasing impetus to develop action plans to reduce the national stillbirth rate. Stillbirth is a known outcome of VP through exsanguination.

### **2(i) Epidemiology**

Papers published since the previous review have continued to emphasise the association between VP and a number of risk factors, these being IVF, multiple pregnancy, placental abnormalities and velamentous cord insertion. The lack of population level data was identified as a limitation in estimates of incidence by Smorgick et al (2009). There were no papers addressing the epidemiology of VP in the UK population.

Hasegawa et al (2010) identified the frequency of velamentous cord insertion in 1.6% of a quoted control group of 4532 women (4692 placentas). They also identified that the odds ratio (OR) of a VP with abnormal placental forms (multiple-lobed, succenturiate and accessory placentas) was 21.9 and that with a low-lying placenta was 28.0. They concluded that confirmation of the placental cord insertion (including velamentous cords and cords located on the lower uterine segment) was the best way of detecting VP. They recommended the detection of at least low cord insertion and

velamentous cord insertion during the second trimester to be a useful strategy for making a timely diagnosis of vasa previa.

The authors concluded that in their view the number of cases identified with VP is increasing because of the improvement in the precision of ultrasonographic scanning technologies and that this highlights the potential historical under-reporting referred to earlier.

Further case reports have reinforced the association between VP, multiple pregnancies and abnormal placentation.

Suzuki et al (2010) confirmed that the incidence of succenturiate lobes was significantly higher in twin pregnancies, and that in singleton pregnancies placental complications including abruption, VP and retained placenta were associated with an abnormally shaped placenta. The OR for VP in pregnancies with bilobed and succenturiate lobes was 22.11.

There are now adequate numbers of case reports in the literature which describe clinical circumstances in pregnancy that are at increased risk of VP, with e.g. assisted conception becoming increasingly common. The quoted incidence of VP has been 1:202 following in vitro fertilisation (IVF) (c.f. 1:2200 in non-IVF pregnancies; OR 7.75) (Gagnon et al 2009).

The recognised risk associations are all generally accepted in the literature, including for instance when considering the role of ultrasound in placental imaging (Nguyen et al 2012), and may define a relatively small population in which the burden of disease is concentrated and in which the option of selective diagnostic testing might be considered without compromising the detection rate to any significant degree. The Appendix includes two tables that explore the incidence of risk factors from case reports and other studies. Up to 80% of cases of VP had one or more identifiable maternal risk factors.

## **2(ii) Natural History**

The two main types of VP occur when:-

(a) The umbilical cord inserts directly into the membranes rather than the placenta (a velamentous insertion) **(Type I)**

(b) There is as an additional separate (succenturiate) placental lobe with vessels crossing over from one portion of the placenta to the other **(Type II)**.

This binary typing is helpful in understanding VP and increasing awareness of the condition. As a consequence of its use it is generally agreed that women with a velamentous insertion or a placental abnormality would be best served by having vasa praevia excluded.

However focusing on a binary typing approach can obscure important elements of maternal risk profiles in many cases of VP. This has practical implications for the development and assessment of prevention strategies. The approach tends to focus attention on universal screening for velamentous cord insertion. However it needs to be understood that other placental and cord variants can also result in VP without a classical velamentous insertion and that a velamentous insertion can be combined with other risk factors, for example multiple pregnancy, placenta praevia and / or IVF conception.

## **2(iii) Recognised latent period or early symptomatic stage**

The 2008 review concluded that there was no accepted early symptomatic stage, but bleeding in pregnancy could be considered a possible alert system for VP. This is likely to have a low positive predictive value given the relatively common occurrence of vaginal bleeding in pregnancy. No papers addressing this issue were retrieved by the literature search for this review.

Since the previous review, the RCOG Guidelines state that in the absence of vaginal bleeding there is no method to diagnose VP on clinical examination in the antenatal period. Occasionally however the vessels can be palpated in labour during the course of a vaginal examination, and this can be confirmed using an amnioscope. They advise that delivery should not be delayed in an attempt to diagnose VP in women with vaginal bleeding, especially when associated with membrane rupture and

fetal compromise. Various tests that can differentiate between maternal and fetal blood are often not applicable in the clinical situation (RCOG 2011).

