# PLACENTAL ABNORMALITIES (PLACENTA PREVIA, PLACENTA ACCRETA AND VASA PREVIA) MANAGEMENT OF THIRD TRIMESTER HAEMORRHAGE

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## 1. PLACENTA PREVIA

The term placenta previa (PP) refers to an abnormal placenta overlying the endocervical os. Placenta previa affects 0.25-0.5% of singleton pregnancies (approximately 4/1000 births). The risk is higher in the case of previous caesarean sections and increases proportionally with an increasing number of prior caesarean sections. There is also an increased risk in other cases of uterine surgery, such as myomectomy, history of curettage or manual removal of a retained placenta. Other risk factors for placenta previa have been described: maternal age, smoking, black and Asian race, multiparity, multiple gestations, assisted reproductive technology, placenta previa in previous pregnancies, cocaine use and history of embolisation.

PP accounts for 20% of third-trimester bleedings. It is a common cause of maternal transfusion and obstetric hysterectomy, and it is associated with significant perinatal morbidity and mortality. Women with PP are almost 10 times more likely to have bleeding during the third trimester. Fetal complications are mainly associated with prematurity.

The most common presentation of PP is an incidental finding during the routine second-trimester ultrasound. Currently, it is diagnosed in 1-6% of pregnancies, but the vast majority of these will not have a placenta lining the internal os in the third trimester (90% resolve before delivery).

In recent years, the terms ‘partial’ and ‘marginal’ placenta previa have been deleted. All placentas that overlie the internal cervical os (to any degree) are termed previa and those that extend into the lower uterine segment without covering the os are termed low-lying. This term is usually applied when the placental edge is within 2 cm from the internal cervical os (Figure 1).

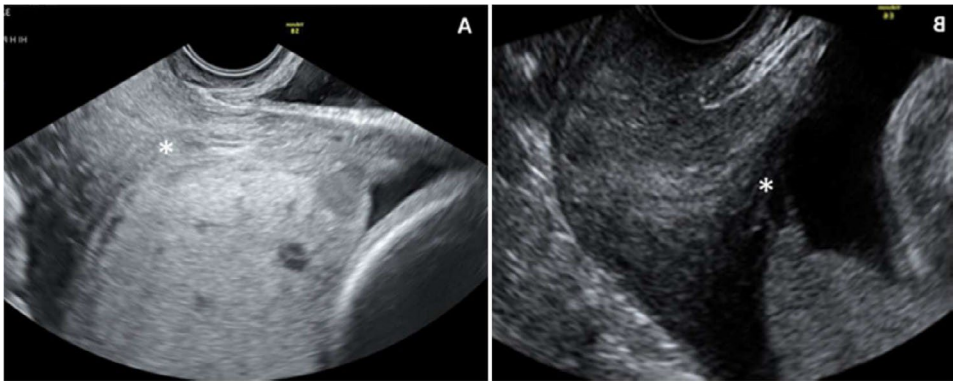

Figure 1. A) Placenta previa. B) Low-lying placenta.

### 1.1 CLINICAL FINDINGS

The main symptom of PP is abundant isolated metrorrhagia of bright red blood of maternal origin, associated with uterine contractions in 10-30% of cases. Approximately 30% of patients will have bleeding before 30 weeks, 30% between 30 and 36 weeks and 30% after 36 weeks. Only 10% of patients with PP will remain asymptomatic throughout pregnancy. Although the exact mechanism of bleeding is unknown, it is thought to be associated with the occurrence of uterine contractions, even if subclinical.

### 1.2 DIAGNOSIS

The placental location should be determined during the routine second and third-trimester scans. If PP is suspected, or in the case of bilobed placentas or twin gestations, a transvaginal ultrasound can help confirm or exclude the diagnosis of PP.

Ultrasound assessment of placenta previa should include:

- Transabdominal ultrasound to evaluate placental territory, insertion of the umbilical cord and ruling out of the presence of haematomas.
- Transvaginal ultrasound (performed with partially filled bladder) to evaluate the lower uterine segment: anterior, posterior and lateral (transverse view). Sometimes it is necessary to push back the fetal presentation.
- Colour Doppler ultrasound to rule out vasa previa.
- Evaluation of typical signs of placental accretism, especially if there is a history of previous caesarean section.
- Evaluation the precise relationship between lower placental edge and internal cervical os (with empty bladder) and cervical length measurement. The distance that the placenta overlies or is away from the os should be reported.

### 1.3 MANAGEMENT

The relationship between the cervix and the placenta changes over time with the placenta typically moving away from the cervix. The optimal time for subsequent imaging in pregnancies

with PP has not been well established. It is reasonable to perform a follow-up ultrasound at approximately 28 weeks in pregnancies thought to have placenta previa or low-lying placenta located <10 mm from the internal cervical os, in order to confirm the diagnosis and give recommendations or explanations to the patient (relative rest, avoid sexual relations, prevention of maternal anaemia, possible onset of bleeding).

Follow-up in the third trimester will not be necessary in asymptomatic patients with low-lying placenta located 10 mm or more from the internal cervical os, given the high probability of migration (more than 90%, especially anterior placentas).

If the diagnosis of PP is confirmed at 28 weeks, ultrasound monitoring will be scheduled approximately monthly, or more frequently depending on the clinical features and cervical length. There is no clear benefit from more frequent ultrasounds in stable cases.

-Asymptomatic PP: follow-up ultrasound every month from 28 to 36 weeks to rule out associated complications. If PP persists, at 36 weeks we perform an ultrasound to determine the optimal route and timing of delivery.

-Symptomatic PP: depending on the degree of metrorrhagia and the patient's history, we will decide whether to keep the patient under observation or admit her.

1. Under observation: patients presenting with mild to moderate bleeding and who are haemodynamically stable without additional haemorrhagic risk factors.
    - Anamnesis and physical examination: transvaginal ultrasound is preferred to avoid vaginal examination.
    - Complete blood count (CBC), blood coagulation test and basic blood chemistry test.
    - Auscultation of fetal heart rate (FHR) and recognition of uterine contractions. cardiotocography (CTG) is indicated after 24 weeks to check fetal well-being.
    - Obstetric ultrasound: fetal assessment, placental location, site of umbilical cord insertion into the placenta, cervical length and integrity of membranes. Other complications must be excluded: vasa previa, placental accretism and placental haematomas.
    - Relative rest
    - Discharge to go home after a few hours under observation if there is no associated complication and the patient remains haemodynamically stable and asymptomatic. The timing of the next follow-up appointment will be in 1-2 weeks.

