Placental pathology: A review of placenta previa, placental abruption and placenta accreta

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doi: 10.1029/WFSA-D-18-00010

INTRODUCTION
Although placental pathology is relatively rare, escalation in associated risk factors – including history of caesarean delivery (CD) - portend an increased incidence in placenta-related morbidity and mortality. Between 1990 and 2014, the global CD rate increased an average of 4.4% per year from 12.4% to 19.1% overall. Regional increases in CD rates are variable. Eastern and Western sub-regions of Africa report CD rates less than 4%, while China’s CD rate exceeds 54%. Many middle- and high-socioeconomic status countries have reported an almost 10-fold increase in the incidence of placental pathology. This trend carries implications for increased risk of emergent delivery, preterm birth and peripartum haemorrhage.

DEFINITIONS
Placental pathology comprises conditions related to abnormal implantation and separation. Placenta previa is abnormal placental tissue development, overlying or in close proximity to the internal cervical os, in advance of the presenting fetus. Placenta previa can be “total” (completely covering the os of the cervix) or “partial”; the condition is termed “marginal” if the placenta lies within 2 centimetres of but does not cover the os. Placental abruption refers to complete or partial separation of the placenta from the decidua basalis layer of the uterine endometrium, occurring progressively or suddenly before delivery and leading to uteroplacental insufficiency. Diagnoses on the abnormally invasive placenta (AIP) or placenta accreta spectrum (PAS) include placenta accreta vera (direct placental adherence to uterine myometrium), placenta increta, (invasion of the placental chorionic villi into the myometrium), and placenta percreta (invasion through the myometrium into the serosa and possibly adjacent organs, usually the bladder). Placenta accreta is the least severe and most common presentation (78%) of PAS, while placenta percreta (also termed “morbidly adherent placenta” MAP), though rare (5%), is most severe.

INCIDENCE
The worldwide prevalence of placenta previa is between 4 to 5 per 1000 pregnancies. The highest prevalence was detected in Asia (12.2 per 1000 pregnancies), and a lower prevalence was reported in Europe (3.6 per 1000 pregnancies), North America (2.9 per 1000 pregnancies) and Sub-Saharan Africa (2.7 per 1000 pregnancies). Seven to twelve of every 1000 pregnancies in North America end in placental abruption, with the highest trends reported in the United States (US), especially among African Americans. European countries have demonstrated a temporal decline in placental abruption with a prevalence of 3 to 6 per 1000 pregnancies. Complicated by variation in definition of diagnosis and clinical confirmation, estimates for the incidence of placenta accreta range from 1.7 to 900 per 100,000.
deliveries, with the highest incidence reported in Israel. The reported rate of placenta accreta in the US is 40 per 100,000, in the United Kingdom is 17 per 100,000, and the reported average incidence worldwide is 189 per 100,000 deliveries. Variation in birth rate and inter-pregnancy intervals will potentially delay the increased incidence of PAS disorders corresponding to rising CD rates. The International Federation of Gynaecology and Obstetrics estimates that for the US alone, if the CD rate continues its current trend, the 2020 CD rate will be greater than 50%, resulting in over 4500 annual cases of PAS disorders and 130 deaths due to resulting obstetric complications.

**RISK FACTORS**

Several studies have investigated possible risk factors for placental pathology. Advanced maternal age is associated with increased risk of placenta previa. Compared to women <20 years old, primiparous women >39 years old are at an almost 10-fold higher risk of placenta previa. Other risk factors include previous placenta previa, multiparity, multifetal gestation, smoking and cocaine use, male fetal gender, prior uterine surgical history or myometrial scarring, prior pregnancy terminations, polyhydramnios, and birth intervals < 1 year or >4 years. The direct relationship existing between the risk of placenta previa and prior history of CD is most significant. Gurol-Urganci et al found that risk of placenta previa increased by 60% after a women’s first CD.

History of CD has also been studied as a risk factor for placental abruption. Getahun et al found that following their first birth by CD, women were more likely to have a placental abruption in their second pregnancy compared to women who had a vaginal first birth. Two consecutive CDs were associated with a 30% increased risk of placental abruption in the third pregnancy. A population-based, retrospective cohort comparison of risk factors between placenta previa and placental abruption among primiparous and multiparous singleton pregnancies in the US found the effects of advanced maternal age, parity and previous CD to be stronger for risk of placenta previa. The same study also found cigarette smoking, two or more alcoholic beverages per week during pregnancy and prenatal care to have stronger effects on risk of placental abruption. The authors concluded that risk of placenta previa is more likely affected by conditions prior to pregnancy whereas risk of placental abruption is more likely affected by conditions occurring during pregnancy. Other conditions associated with placental abruption include preclampsia and hypertensive disease, premature rupture of membranes, chorioamnionitis, cocaine abuse and trauma. Historically, women with placenta previa were found to be 13 to 14 times more likely to have a placental abruption than women without, possibly due to inadequate placental development at the abnormal implantation site. A growing number of studies suggest that environmental conditions, including variation in temperature, can affect the risk of placental abruption.

The most important risk factor found in approximately half of all cases of PAS disorder is placenta previa. Existence of placenta previa combined with history of CD synergistically increases the risk of placenta accreta. Women with placenta previa face a 3% risk of an abnormally invasive placenta if without prior uterine surgery, versus an 11% risk having a history of one previous CD, a 40% risk having two previous CDs and greater than 60% risk having a history ≥ 3 CDs. Interestingly, the incidence of placenta accreta was found to be <1% in the absence of placenta previa, unless the woman had undergone ≥5 previous CDs. More recent, large population-based pregnancy cohort study in Scandinavian countries confirmed similar elevation in risk of abnormally implanted placenta after one prior CD versus after ≥ 3 CDs. This study also newly identified history of postpartum haemorrhage as a risk factor for placenta accreta.