Sinha et al (2008) describe a series of three cases of VP where the presentation was not only that of that of intrapartum but also antepartum bleeding, warning of the need for vigilance in the antenatal period especially with low-lying placentas, velamentous insertions, IVF and multiple pregnancies. Consideration of VP in cases of antepartum bleeding has also been highlighted by Komatsu et al (2011) as a missed diagnosis even when ultrasound is performed under the best circumstances in tertiary centres. A policy of careful evaluation for VP in women with multiple pregnancies, low-lying placentas (even if this resolves later in the pregnancy), velamentous cord insertions and history of assisted conception has been consistently advocated (Gandhi et al 2008, Ioannou & Wayne 2010, Komatsu et al 2011) as cases of placenta praevia, low-lying placenta and bilobed or succenturiate placenta has been estimated as accounting for 89% of pregnancies complicated by VP.

Attempts to exclude VP in clinical situations that are recognised as being associated with the condition have been considered as reasonable by this author in 2012 (Nishtar & Wood). Ioannou & Wayne (2010) also advocate transvaginal scanning as a screening tool for VP in a defined group of women who are known to be at increased risk of the condition.

### **3 Any cost-effective primary prevention interventions practicable?**

There are no cost-effective primary prevention interventions that are practicable. The previous review pointed out that antenatal diagnosis can be expected to reduce perinatal morbidity and mortality.

#### ***The Test***

### **4 Simple safe precise and validated screening test**

The previous review concluded that there was a lack of evidence relating to the sensitivity of ultrasound detection of VP. No studies were retrieved by the literature search which significantly alters this view.

The 2011 RCOG Guidelines conclude that VP can be accurately diagnosed with colour flow Doppler ultrasound, often utilising the vaginal route. Screening for VP would involve scanning to identify placental and cord variants associated with VP, and if these are present diagnosis would involve the use of colour flow Doppler (often transvaginal) to identify any fetal vessels in the region of the cervical os. Recognition is given to the practical difficulties associated with ultrasound diagnosis - VP can be diagnosed with good specificity, but sensitivity has not been determined given its low prevalence.

Hasegawa et al (2010) identified 10 cases of VP in a total population of 4532 women. In 9/10 cases the cord insertion was velamentous and this was also the case with location of the umbilical cord insertion sites on the lower uterine segment.

Rao et al's overview in 2012 stated that the specificity and sensitivity for VP with Doppler ultrasound was high. Gagnon et al's practice guideline (2009) comments on how under the best circumstances the false positive rate is extremely low. Current specificity of using transvaginal ultrasound in women with any risk indicator for VP is quoted as >99.95% by Cipriano et al (2010) on review of the literature.

Hasegawa et al 2011 investigated the risk for VP at 9-13 weeks of pregnancy by looking at the usefulness of identifying the cord insertion site in the lower third of the uterus in 1270 mothers. No significant risk factors were found for low cord insertion between 9-13 weeks including in vitro fertilisation. The cases however had more frequent abnormal placental forms including succenturiate lobes, lobed and accessory placentas and placenta praevia. 10.6% of cases (n=139; controls 1172) were seen to have low cord insertions. The frequency of velamentous cord insertion was 7.2% (n=21) in these cases and 0.2% in controls. Three cases of VP were diagnosed from the cases identified (2.2%) and none in the control group. Placental abruption occurred in 4.3% of the cases and 0.9% of the controls (relative risk 4.7). The authors concluded that screening with ultrasound in the late first

or early second trimesters and following up at the second trimester in cases with low cord insertion is a usefully was to detect VP. This study however only predicted three cases of VP using evaluation of the umbilical cord insertion site with statistically significant relative risk. The relationship between a low cord insertion site and subsequent development of placenta praevia was noted to be close.

There appears to be little benefit in attempting to identify potential cases of VP in the first trimester, with a real risk of increasing the false positive rate.

The focus of attention for antenatal screening for vasa praevia remains the second trimester. The majority of risk factors for vasa praevia can be identified within current practice. For example pregnancies conceived through assisted reproduction, multiple pregnancies, low lying placenta and bilobed placenta. Kanda et al's (2011) case series discussed 10 cases of vasa praevia among 5131 deliveries over six years. All the cases had one or more risk factors for vasa praevia. 9 of the 10 had a low lying placenta at mid term.

There are no national guidelines addressing the cord insertion site. Ionnou and Wayne's survey of UK obstetric practice suggested that detection of velamentous cord insertion as a screening strategy would be a major step change in UK practice.