2. Hospital admission: patients who do not meet the criteria for admission under observation. In addition to the actions that would be carried out in an admission for observation, the following points should be taken into consideration:
    - Blood reservation and assess the need for transfusion.
    - Vital signs monitoring including urine output.

- Anti-D immunoglobulin should be administered to RhD negative patients (intramuscular injection of 300 µg or 1500 UI).
- Daily cardiotocography in gestations > 24 weeks.
- Tocolytic therapy will be administered despite normal cervical length or absence of uterine contractions. The drug of choice may vary according to the clinical guideline for threatened preterm labour, but indomethacin should be avoided due to its inhibitory effect on platelet function, as well as nifedipine in cases of clinical hypotension.
- Antenatal corticosteroids for fetal lung maturation between 24.0 and 34.6 weeks.
- Magnesium sulphate for fetal neuroprotection between 24.0 and 31.6 weeks.
- Absolute rest until the condition stabilises.
- Severe bleeding that does not stop after tocolytic therapy, haemodynamic instability or suspected fetal compromise will be criteria for immediate termination of pregnancy.
- After clinical stabilisation, gestation will be terminated by caesarean section if the gestational age is ≥ 36 weeks. On the contrary, if gestational age is <36 weeks, the patient will be discharged to go home. Relative rest is recommended, and the next follow-up appointment will be in 1-2 weeks. Thereafter, regular ultrasound follow-up is indicated every 2-4 weeks depending on the distance of the placenta from the internal cervical os, gestational age, cervical length and clinical features.

Elective termination of pregnancy

- Asymptomatic PP (patient who has never presented clinical manifestations): elective caesarean section at 37-38 weeks.

- Symptomatic PP (patient who has presented at least one bleeding): elective caesarean section at 36-37 weeks. Assess the need for QuantusFLM to evaluate fetal lung maturation prior to termination.

- In cases of low-lying placenta located 10 mm or more from the internal cervical os, the option of spontaneous vaginal delivery may be contemplated (success rate of 69%).

In all cases, a blood reservation (3 units of packed red blood cells) and pre-anaesthetic visit are requested. Loco-regional anaesthesia should be the first choice whenever possible.

Intraoperative aspects of caesarean section

- An ultrasound prior to the caesarean section allows us to accurately determine the location of the placenta.
- Although transverse lower segment uterine incision is the preferred incision for a caesarean, transplacental incision should be avoided whenever possible and the incision should be made as far away as possible from the site of umbilical cord insertion. In case of transplacental incision, the placenta must be crossed quickly for fetal extraction.
- Early cord clamping is indicated.

### 1.4 COMPLICATIONS

- Perinatal morbidity and mortality: pre-labour rupture of membranes (PROM), preterm birth
- Fetal malposition
- Severe bleeding, need for vasoactive drugs and maternal transfusion, hypovolemic shock
- Placental accretism, vasa previa, velamentous cord insertion
- Postpartum haemorrhage
- Emergency peripartum hysterectomy
- Amniotic fluid embolism

## 2. PLACENTA ACCRETA SPECTRUM (PAS)

Placenta accreta spectrum disorder (PAS) describes a clinical situation where the placenta does not detach spontaneously after delivery due to an abnormal adherence of the placenta to the myometrium and/or neighbouring organs. It is the consequence of damage to the endometrium-myometrial interface that leads to a failure of normal decidualisation at the site of a uterine scar, enabling abnormally deep trophoblast infiltration. Nowadays, the main cause of PAS is uterine surgery and, in particular, uterine scar secondary to caesarean delivery. The decidua potentially regulates trophoblast invasion. The classic histopathological diagnosis criteria is the partial or complete absence of decidua basalis.

PAS is associated with significant maternal morbidity, in particular, major obstetric haemorrhage, respiratory distress, need for transfusion, thromboembolism, intraabdominal infection, peripartum hysterectomy, and damage to surrounding organs. It has been associated with high maternal mortality of up to 7%.

### 2.1 EPIDEMIOLOGY AND RISK FACTORS

The accurate estimation of the incidence of PAS is challenging. Today the incidence is 3/1000 pregnancies, although it varies among different populations according to the prevalence of the

risk factors associated with this condition. In recent years, the increasing incidence of caesarean delivery has resulted in a rise in PAS, as previous caesarean section is the main risk factor. Over the past four decades, caesarean delivery rates have risen globally from less than 10% to over 30%. This has been accompanied by a simultaneous increase of up to 10 times in the incidence of PAS.

PAS may occur after any kind of procedure that causes damage to the endometrium, including uterine curettage, manual removal of the placenta, endometrial resection, uterine artery embolisation, or myomectomy. Other acknowledged risk factors include assisted reproductive technology, advanced maternal age (greater than 35 years), endometritis, Asherman syndrome, intrauterine device, prior history of pelvic irradiation and a diagnosis of PAS in a previous pregnancy. Finally, some cases with no relevant history, but presenting with a uterine pathology, have also been reported: adenomyosis, submucous fibroids, placenta previa, bicornuate uterus and myotonic dystrophy.

However, the major risk factor for PAS is a prior caesarean delivery in combination with placenta previa.
Both are risk factors for PAS individually (present in more than 90% of cases), but the combination of the two results in a 10-20 fold increase in the risk of PAS (Figure 2).

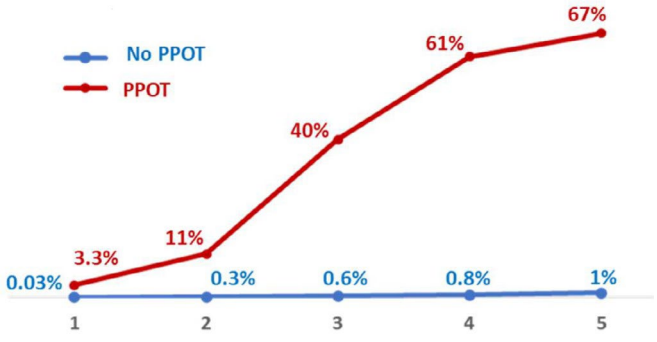


Figure 2. Risk of PAS depending on the number of previous caesarean deliveries and its association with placenta previa (adapted from Silver RM, Obstet Gynecol 2006).

Therefore, patients with a history of previous caesarean section who present with a placenta previa or a low-lying anterior placenta in the second trimester of gestation represent the main risk group for PAS and should be evaluated by the specialist in placental/myometrial pathology.

Another important risk factor for PAS is the history of caesarean scar ectopic pregnancy. There is increasing evidence that this entity could be a precursor of PAS disorders. It has been demonstrated that more than 90% of caesarean scar ectopic pregnancies diagnosed during the first trimester and managed expectantly develop PAS disorder in the third trimester. Early diagnosis and treatment of this condition will prevent further development of PAS.