## **5 Distribution of test values in target pop and suitable cut-off**

The previous review concluded that given the nature of the diagnostic test (ultrasonic identification of blood vessels over the cervical os) there was no practical formal numerical cut-off. This remains the case.

Hasegawa et al (2010) identified low cord insertions in the uterus were seen in 9/10 women with VP compared to 0.4% of controls (Odds Ratio – OR - 2470). A multivariable regression analysis resulted in an OR of 65.1 (95% Confidence Interval – CI - 5.8-733) for velamentous cord insertion with regard to the risk of VP. The OR for low cord insertion was 344.7 (CI 31-3838).

## **6 Test acceptable to population**

No studies retrieved by the literature search addressed this issue.

The previous review noted that, in the UK, the average uptake of fetal anomaly scans is to the order of 97%, so that the overwhelming majority of pregnant women therefore accept the offer of a midtrimester ultrasound scan for fetal anomaly, and with appropriate counselling do so in the expectation that they will obtain reassurance with recognition that there is value in the detection of abnormalities in the antenatal period.

## **7 Agreed policy on further diagnostic investigation/choices**

The previous review noted that prenatal diagnosis allows for the closer monitoring of symptoms of vaginal bleeding and facilitates planned delivery under controlled circumstances.

The 2011 RCOG Guidelines advise that in cases of suspected VP transvaginal colour

Doppler ultrasonography (TVS) should be carried out to confirm the diagnosis. Imaging should be repeated in the third trimester to confirm the ongoing diagnosis, given that VP can

resolve in up to 15% of cases this repeat scan was considered essential in order to avoid unnecessary anxiety, hospital admissions, preterm birth and caesarean sections.

Modelling work has since been published which helpfully expands upon the available knowledge base.

Cipriano et al's (2010) cost effectiveness study estimated that in their population of over 130,000 women (and compared to the status quo of no screening at all) TVS in singleton pregnancies affected by one high risk indicator would result in approximately 8726 more women receiving at least one transvaginal examination during their pregnancy, 33 more caesarean sections in total but 24 fewer emergency caesarean sections and 19 fewer late fetal or neonatal deaths per year in singleton

pregnancies. This compares to 23 fewer late neonatal or fetal deaths if universal screening with TVS were to be adopted. Expanded prenatal TVS of all twin pregnancies and at-risk singleton pregnancies would result in approximately 27-28 fewer late fetal and neonatal deaths each year in a population of approximately 132,000 pregnancies.

On this basis, multiplication of these figures 5.5 fold should provide an indication of the total anticipated reduction in late fetal and neonatal deaths in England and Wales based on the total number of live births in 2011.

- 104-105 fewer late neonatal or fetal deaths in singleton pregnancies with selective screening linked to at least one high risk indicator,
- 115 fewer deaths in singletons with universal screening with TVS and
- 148-154 fewer deaths with screening expanded to all twin pregnancies and singleton pregnancies with at least one high risk indicator.

The authors accept that not all of cases will be detected even with a screening programme as scarring of the abdominal wall, maternal obesity and fetal position potentially prevent optimal visualisation. Their analysis indicates that 7.5 affected singleton pregnancies and 0.9 affected twin pregnancies would remain undetected each year (total population >130,000) even if all risk indicators were used to indicate diagnostic follow up in singleton pregnancies and twin pregnancies compared with universal screening.

The paper suggests that universal screening with TVS is not cost effective in singleton pregnancies as compared to targeted screening. The authors also concluded that selective TVS was almost certainly cost effective and that the probability that having no TVS follow up of identified risk factors was the cost-effective choice was negligible (see section 14).

The general view remains that women with risk factors should undergo transvaginal colour Doppler ultrasound of the region over the cervix if VP cannot be excluded by transabdominalultrasound (Gerretto et al 2012). This should be followed up for confirmation in later pregnancy.

## **8 Effective treatment or intervention**

Guidelines and publications since the previous review continue to recommend delivery by caesarean section and this is based on clinical pragmatism and natural logic. The low frequency of diagnosed cases of VP remains likely to preclude any prospective trial to address the proper timing of delivery. As such modelling and decision analysis may be the only tool whereby this question can be explored in a logical manner. This approach was used by Robinson & Grobman (2011) in a comprehensive evaluation of timing strategies for delivery in cases of VP. Their decision tree compared 11 different strategies for delivery timing in singleton pregnancies affected by VP. The authors accept that this was not a clinical trial or study and highlighted the small amount of evidence which limited choice and precision in the estimates employed in the model.

### *Prophylactic steroids*

Administration of prophylactic steroids to aid lung maturity between 28-32 and before 34 weeks in cases of VP in case of early preterm delivery is consistently recommended (Chmait et al 2010). The risk of superadded threatened preterm labour and intervention in cases where VP has been diagnosed has been stressed by Garretto et al (2012) whose unit is one where routine identification of the placental umbilical cord insertion as part of the second trimester obstetric ultrasonographic examination is performed (despite this not being a requirement of the American Institute of Ultrasound in Medicine Practice Guideline for the Performance of Obstetric Ultrasound Examination).

### *Early hospitalisation*

The Society of Obstetricians and Gynaecologists of Canada Guidelines released in 2009 recommended hospitalisation at 30-32 weeks of pregnancy for women whose pregnancies were shown to be affected by VP (Gagnon et al 2009). The budgetary implications and cost-effectiveness of these recommendations were not evaluated.

Case reports also allude to an anticipated admission at 32 weeks once vasa praevia has been diagnosed (Gandhi et al, 2008) and delivery between 34-35 weeks of pregnancy after the administration of steroids. Early admission is advocated on the basis of a 10% risk of rupture of the membranes before labour and the high associated perinatal mortality with VP.

### *Timing of planned delivery*

In Cipriano et al's study (2010) pregnancies with VP were delivered by planned caesarean section at 35 weeks for singletons and at 34 weeks' gestation for twins. When considering cost-effectiveness the authors were aware of the risks to both mother and baby inherent in unnecessary early delivery by caesarean section.

There appears to be consensus with respect to delivery at 34-35 weeks of pregnancy in case reports (Sinha et al, 2008, Gandhi et al 2008). Chmait et al (2010) explain how, although there has been a significant fall in the perinatal morbidity and mortality with hospitalisation and preterm planned caesarean section to precede rupture of the membranes, there remained an approximate 3% perinatal mortality rate with VP using this approach.

Robinson & Grobman's (2011) modelling study in singletons concluded that scheduled delivery at 34 weeks of pregnancy was the preferred approach to delivery resulting in the highest quality-adjusted life-years, the optimal timing remaining at 34-35 weeks of pregnancy, taking into account both long and short term outcomes for the child. Under all circumstances strategies incorporating confirmation of fetal lung maturity by amniocentesis failed to result in a better outcome than in strategies that incorporated delivery at the same gestational age without amniocentesis. There was no advantage in delivering any later than 37 weeks of pregnancy.

Delivery at 34-35 weeks of pregnancy as a preferred strategy (under most but not all circumstances) may at the very least balance the risk of perinatal death with the risks of infant mortality, respiratory distress syndrome, developmental delay and cerebral palsy relating to prematurity at that stage of pregnancy, and this approach would similarly apply to multiple pregnancies where VP has been identified antenatally.

### *Laser ablation*

Chmait's team (2010) reports offering patients with VP:-

- expectant management with hospitalisation between 28-32 weeks of pregnancy and caesarean section at approximately 35 weeks of pregnancy,
- termination of the pregnancy or
- operativefetoscopic laser ablation between 28-30 weeks of pregnancy; this was first reported in the literature some three years earlier.

They went on to report their experience with two cases of *in vivo* laser ablation in the third trimester treatment of Type II VP (when the vessels bridge separate placental lobes) diagnosed prenatally at 28 and 30 weeks of pregnancy. Ablation of the aberrant blood vessels alleviated the risk of fetal exsanguination although the risks of VP were replaced by those of operative fetoscopy (preterm rupture of the membranes and preterm birth) and placental insufficiency (intrauterine growth restriction). The authors advised how prolonged hospitalisation could be avoided in this way and how there was then the possibility of a vaginal delivery at term. Consideration to laser treatment should be assessed on an individual basis with due consideration to the relative amount of placental tissue supported by the aberrant vessel(s). The authors confirm that in their opinion further study is



required to determine whether VP ablation is justified as a prophylactic procedure or as a treatment to prolong pregnancy in patients at risk of preterm delivery.