### 2.2. CLASSIFICATIONS

There are different classifications, but the most commonly used is the classical or anatomopathological classification, based on the depth of villous tissue invasiveness inside the myometrium. Pathologists separated PAS into three categories representing the range of pathologic invasiveness of the placenta:

- Placenta accreta (80%): the chorionic villi simply adhere to the superficial myometrium without interposing decidua.
- Placenta increta (15%): the chorionic villi penetrate deeply into the myometrium reaching the external layer.
- Placenta percreta (5%): the chorionic villi invade the full thickness of the myometrium and penetrate through the uterine serosa and potentially to the nearby organs (such as the bladder).

The placenta may show different degrees of invasion along its entire length. According to the lateral extension of invasion, PAS disorders are subdivided into focal, partial, and total, depending on the number of placental lobes involved.

### 2.3. CLINICAL FINDINGS

The clinical manifestations of placenta accreta during pregnancy are comparable to those of placenta previa, as in most cases they are associated. In case of invasion of neighbouring organs (placenta percreta), other symptoms may occur (haematuria due to bladder involvement or hydronephrosis due to ureteral entrapment).

When the diagnosis is made during labour, it manifests as difficult or incomplete removal of the placenta with or without associated postpartum haemorrhage. There is evidence of a lack of placental cotyledons (focal or partial accretism) or total impossibility of placental expulsion because a cleavage plane between the maternal placental surface and the uterine wall cannot be formed (total accretism).

If no prenatal diagnosis is made, the diagnosis will be made at the time of delivery based on the findings at this time (Table 1). The process of placentation in cases of PAS has an impact on the development of the surrounding deep uterine circulation. The area affected by accretism will not spontaneously deliver and any attempt to do so may result in an uncontrollable bleeding from the deep uterine vessels or neovascularisation around the placenta accreta. The deeper and larger the area affected by accretism, the greater the risk of serious haemorrhagic complications.

| GRADE | | DEFINITION | |
|---|---|---|---|
| | | Clinical criteria | Histologic criteria |
| 1<br>Abnormally adherent placenta (accreta) | | At vaginal delivery:<br>-no separation with synthetic oxytocin and gentle controlled cord traction<br>-attempts at manual removal of the placenta results in heavy bleeding from the placenta implantation site, requiring mechanical or surgical procedures | Microscopic examination of the placental bed samples from the hysterectomy specimen shows extended areas of absent decidua between villous tissue and myometrium with placental villi attached directly to the superficial myometrium. |
| | | If laparotomy is required (including for caesarean delivery):<br>-same as above<br>-macroscopically, the uterus shows no obvious distension over the placental bed (placental "bulge"), no placental tissue is seen invading through the surface of the uterus, and there is no or minimal neovascularity | |
| 2<br>Abnormally invasive placenta (increta) | | At laparotomy:<br>-abnormal macroscopic findings over the placental bed: bluish/purple colouring, distension (placental "bulge")<br>-significant amounts of hypervascularity (dense tangled bed of vessels or multiple vessels running parallel craniocaudally in the uterine serosa)<br>-no placental tissue seen to be invading through the uterine serosa<br>-gentle cord traction results in the uterus being pulled inwards without separation of the placenta (so-called dimple sign) | Hysterectomy specimen or partial myometrial resection of the increta area shows placental villi within the muscular fibres and sometimes in the lumen of the deep uterine vasculature (radial or arcuate arteries). |
| 3<br>Abnormally invasive placenta (percreta) | 3a Limited to the uterine serosa | At laparotomy:<br>-abnormal macroscopic findings on uterine serosal surface (as above) and placental tissue seen to be | Hysterectomy specimen showing villous tissue within or breaching the uterine serosa. |

| | | | |
|---|---|---|---|
| | | invading through the surface of the uterus<br>-no invasion into any other organ, including the posterior wall of the bladder (a clear surgical plane can be identified between the bladder and uterus) | |
| | 3b With urinary bladder invasion | At laparotomy:<br>-placental villi are seen to be invading into the bladder but no other organs<br>-a clear surgical plane cannot be identified between the bladder and uterus. | Hysterectomy specimen showing villous tissue breaching the uterine serosa and invading the bladder wall tissue or urothelium. |
| | 3c With invasion of other pelvic tissue or organs | At laparotomy:<br>-placental villi are seen to be invading into the broad ligament, vaginal wall, pelvic sidewall, or any other pelvic organ (with or without invasion of the bladder) | Hysterectomy specimen showing villous tissue breaching the uterine serosa and invading pelvic tissues/organs (with or without invasion of the bladder). |

Table 1. Clinical and Histologic Grading System to assess and categorise placental adherence or invasion at delivery according to FIGO Guidelines.

### 2.4. DIFFERENTIAL DIAGNOSIS

- Uterine window: this an area of uterine dehiscence with normal placentation underneath (thinning of the uterine wall at the caesarean section scar site may allow the placenta to be seen through the myometrium). In this case, the surrounding uterine tissue appears relatively normal with no severe vascular changes or placental bulging. A normal delivery of the placenta can be attempted with subsequent surgical repair of the dehiscence.

- Manual removal of a retained normal placenta: this may be associated with severe bleeding due to secondary uterine atony, but, in these cases, conservative management techniques such as the administration of uterotonic agents, intrauterine balloon or compressive sutures, are usually effective in controlling the bleeding.

## 2.5. PRENATAL DIAGNOSIS

Recent population-based studies showed that approximately one-half to two-thirds of PAS disorders were not diagnosed antenatally. On the other hand, there is evidence that maternal mortality and morbidity are significantly reduced when pregnant women with PAS disorder are referred to a referral centre and managed by a multidisciplinary team with experience in this pathology, demonstrating the need for targeted prenatal screening for PAS.

### Prenatal screening

Prenatal screening for PAS disorders is based on the identification of patients at risk for this complication so that they can be referred to and evaluated by a specialised team.

The main risk factor is a prior caesarean delivery in combination with placenta previa or low-lying placenta. Therefore, all patients presenting with placenta previa or low-lying placenta should undergo a detailed anamnesis in order to determine associated risk factors for PAS. If identified, they should undergo ultrasound evaluation in a centre with expertise in this condition, as well as in case of detecting ultrasound signs of PAS in prenatal screening scan.

### Ultrasound diagnosis

Obstetric ultrasonography is the technique of choice for prenatal diagnosis of PAS during the second and third trimester of pregnancy, with a sensitivity of 91% and a specificity of 97% in pregnant women at high risk of PAS.

The European Working Group on Abnormally Invasive Placenta (EW-AIP) has proposed a terminology and detailed description for all ultrasound signs used in prenatal diagnosis of PAS.

- <u>2D grayscale ultrasound findings:</u>

  -Loss of “clear zone” (sensitivity: 58-74%; specificity: 95-97%): Loss, or irregularity, of hypoechoic plane in myometrium underneath placental bed (‘clear zone’), representing an abnormal extension of the chorionic villi through the basal decidua and into the myometrium (Figure 3).

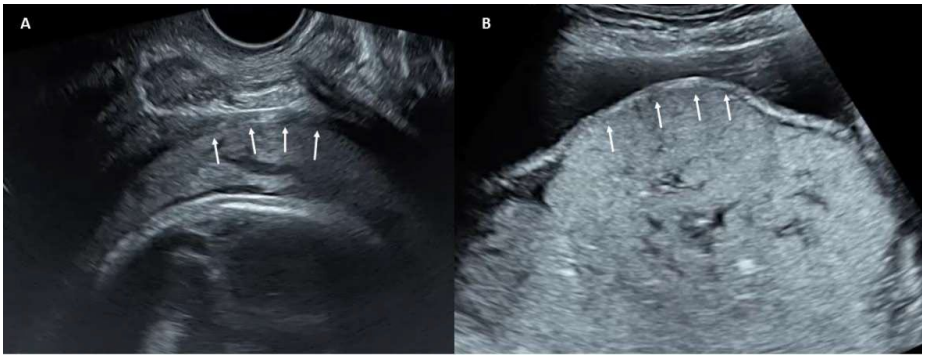


Figure 3. Ultrasound evaluation of the clear zone. A) Case without suspected PAS: the clear zone is correctly identified. B) Suspected PAS: loss of the retroplacental hypoechoic plane or clear zone.

-Abnormal placental lacunae (sensitivity: 70-83%; specificity: 94-96%): Presence of numerous lacunae, including some that are large and irregular (Finberg Grade 3), often containing turbulent flow visible on grayscale imaging, and of high velocity (Figure 4).

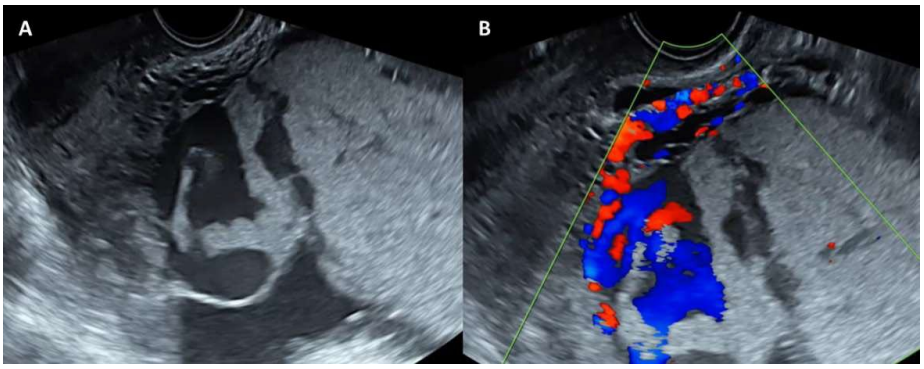


Figure 4. Large and irregular vascular lacunae (A). With Colour Doppler (B), high velocity turbulent flow is observed.

-Bladder wall interruption: Loss or interruption of bright bladder wall (hyperechoic band or 'line' between uterine serosa and bladder lumen).

-Myometrial thinning (Figure 5): Thinning of myometrium overlying placenta to < 1 mm or undetectable.

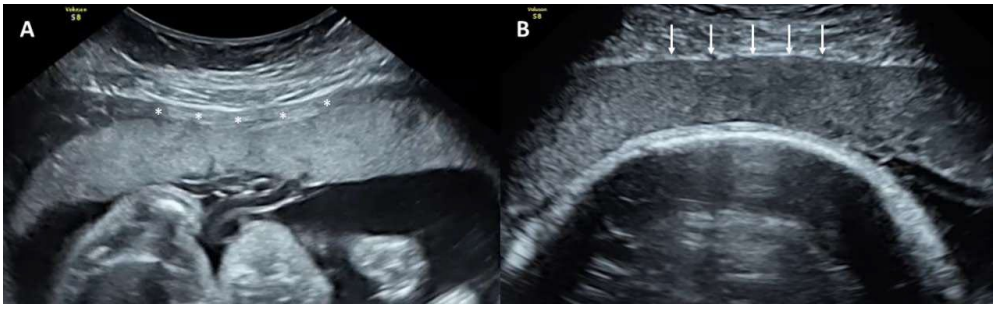


Figure 5. Assessment of retroplacental myometrial thickness. A) Normal myometrial thickness. B) Absence of retroplacental myometrium in a patient with previous caesarean section.

-Placental bulge (Figure 6): Deviation of uterine serosa away from expected plane, caused by abnormal bulge of placental tissue into neighbouring organ, typically bladder; uterine serosa appears intact, but outline shape is distorted.

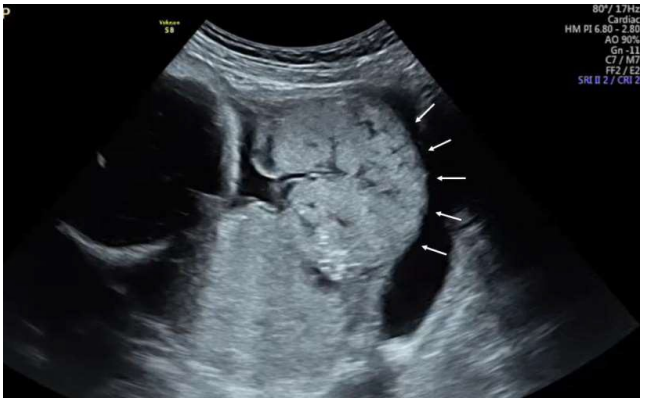

Figure 6. The image shows the abnormal bulging of the placenta towards the bladder (white arrows).

-Focal exophytic mass: Placental tissue seen breaking through uterine serosa and extending beyond it; most often seen inside filled urinary bladder.

- 2D colour Doppler ultrasound findings:

-Uterovesical hypervascularity (Figure 7): Striking amount of colour Doppler signal seen between myometrium and posterior wall of bladder; this sign probably indicates numerous, closely packed, tortuous vessels in that region (demonstrating multidirectional flow and aliasing artifact).