#### *Cervical length measurement*

The use of transvaginal cervical length measurements in the management of a pregnancy with vasa praevia has not been formalised (Garretto et al 2012), although a cervix that is seen to be long and closed at 24 and 28 weeks of pregnancy is likely to provide additional reassurance that prophylactic admission can be avoided prior to 30-32 weeks' gestation. The role of cervical cerclage in women with VP is unknown.

### **9 Evidence based policies covering who should be offered treatment and the appropriate treatment to be offered**

The last review concluded that the offer of delivery by planned caesarean section in cases where VP has been diagnosed prenatally and the resultant prevention of perinatal mortality in this way is essentially intuitive and logical rather than based on any randomised trials.

### **10 Optimise clinical management and patient outcomes prior to screening**

The need for education and ultrasonography training remains. There is already widespread access to mid-trimester ultrasound scans with a Doppler flow facility.

While clinical management guidelines appear to be evolving towards a consensus, the extent to which they have been applied in the clinical setting is unclear.

The following guidelines have been published since the previous review:

The ACR Appropriateness Criteria (2012) Evidence-based Guidelines refer to the increased risk of VP with monochorionic twins and triplets.

The RCOG published Guidelines on the Management of Monochorionic Twin Pregnancies in December 2008. The Guideline highlighted how there has been a recent increase in multiple pregnancies as a result of increasing use of assisted reproductive techniques and described the challenges arising from the vascular placental anastomoses and in particular twin-twin transfusion syndrome. Unequal placental sharing and peripheral 'velamentous' cord insertions were identified as being common in cases of twin-twin transfusion syndrome.

In August 2009 the Society of Obstetricians and Gynaecologists of Canada released Guidelines for the management of VP and stated that cord insertion should be identified at the time of the second-trimester ultrasound scan when the placenta was seen to be low-lying. Transvaginal ultrasound may be considered for all women at high risk of VP including those with low or velamentous cord insertion, a bilobed or succenturiate placenta, or those with a history of vaginal bleeding.

The RCOG Guidelines on "Placenta praevia, placenta praevia accreta and vasa praevia: diagnosis and management" (2011) confirmed the recognised risk factors for VP as placental anomalies, a low-lying placenta in the second trimester, multiple pregnancy and in vitro fertilisation. These Guidelines conclude that there is insufficient information on the case definition, natural history and epidemiology of VP to advocate universal ultrasound checks for the condition, but that by investigating women with a risk factor, including velamentous insertion, a significant minority will be at increased risk of vasa praevia "and require further counselling and screening".

These Guidelines also recommend routine ultrasound scanning for placental localisation at the time of the mid-trimester fetal transabdominal anomaly scan. The RCOG policy of identifying a low-lying placenta at the time of the routine 20-week fetal ultrasound scan is a longstanding element of antenatal care packages and supported by the National Screening Committee, the RCOG and the National Institute for Health and Clinical Excellence. A transvaginal scan is advocated to improve the accuracy of the transabdominal scan in cases where the placenta is seen to encroach on the cervical os. Asymptomatic women with suspected minor placenta praevia can be reassessed on ultrasound

scan at 36 weeks of pregnancy, although cases where placenta praevia is suspected as being major were advised to have this ultrasound scan at 32 weeks' gestation to clarify the diagnosis and allow for a management plan in the third trimester.

### ***The Screening Programme***

#### **11 Evidence from high quality RCTs that the screening programme is effective in reducing mortality or morbidity**

The last review concluded that despite the absence of large prospective studies relating to VP there is probably no place for a randomised controlled trial to investigate whether screening for VP would decrease fetal mortality. This would be ethically unjustifiable given the poor fetal prognosis. It would seem difficult to counter the premise that a substantial improvement in fetal outcome in affected cases would be reliant on appropriate prenatal detection. There were no cases of fetal loss in Hasegawa et al's study (2010) where universal screening for vasa praevia was conducted over a period of four years.

#### **12 Evidence that complete screening programme is acceptable to public and health professionals**

The last review concluded that there is no evidence for or against the complete screening programme being acceptable to the public and to health professionals.

Ioannou & Wayne et al (2010) assimilated the views of obstetricians in England and Wales in 2006 and concluded (on the basis of a 55% response rate to a questionnaire) that most obstetricians (80%) felt that an effective screening policy was not feasible. A more positive response was however elicited from the subgroup of individuals who performed transvaginal scanning.