-Subplacental hypervascularity: Striking amount of colour Doppler signal seen in placental bed; this sign probably indicates numerous, closely packed, tortuous vessels in that region (demonstrating multidirectional flow and aliasing artifact).

-Bridging vessels (Figure 7): vessels appearing to extend from placenta, across myometrium and beyond serosa into bladder or other organs; often running perpendicular to myometrium

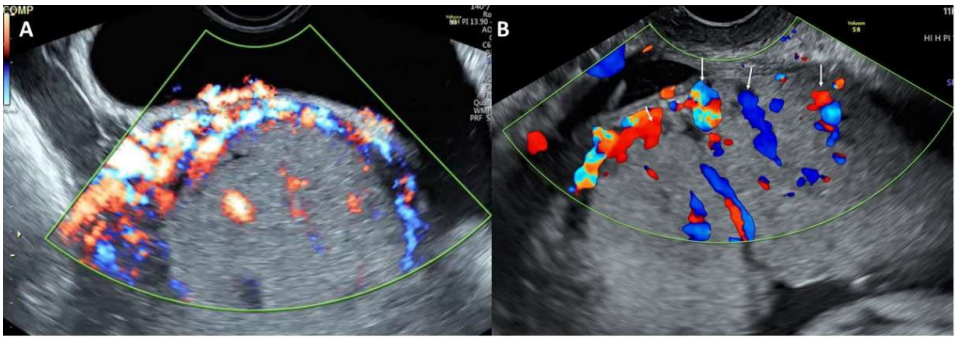


Figure 7. Colour Doppler image showing uterovesical hypervascularization (A) and the presence of bridging vessels (B).

-Placental lacunae feeder vessels: Vessels with high-velocity blood flow leading from myometrium into placental lacunae, causing turbulence upon entry.

The latest systematic reviews, using this new standardised description of the ultrasound signs of PAS, show that loss of clear zone (62%) and the presence of bridging vessels (71%) are the most frequent signs in cases of placenta accreta. In placenta increta, loss of clear zone (85%) and subplacental hypervascularisation (60%) are the most common sonographic signs. Finally, abnormal placental lacunae (82%) and subplacental hypervascularity (54%) are the most frequent sonographic signs in placenta percreta.

Other new ultrasound markers have been recently described. They need to be validated in the coming years.

- Placental thickness > 4.5 cm: sensitivity of 50% and specificity of 90%.
- Separation sign: dynamic sign that consists of applying pressure on the placenta using an ultrasound probe so that the hypoechoic retroplacental clear zone normally observed between the placenta and myometrium disappears. The pressure was then rapidly released to see movements of tissues when they return to their natural position. In cases with normal placentation, the placenta keeps moving away from the probe after the myometrium has snapped back into place. With a negative separation sign, no separate movement of the placenta from the myometrium can be seen. The separation sign was recorded as positive if separation of the myometrium from the placenta was observed in all areas of the placenta. The sign was recorded as negative if the myometrium and placenta moved as one structure and no clear zone could be seen over any part of the placenta after release. In high risk patients, a positive separation sign has a sensitivity and specificity of 95% and 100% respectively for a normal delivery of the placenta.

Some technical aspects should be taken into consideration during ultrasound examination:

1. Transvaginal ultrasound provides data that we cannot obtain with abdominal ultrasound (assessment of the cervical canal, the internal cervical os and the relationship between the leading edge of the placenta and the internal os). Is also allows better assessment of the lower uterine wall and the uterine-bladder interface.
2. Panoramic view (anterior and posterior): it is important to begin the ultrasound examination with a panoramic view that allows the examination of the anterior and posterior uterine wall, as well as the relationship between the location of the placenta and the different anatomical structures. Subsequently, a more detailed study of the areas of interest will be carried out using the zoom.
3. Ultrasound examination should be performed with a full bladder. The contour of the bladder is important to identify the lower uterine segment, thus allowing assessment of the placental location in relation to the caesarean scar. If the bladder is not full, signs such as bladder wall interruption, placental bulge and uterovesical hypervascularity cannot be correctly assessed.
4. Avoid transducer pressure during transabdominal scanning. Excessive probe pressure may cause a loss of the retroplacental clear zone. This mistake is much less likely to occur with the transvaginal probe.
5. Optimisation of colour Doppler. Proper ultrasound settings and knowledge of how changes in these settings will affect the visualisation of the vascular structures are critical to avoid mistakes.

Magnetic Resonance Imaging (MRI)

Although ultrasound is the first-line imaging tool for the screening and diagnosis of PAS, it is well-established that magnetic resonance imaging (MRI) has a role in the diagnosis of PAS, with high sensitivity (83-95%) and specificity (84-94%). MRI has not demonstrated superiority over ultrasound in the diagnosis of PAS except in some specific cases, which are its main indications:

- Patients at high risk of PAS where ultrasound is inconclusive (high maternal BMI, posterior placenta, etc.)
- Suspected placenta percreta. MRI has a better potential to evaluate the invasive depth of PAS including myometrial, parametrial and bladder involvement.

The indication for MRI will always be made after ultrasound evaluation of the patient at risk of PAS. MRI images should be analysed by a radiology team experienced in the evaluation of PAS disorders.

MRI features associated with PAS disorders are the following:

- Placental bulge, which may bulge the uterine surface and invade adjacent structures. It is the most specific sign of placental accretism.
- Heterogeneous signal intensity within the placenta, mainly due to increased vascularisation.
- Heterogeneous signal intensity.
- Bands of hypointensity in T2 sequences, extending from the myometrial interface.
- Decreased myometrial thickness.
- Focal areas of myometrial line loss (thin hypointense line).

The use of intravenous Gadolinium may significantly improve the diagnostic capability, as it allows better delineation of the margin between the placenta and the myometrium. Its use is not safe in pregnancy and is reserved for selected cases in which the benefit outweighs the risk.

### 2.6. PRENATAL MANAGEMENT

Generally, the management for the three different types of PAS disorders is essentially the same. When the diagnosis is made, follow-up will be every two weeks. The indication of MRI will be assessed and, if considered, it will be requested at approximately 32 weeks of gestation.

Given the potential for haemorrhage, it is desirable to optimise haemoglobin values prior to delivery and to correct anaemia, especially iron deficiency anaemia. Most PAS disorders are associated with placenta previa, thus the risk of antepartum haemorrhage increases with increasing gestational age. In case of third trimester bleeding, we will act according to the indications given for symptomatic placenta previa.

Management by a multidisciplinary team significantly reduces maternal morbidity (reduces the amount of blood product transfusion, the need for ICU admission, etc.). It is important to arrange a meeting for surgical planning at 30-32 weeks. The multidisciplinary team should be composed of a maternal-fetal medicine team, a surgical team with expertise in gynaecological/oncological pelvic surgery, anaesthesiologists experienced in the management of massive haemorrhage, neonatologists, interventional radiologists, urologist and blood banks.

At the meeting, each case will be assessed individually, and a consensus will be reached on the different aspects related to termination of pregnancy (gestational age, surgical approach and technique, equipment involved in the surgery, need for ureteral catheters or intravascular balloons, etc.)

The routine strategy for the delivery of women with PAS disorders is planned caesarean section. The optimum timing of such planned delivery remains unclear. Most guidelines consider a reasonable delivery be scheduled at 35-37 weeks, in order to avoid the need for emergency surgery, which is associated with higher maternal morbidity. Elective caesarean section may be considered from 34 weeks in patients presenting with antepartum bleeding, uterine contractions, or preterm premature rupture of membranes.

A pre-anaesthesia evaluation will be performed 2-4 weeks prior to termination of pregnancy and reservation of blood is essential (four units of packed red cells).The estimated average blood loss in these patients is approximately 2-3 litres, so the blood bank must be prepared for major transfusion needs (in our centre it is possible to activate “code red” for the management of massive haemorrhage). The use of rapid infusion systems and interoperative blood salvage systems (to recover blood from the surgical field) with subsequent retransfusion may reduce the need for allogeneic red blood cell transfusion.

A distinction is made between nonconservative management (the most common) and conservative management (for selected cases). Each case should be evaluated by a specialised multidisciplinary team and discussed with the patient in order to plan the most appropriate management.

Informed consent must be provided with discussion of all potential complications (blood transfusion,urinary and/or intestinal lesions, fistula, hysterectomy, etc.). If a PAS disorder is confirmed, the definitive treatment is hysterectomy. However, conservative management may be considered if the patient wishes to preserve her fertility and the situation allows it.

### 2.7. PREOPERATIVE CONSIDERATIONS

Classically, the anaesthetic technique of first choice has been general anaesthesia. However, there is increasing experience in the management of these patients under loco-regional anaesthesia. Both general and regional anaesthetic techniques have been shown to be safe for the surgical procedures required for the delivery of PAS. Therefore, the choice of anaesthetic techniques for caesarean section should be made by the anaesthetist conducting the procedures and the patient. Neonatal outcomes appear to be improving with the use of regional anaesthesia compared to general anaesthesia.

Insertion of intra-arterial balloon occlusion catheter is one of the strategies used to reduce perioperative bleeding. These devices are placed by an interventional radiologist at the

common iliac or internal iliac arteries. Balloon inflation is performed after fetal extraction in order to decrease blood flow to the pelvis. The current evidence does not allow a strong recommendation for its use. In our centre, in selected cases with special surgical complexity and after multidisciplinary evaluation, the placement of intravascular balloons is considered useful in reducing intraoperative bleeding and the need for transfusion and has allowed better visualisation of the surgical field during surgery.

### 2.8. NONCONSERVATIVE MANAGEMENT

Caesarean hysterectomy, with the placenta left undisturbed in situ after delivery of the foetus, is considered the gold standard for the treatment of PAS disorders. Available evidence shows that almost 90% of antenatally suspected cases of PAS underwent caesarean hysterectomy. This radical approach is a high-complexity procedure associated with high rates of complications, the most common being massive haemorrhage that can lead secondarily to coagulopathy with a risk of multiple organ failure and maternal death. Table 2 shows the frequency of the different complications associated with this surgery.

| Table 2. Complications associated with surgery for PAS disorders | |
|---|---|
| Average blood loss | 2-3 L |
| Average packed red blood cellstransfused | 3.5 – 5.4 L |
| Massive transfusions (>10 L) | 5-40% |
| Bladder injury | 7-48% |
| Ureteral injury | 0-18% |
| ICU admission | 15-66% |
| Infection | 18-32% |
| Bowel injury / intestinal obstruction | 2-4% |
| Thromboembolism | 4% |
| Reintervention | 4-18% |
| Maternal mortality | 1-7% |

Surgical technique

- Incision type: midline skin incision is the preferred option for most authors, as it allows adequate access to the uterus and pelvic walls. A large extended transverse incision can be used to avoid a vertical incision. There is no strong evidence to recommend one type of skin incision over another. Therefore, the decision should be made according to the location of the placenta, the degree of invasion and the gestational age.

If the placenta is anterior and extending towards the level of the umbilicus or a hysterectomy is planned, a midline laparotomy is often needed. A low transverse skin incision allowing access to the lower half of the uterus may be adequate if the upper placental edge does not reach the upper segment of the uterus and hysterectomy is not considered.

- Avoid transplacental uterine incision: the uterine incision should be performed avoiding placental transection in order to reduce maternal morbidity related to blood loss from the placental bed, so in many cases the hysterotomy should be a fundal incision. Intraoperative ultrasound of the exposed uterus can help to identify the upper placental edge and guide the decision regarding the site of hysterotomy.

- Avoid placental removal: the most universally accepted procedure in the nonconservative management of PAS is caesarean hysterectomy with the placenta left undisturbed in situ after delivery of the foetus. No attempt should be made to manually remove the placenta because leaving the placenta in situ reduces the risk of massive haemorrhage. In case of intraoperative clinical confirmation of PAS disorder, after fetal extraction, the umbilical cord is tied with suture, cut at the insertion site, and the uterine cavity is closed, leaving the placenta in situ. Uterotonic drugs should not be administered.

  In cases of doubtful diagnosis or prenatal suspicion of focal placenta accreta, if the uterine surface is preserved and there are no signs of placenta increta or percreta, controlled cord traction may be considered to attempt delivery. If spontaneous partial separation of the placenta occurs, conservative strategies should be considered if the area affected by accretism is limited.

- Hysterectomy: in the majority of cases, a total hysterectomy is the preferred method although it is a radical technique. Subtotal hysterectomy may not be effective in the treatment of placenta increta or percreta, especially when cervical involvement is present.

- Minimise urinary tract injuries: urinary tract injuries are described in 29% of the procedures performed in women with PAS disorder (the most common is bladder laceration). Modification of surgical technique can reduce the risk of adjacent organ injury.

  In selected cases, preoperative placement of ureteral catheter (JJ stent) may reduce the risk of urinary tract injury, especially in placenta percreta with lower invasion. Cystoscopy should be considered in cases of suspected bladder invasion. In case of placenta percreta with confirmed bladder invasion, partial cystectomy may be an option.