This study highlighted that just 80% of UK obstetricians would recommend caesarean section as a result of antenatal suspicion of VP (a sine qua non), and most would not offer this until 38 weeks of pregnancy.

One third could not name one risk factor for the condition (with only 1.5% being able to name up to 4 risk factors). Over half had no experience of diagnosing VP on scan or indeed managing this antenatally before rupture. Only 60% of those who performed obstetric ultrasound scanning considered themselves able to identify VP on transvaginal scan.

Lack of published guidelines and lack of knowledge appear to loom large in this respect, so that education and application of knowledge would seem to be a priority within UK obstetric practice. The authors concluded that there was a need to increase the awareness and understanding of the major risk factors for this condition.

A 20-year retrospective study (Smorgick 2010) concluded that antenatal ultrasound screening using selective scans for VP in women at risk or as part of routine mid-pregnancy scanning may impact significantly on the adverse obstetric manifestations of this condition. The overall incidence of VP in this retrospective study was 1.7/10,000 deliveries but the prenatal detection rate increased from 25% in the first ten years to 60% in the second ten-year period, effects of increasing education and awareness of VP (explained by the obstetric community's "alertness" to the condition). During these two time periods the perinatal mortality from VP fell from 25% to 0%. The authors also found an apparent increase in the incidence of VP during the second decade explained by the increased proportion of pregnancies with risk factors including in vitro fertilisation and multiple pregnancies but also potentially because of improved reporting structures and general awareness.

The need for increasing awareness of the condition was also highlighted by Nishtar and Wood in our review of the literature in 2012.

### 13 Benefits to outweigh harm

The last review listed the potential benefits to the neonate in respect of survival and morbidity versus the risks of preterm birth. Robinson's (2011) modelling study took potential harms into account. However no papers in the literature search addressed the benefits and harms of a national screening programme for VP.

In Hasegawa et al's study (2010) cases where VP was diagnosed antenatally (n=10) the gestation at delivery was earlier (34.6 weeks c.f. 38 weeks). The birthweight (1.942 kg c.f. 2.837 kg), Apgar score (albeit still scoring 8 at one minute c.f. 9 in the control group) and placental weight (399 g c.f. 591 g) were all lower than in those cases without VP. However half of those 10 cases of VP were also associated with intrauterine growth restriction (OR 9.2). Two cases were also associated with a reduction in the liquor volume (oligohydramnios). The authors suggested consideration of assessment for VP when the cause of intrauterine growth restriction cannot be explained, but this is an association which has not been extensively studied.

Pregnancies affected by VP were found by Weintraub et al's (2012) conference abstract to have an OR of 4.6 for preterm delivery, 4.3 for intrauterine growth restriction and 8.2 for placental abruption.

### 14 Opportunity cost economically balanced in relation to medical care as a whole

In 2008 the cost of a national screening programme in the United Kingdom based on additional identification of umbilical cord insertion in the antenatal period had not been estimated.

Ioannou & Wayne (2010) note that the sensitivity of screening for VP is unclear. As a result the impact of missed cases in a screening policy's overall effectiveness and cost-effectiveness is difficult to quantify at present.

Following the publication of the 2009 Canadian Guidelines on VP, Cipriano et al (2010) evaluated the cost effectiveness of both targeted and universal screening for VP using TVS at 18-20 weeks of pregnancy in a Canadian population against the status quo of no routine screening in over 130,000 women. Recognition was given to the fact that not all inputs applied to the analysis could be specific to VP. The study was based on a decision-analytical model comparing relevant strategies and life-long outcomes for mothers and infants. A total of 9 strategies including 7 primary VP screening strategies were considered and 2 involving selective screening of women with known high risk factors. Screening decreased late fetal and neonatal mortality but cost more than not screening at all.

However once cost effectiveness was analysed the study identified that the Incremental Cost-Effectiveness Ratio (ICER) for targeted TVS screening in women with identified risk factors (low placenta, IVF, accessory lobes, velamentous cord insertion) was \$15764 (Canadian) per quality-adjusted life year. Screening women with a marginal cord insertion cost an additional \$27603 per quality-adjusted life year. The individual cost of the additional resources to provide these services was \$12.28. Costs were based on the management plan described earlier including hospitalisation and caesarean section. Benefits included late fetal and neonatal deaths averted, life-years gained and improvements in quality of life and included consideration of the risks of caesarean section.