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## 2.9. CONSERVATIVE MANAGEMENT

Conservative management of placenta accrete is defined as all procedures or strategies aiming to avoid a peripartum hysterectomy.

Expectant management (leaving placenta in situ)

This approach consists of leaving the placenta in situ, totally or partially, and waiting for its complete resorption. The main objective is avoiding the maternal morbidity associated with peripartum hysterectomy. If successful, this strategy will preserve fertility. This strategy can be used alone or in combination with additional procedures oriented to prevent and treat postpartum haemorrhage.

The main situations in which this therapeutic option may be considered are focal placenta accreta, either with prenatal suspicion or due to incomplete removal of the placenta intrapartum, placenta percreta with invasion of surrounding organs and intraoperative diagnosis of PAS.

Antibiotic therapy is usually administered prophylactically to minimise the risk of infection. The treatment of choice will be Piperacillin-Tazobactam 4 g/6h. In case of penicillin allergy, we will use Tigecycline 100 mg (first dose) followed by 50 mg/12h and Metronidazole 500 mg/12h.

The rate of uterine preservation in placenta accreta reported in the literature is high (75%). Only 6% of the cases show severe maternal morbidity (septic shock, peritonitis, uterine necrosis, postpartum uterine rupture, adjacent organ damage, pulmonary oedema, acute renal failure, thromboembolism, or maternal death). A spontaneously complete resorption of the placenta was achieved in 75% of cases with a mean of 13.5 weeks (ratio 4-60 weeks). Experience with conservative management of placenta percreta is more limited. Hysterectomy could be avoided in 50-60% of cases, but 16-42% had severe complications (the most common being maternal sepsis). In the event of complications, delayed hysterectomy will be the definitive treatment.

Different additional procedures have been proposed in the conservative management of PAS to decrease morbidity and accelerate placental resorption.

1. Prophylactic uterine devascularisation. This can be achieved by techniques used to treat postpartum haemorrhage: embolisation, bilateral uterine artery ligation, etc.)
2. The use of methotrexate to hasten placental resolution is not recommended until more evidence on its efficacy and safety is available. The low rate of placental cell division in the third trimester compared with early pregnancy implicates a lower efficacy of this drug in postpartum compared to early pregnancy.

3. Hysteroscopic resection of retained tissues. It seems that this procedure may shorten recovery time in symptomatic patients. The role of prophylactic hysteroscopy in asymptomatic women is unknown.

Before discharge, the woman should be advised about the need for long term monitoring because there is still a risk for bleeding and infection. Patients are seen for outpatient clinic visits weekly for the first 2-3 weeks, and every 2 weeks for the first 2 months. After that, monthly follow-up is needed until complete resorption of the placenta (it may require more than 6 months). The visits include an anamnesis, physical examination (bleeding, temperature, pelvic pain), pelvic ultrasound (size of retained tissue) and laboratory test screen for infection (haemoglobin, leukocytes, c-reactive protein, coagulation test and βhCG). It is important to evaluate serum βhCG at each follow-up visit to verify its progressive decrease until it becomes negative, although this does not guarantee complete placental resorption and it should be confirmed by ultrasound. There is insufficient evidence to recommend the use of MRI for monitoring.

Delayed interval hysterectomy

Delayed hysterectomy is an alternative radical procedure for the management of PAS. It means that a planned hysterectomy will be scheduled 3-12 weeks after the caesarean section. This approach has the advantage of the involution of the uterus and reduction of the vascularity, making the later surgery less risky for the patient and reducing surgical morbidity.

Delayed hysterectomy should be applied in case of unsuspected highly invasive PAS disorder diagnosed at the opening of the abdomen for an elective caesarean section, if the operating team has limited surgical experience in performing complex surgical procedures. There is an associated risk of complications such as coagulopathy, haemorrhage and sepsis during the period between surgeries and, therefore, patients should be followed up.

The Triple-P procedure

A novel technique of uterine preservation has been proposed for PAS disorders. It consists of resection of the area affected by placenta accreta (partial resection of the myometrium) at the time of caesarean section, followed by immediate uterine reconstruction. It aims to combine the advantages of both conservative treatment (preservation of the uterus) and nonconservative management (minimal risk of haemorrhage and infection). The steps of the Triple-P procedure include the following:

1. Preoperative placental localisation using transabdominal ultrasound to identify the upper edge of the placenta in order to deliver the foetus by an incision above the upper placental edge.
2. Pelvic devascularisation (preoperative placement of intra-arterial balloon catheters).
3. No attempt to remove the placenta, myometrial excision of affected area and uterine repair. If the posterior bladder wall is affected, the placental tissue invading the bladder is left in situ, to avoid cystotomy.

This procedure may be indicated in cases of non-extensive or localised placental accretism in uterine zones other than the segment. Removal of the area completely invaded by placental tissue and subsequent uterine reconstruction with surrounding healthy myometrium results in a low recurrence rate (2%) in future pregnancies.

Long-term obstetric outcomes and fertility

Successful conservative treatment for PAS disorders does not appear to compromise subsequent fertility. Subsequent pregnancies are at increased risk of adverse maternal outcomes: recurrent PAS disorders (20-30%), postpartum haemorrhage (5-20%), uterine rupture and peripartum hysterectomy.

Long-term complications include intrauterine adhesions and secondary amenorrhea. At the moment, there are no data on pregnancies after the conservative or Triple-P surgical procedure.

## 3. VASA PREVIA

Vasa previa is defined as the presence of fetal vessels in the membranes, unprotected by placental tissue or cord, crossing through the lower uterine segment or over the cervix. It can be classified into two main types (Figure 8):

- Type I: there is a velamentous cord insertion and vessels run between the umbilical cord insertion site, through the fetal membranes, and the placenta.
- Type II: the free vessels course through the membranes between two lobes of the placenta in the lower segment. It can occur in pregnancies with a bilobed or succenturiate placenta.

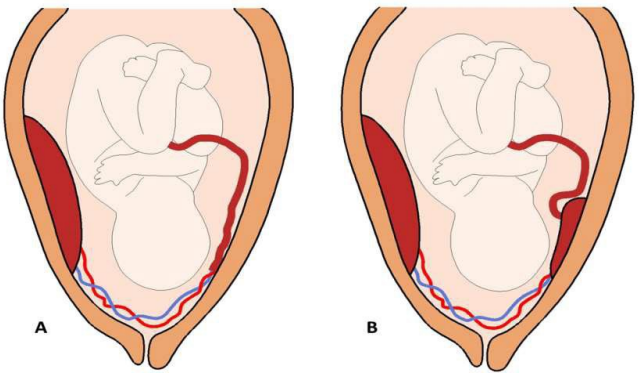


Figure 8. Types of vasa previa. A) Type I. B) Type II

The overall incidence is low, ranging from 1/1275-2500 pregnancies, but it increases in the presence of risk factors. Between 80-90% of cases will have one of the following risk factors: IVF pregnancy (incidence up to 1/260), velamentous or marginal cord insertion into the placenta, resolving placenta previa, bilobed or succenturiate placenta and multiple pregnancy.