- Screening all twin pregnancies for VP with transvaginal ultrasound was almost certainly cost effective and considered to be robust in sensitivity analysis.
- The use of colour Doppler at all transabdominal ultrasound examinations and the targeted use of transvaginal ultrasound for IVF pregnancies or when the placenta is seen to be associated with one or more risk factors was cost-effective.
- Universal transvaginal ultrasound screening of singleton pregnancies was not cost effective when compared to targeted screening
- The probability that that having no screening for VP is the cost-effective choice is negligible.

The authors were circumspect over whether marginal cord insertion was a cause of VP and suggested that more information about this potential risk factor may be necessary before routine transvaginal scanning for women with marginal cord insertion should begin. They however recommend policies for adoption wherein women with multiple pregnancies, low-lying placentas, velamentous cord insertion, or even marginal cord insertion are referred to transvaginal ultrasound to screen for VP.

**15 Plan for managing and monitoring the screening programme with an agreed set of quality assurance standards**

The conclusion reached in the 2008 review that in the absence of national screening in the United Kingdom, no quality assurance standards have been agreed remains.

**16 Adequate staffing and facilities available**

When estimating the base-cost analysis of screening for VP Cipriano et al (2010) did not include the one-time cost of training obstetricians and sonographers in the use of colour Doppler, the detection of velamentous vessels or VP or in the appropriate management of women with VP. The RCOG Guidelines note that scanning for velamentous cord insertion and VP is not routinely taught during ultrasound training courses in the UK, and that the training implications of introducing such a screening programme require careful consideration.

Ioannou & Wayne (2010) highlighted the need for a system that ensures skill validation and quality control across the board. They found that the self-assessed ability of obstetricians to perform this investigation was variable but that those in possession of the necessary scanning skills were more likely to support a policy of screening for VP.

Magnetic Resonance (MR) imaging has also been used to differentiate between placental tissue and haemorrhage between placental lobes with a VP (Kikuchi et al 2011). Whereas MR appears to be an accurate tool with which the antenatal diagnosis of VP can be made without adverse fetal effects, this is an expensive option and not a method that can be used in day to day obstetric practice to diagnose VP.

**17 Other options for managing the condition**

Other than for ultrasonography, the antenatal diagnosis of VP can be made by MR scanning, amnioscopy, palpation of the vessels by digital vaginal examination or by identification of fetal blood in vaginal blood. Prenatal ultrasonography appears to be the least invasive option. No studies discuss the alternatives to ultrasound as viable options to an approach based on the main risk groups, and therefore the notion of a screening “history” followed by a diagnostic test. . A similar approach currently exists in the diagnosis of gestational diabetes where a diagnostic test is offered to women identified as being at increased risk of the condition

**Placenta Praevia Update:-**

Conclusions - November 2008

Placenta Praevia(PP)

- Antenatal detection of PP is desirable in order to manage cases appropriately and reduce maternal and perinatal complications arising from this condition.
- Placental localisation at the time of the fetal anomaly ultrasound scan is an established part of UK clinical practice.
- The earlier a scan is carried out to look for PP, the higher the false positive rate compared to the prevalence of PP at term. The midtrimester scan overestimates the prevalence of PP at term by 1:10. First trimester scans will demonstrate a placenta reaching or overlapping the internal os in as many as 42% of cases.
- Additional work is required before conclusions can be reached on the merits of measurement of the angle of the lower placental edge in the first trimester of pregnancy in reducing the overall false positive rate.
- A low-lying placenta is a shared risk factor for velamentous cord insertion and VP as is in vitro fertilisation.
- The present NICE guideline concludes that women in whom the placenta extends over the internal cervical os at the time of the fetal anomaly scan should be offered another transabdominal scan at 32 weeks, with an additional transvaginal scan if there is still uncertainty.
- The extent to which additional later scans are necessary could be reduced by the offer of a transvaginal scan at the time of the anomaly scan in selected cases. There is insufficient evidence to draw reliable conclusions on the advantages and disadvantages of offering a transvaginal scan at the time of the routine fetal anomaly scan in selected cases as opposed to bringing women back for a repeat ultrasound examination in the third trimester. These factors would include practical issues of time allocation and patient considerations.
- The timing of a confirmatory ultrasound scan in the third trimester has varied between 32-36 weeks depending on the extent of the placenta praevia. Although the shift from the RCOG guidance by NICE to 32 weeks for all women whose placenta extends over the os at the time of the fetal anomaly scan is based on a perceived need for awareness in the context of the risk of antepartum haemorrhage there does not appear to be strong evidence to demonstrate that this actually makes a difference to the management of asymptomatic patients.
- The general shift in emphasis to reporting on the basis of actual distance from the placental edge to the cervical os (and the degree of overlap) as opposed to the adoption of a broader and more subjective classification is good practice which should be encouraged.
- The evidence indicated that transvaginal scanning is the gold standard for the diagnosis of PP and was superior to transabdominal and transperineal approaches.