### 3.1 CLINICAL FINDINGS

The main sign is the occurrence of metrorrhagia after spontaneous or artificial rupture of the membranes associated with suspected fetal distress (pathologic CTG recording: bradycardia, sinusoidal pattern, etc.). Rupture of vasa previa may result in catastrophic delivery events, including fetal or neonatal death, severe fetal anaemia and cerebral palsy. Exceptionally, bleeding may occur without rupture of membranes.

### 3.2 DIAGNOSIS

Prenatal diagnosis of vasa previa significantly improves perinatal outcomes (increased survival, reduced neonatal morbidity and reduced need for neonatal transfusion).

Transvaginal and transabdominal ultrasound using colour and pulsed wave (spectral) is the first line diagnostic method. Ultrasound findings of suspected vasa previa are the following:

- Visualisation of vessels on grayscale imaging as circular or linear hypoechoic structures in the lower uterine segment (it can be recognised as either “bubbles” or “lines” in the lower segment.
- Arterial or venous vessel at the internal cervical os. Pulsed wave (spectral) Doppler is helpful to determine the origin of the vessel.
- Velamentous or marginal cord insertion into the placenta. Try as far as possible to visualise the path of the vessel up to its insertion into the placenta or umbilical cord.

Differential diagnosis includes free cord loop, chorioamniotic membrane separation, uterine varicosities of maternal origin or an amniotic band.

Screening for vasa previa is not recommended as part of the routine anatomic survey due to its low incidence in the absence of associated risk factors. However, it is relatively easy to do and may be cost-effective. It is recommended to perform a targeted screening for vasa previa in the routine second and third trimester ultrasound in women presenting with risk factors: low-lying placenta, accessory placental lobe, succenturiate placenta, velamentous or marginal cord insertion and multiple gestation.

The screening ultrasound should include systematic evaluation of the insertion site of the umbilical cord into the placenta and assessment of the location and morphology of the placenta. Other diagnostic methods may include MRI, direct visualisation with an amnioscope or palpation of vessels during vaginal examination.

### 3.3 MANAGEMENT

Asymptomatic vasa previa

Ultrasound monitoring (confirmation of the diagnosis, evaluation of placental location and measurement of cervical length) will be performed every month until 32 weeks of pregnancy, and every 2 weeks thereafter.

Vasa previa may resolve in up to 15-20% of cases. In cases where vasa previa is still suspected at 34-35 weeks, an elective caesarean section will be scheduled around 35 weeks (between 34 and 37 weeks). In case of significant cervical shortening (cervical length<15 mm) or uterine contractions, admission of the patient for maternal and fetal monitoring and administration of fetal lung maturation may be indicated. Termination of pregnancy should be individualised depending on the gestational age and clinical situation of the patient.

Symptomatic vasa previa

Emergent caesarean section is indicated in case of antepartum or intrapartum bleeding in a patient with a previous diagnosis of vasa previa. In these cases, early cord clamping should be performed. An anatomopathological study of the placenta is recommended to confirm the diagnosis.

## 4. MANAGEMENT OF THIRD TRIMESTER HAEMORRHAGE

Third trimester bleeding is an obstetric emergency associated with increased maternal and fetal morbidity and mortality. There is an increased risk of preterm delivery, fetal death and IUGR. On the other hand, there is also a higher rate of induction of labour at term. The following aspects should always be considered in the event of third trimester haemorrhage: gestational age, cause of the bleeding, amount of bleeding and maternal/fetal involvement. Every effort should be made to establish an accurate, early diagnosis, thus determining the management to be employed. The two most common causes are placental abruption and placenta previa, which account for about half of all cases.

The management of third trimester bleeding will be specific to the suspected diagnosis. It may be physiological bleeding when the pregnant woman is expelling the mucus plug. It can be seen as a pink or little bloody increased vaginal discharge due to rupture of small capillaries during the initial changes of the cervix (cervix softening and initial dilation). It can appear from several days to a few hours before delivery. If third trimester bleeding is attributed to the loss of the mucus plug (after excluding other causes by anamnesis and physical examination), the pregnant woman will be discharged and will continue with her usual obstetric follow-up. The same management is needed in case of self-limited spotting.

When evaluating a third-trimester bleeding greater than spotting and/or persistent, admission under observation will be considered. The initial management of significant bleeding in late pregnancy is similar regardless of the aetiology:

- An examination starts with the review of vital signs, particularly blood pressure and maternal fetal heart rate, for signs of hypovolemia. Hypotension, tachycardia and maternal symptoms of haemodynamic instability are important indicators, and women with these signs require immediate intravenous access, fluid resuscitation, and the availability of blood products.
- Targeted anamnesis with particular attention to details of a recent history of bleeding in the present pregnancy and a history of hypertension or preeclampsia.
- Physical examination: the abdomen is palpated for uterine size, tenderness, and tonicity. A digital cervical examination is not recommended when bleeding occurs during later pregnancy until ultrasonography confirms normal placental and vessel location. Careful speculum examination can be done to rule out local causes of bleeding (cervical ectropion, cervical polyps, cervicitis, etc.)
- Transvaginal ultrasonography: a normal placenta and normal cord and vessel insertion exclude placenta previa and vasa previa as the cause of the bleeding.
- Obstetric ultrasound: evaluation of the placenta (haematomas), membranes, estimated fetal weight, amount of amniotic fluid and assessment of fetal anaemia.
- Continuous fetal monitoring is recommended. Persistently non-reassuring fetal heart rate tracing may require emergency caesarean delivery before the aetiology of the bleeding is established.
- Laboratory test (cell blood count, coagulation test) and blood reservation.

The administration of corticosteroids for fetal lung maturation and tocolytic treatment depend on gestational age, origin of the bleeding and risk of preterm delivery. Women who are RhD negative should receive anti-D immunoglobulin (intramuscular injection of 300 µg or 1500 UI).

Once the diagnosis has been established, treatment is aimed at the specific cause. In case of unknown cause, termination of pregnancy may be considered if gestational age ≥37 weeks. In case of patient discharge, outpatient follow-up will be every 1-2 weeks.

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