### **Review of Evidence – 2008-12**

**NICE Guidelines** have not been updated since 2008.

The previous review estimated that the prevalence of clinically evident placenta praevia was 2.8/1000 singleton pregnancies and that the placental site was routinely reported at the time of the mid-trimester ultrasound scan, this being the main screening test for PP.

### **RCOG Guidelines**

In 2011 the RCOG published Guidelines on “Placenta praevia, placenta praevia accreta and vasa praevia: diagnosis and management” which is referred to elsewhere in this report.

### **Other Publications**

Rao’s 2012 Continuing Medical Education article on abnormal placentation reviews the existing knowledge base about PP, advocating transvaginal ultrasound in order to localise the placenta in relation to the cervical os with greater precision. The authors reiterate the general importance of avoiding a definitive diagnosis until the third trimester in asymptomatic women as many cases resolve with advancing gestational age. They advise ultrasonographers to describe precisely the relationship between the placenta and the cervix or the actual distance between the two. The incidence of PP is rising related to the increasing rates of caesarean section and maternal age. The authors advocate that transvaginal scanning, the safety of which has been established, be used for all women even if a fundal placenta is seen on abdominal scanning as the placenta can extend from the fundus to the cervix or be associated with a succenturiate lobe. Transabdominal scanning is associated with incorrect diagnoses approximately 25% of the time. Faced with a low-lying placenta, a follow up scan is advised at 32 weeks to confirm the placental position and a final study may be performed at 36 weeks’ gestation.

Other recent publications have essentially served to consolidate information already available with regard to PP in 2008, rather than providing additional information on developments, refinements or resolution. Many relate to management. The effects of the increasing international rates of repeat caesarean section on increasing rates of PP have been stressed.

### **Summary and Conclusions**

#### **Vasa Praevia:-**

Recent published literature does not support universal screening for VP as per the current position of the UK National Screening Committee. However there is increasing evidence that national guidance should be developed focussing specifically on the identification and management of pregnancies with a raised risk of VP at a time that there is an increasing national focus on prevention of stillbirths.

Interest in the active pursuit of prevention of VP is increasing and an albeit small number of important publications since the previous review has helped considerably to inform and provide knowledge relating to screening, diagnosis and management of VP.

Prominent amongst these is information about the cost effectiveness of various screening and diagnostic scenarios and also on the agreed optimal management pathway of pregnancies affected by VP.

Whereas routine population TVS screening for VP does not appear to be cost effective, selective diagnostic ultrasound scanning based on a screening system that identifies known risk associations with VP has much to commend it. The majority of these risk factors are detected within current practice, these being assisted reproduction, multiple pregnancy, low lying placenta and bilobed placenta.

RCOG Guidelines from 2011 concluded and concurred with the position taken by the National Screening Committee in 2008 that there was uncertainty about the balance of benefits versus harm to be derived from screening all pregnant women with a view to offering caesarean section to those at risk. However this may not preclude the development of an approach based on high risk groups. Insofar as effective treatment and intervention is concerned, while it is not in the UKNSC's remit to develop clinical care guidance, this review might provide an opportunity to discuss the issue with the relevant stakeholders.

Consideration should be given to the active exclusion of VP in pregnancies at high risk of the condition using targeted ultrasonography, since this will potentially identify up to 80% of affected cases and could reduce the perinatal loss rate in England and Wales by as many as 150 deaths per year.

### **Research suggestions**

Modelling work to estimate the impact of screening and risk based identification and subsequent management of VP in singleton and multiple pregnancies. Cipriano (2010) and Robinson and Grobman (2011) provide examples.

Exploration of outcomes in existing Units in the UK where prenatal ultrasound diagnosis of VP is actively explored.

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