A study comparing the rate of subsequent placenta accreta in women who had undergone a primary CD without labor to the rate in women who had undergone primary emergency CD following labor onset. After a primary elective CD, women were found to be three times more likely to develop placenta accreta in a subsequent pregnancy complicated by placenta previa. Dowes et al reported a greater than two-fold increased risk of placenta previa in women undergoing previous pre-labor CD compared to women after previous vaginal delivery that was not associated with women undergoing previous intrapartum CD.

**PRESENTATION**

Although the obstetric anaesthesiologist is seldom the primary diagnostician of placental pathology, recognition of characteristic signs and symptoms are critical in expeditious detection and timely management. The classical presentation of placenta previa is painless vaginal bleeding during the second or third trimester. The first bleeding episode commonly occurs preterm, is unrelated to any inciting event, and typically resolves spontaneously without maternal or fetal compromise. Unlike placenta previa, placental abruption often (however not always) presents with uterine tenderness and/or increased uterine activity. Some cases of placental abruption may present with painless vaginal bleeding commonly occurring in late pregnancy, or as idiopathic preterm labor with a broad variety of non-reassuring fetal heart rate patterns. (A helpful overview of cardiotocography interpretation has been previously published).

**DIAGNOSIS**

The gold standard for placental pathology diagnosis is transvaginal ultrasound. While inexpensive and efficient to perform, ultrasound is subject to operator-dependence and limited availability. The expense and expertise required for magnetic resonance imaging (MRI) is not practical in most low- and middle-income countries—and in most obstetric emergencies—yet its described superior sensitivity and specificity compared to that of ultrasound may serve as a promising diagnostic tool in the future. Variable accuracy of antenatal imaging may explain why two-thirds of PAS disorders remain undiagnosed until delivery.

Placental abruption is primarily diagnosed by history and clinical presentation and is often a diagnosis of exclusion in the parturient presenting with vaginal bleeding and no other identified etiology. Normal findings do no exclude the diagnosis.

**MATERNAL COMPLICATIONS**

Abnormal placentation increases the likelihood of serious
complications, such as maternal haemorrhage, peripartum hysterectomy and death. Parturients with placenta accreta are more likely to undergo CD and to require hysterectomy. One third of peripartum coagulopathies are attributed to placental abruption. The increased antepartum bleeding risk of patients with placenta accreta is primarily related to coexisting placenta previa and is greatest at the time of delivery.

Placental pathologies can also be associated with increased risk of peripartum and chronic cardiovascular disease. Placenta previa is associated with higher rates of preeclampsia. Women with a history of placental abruption experience a 3 to 4-fold increased risk of longterm cardiovascular morbidity and mortality.

FETAL AND NEONATAL COMPLICATIONS

Impaired uteroplacental perfusion caused by abnormal placentation threatens fetus wellbeing. In the US, parturients with placental abruption are five times more likely to deliver preterm and face a perinatal mortality rate of 12%. Babies born to women with placenta accreta are more likely to be born preterm and to require neonatal resuscitation and intensive care. Prematurity remains the most common cause of neonatal morbidity and mortality; however, abnormal placental implantation can also increase the risk of fetal growth restriction.

Placenta previa may be associated with an increased risk of major congenital malformations.

OBSTETRIC MANAGEMENT

The obstetric management of placental pathology is based upon symptom severity and the maturity and condition of the fetus. Consensus encourages individualization of care that delays delivery of stable patients with placenta previa, reducing sequelae of premature birth. Positive outcomes have resulted from reservation of outpatient management for stable patients without bleeding for at least 48 hours and with easily available access to a tertiary obstetric and neonatal care centre. American Maternal-Fetal Medicine (MFM) recommendations promote planned delivery of parturients with stable placenta previa and without obstetric complications at 36 to 37 6/7 weeks. Expectant inpatient management of the first bleeding episode has been shown to prolong pregnancy by an average of four weeks. Corticosteroid administration at 24 to 34 weeks is advised to accelerate fetal lung maturity; however delivery should not be delayed for corticosteroid administration in women with active haemorrhage in the late preterm period. Indicators for delivery of placenta previa include active labor, persistent bleeding, and 36 weeks gestational age. Predictors for emergent delivery include history of CD, antepartum bleeding and blood transfusion requirement. A direct relationship has been found between number of bleeding episodes and risk for emergent delivery.

Definitive obstetric management of placental abruption consists of delivery of the infant and placenta. Delivery may be delayed to permit fetal maturation in a preterm parturient with minimal abruption and without evidence of maternal or fetal distress. Vaginal delivery may be appropriate if the fetus is at near term and the maternal and fetal conditions are reassuring. Vaginal delivery is also preferred for stable patients with placental abruption and intrauterine fetal demise. A gestational age of 34 to 37 weeks has been identified as the most appropriate planned CD time for parturients with PAS disorder due to increased risk for severe maternal morbidity associated with emergent bleeding. An urgent CD is indicated for any signs of maternal or neonatal instability.

Multidisciplinary care - specifically experienced personnel plus resources for complex obstetric/surgical intervention and massive haemorrhage resuscitation - reduces maternal morbidity. International guidelines recommend the adoption of formal protocols for prevention and treatment of PPH, including the application of simulation training for dedicated care teams. Obstetric management ranges from conservative techniques aiming to avoid peripartum hysterectomy to scheduled caesarean-hysterectomy with placenta in situ. Current recommendations include reserving prophylactic intra-arterial balloon catheters for “well-counselled” women with a strong desire for fertility preservation, those who decline blood products, and those with unrespectable placenta percreta. Partial myometrial resection of the accreta area and immediate uterine reconstruction and bladder reinforcement is specifically recommended for low- and middle-income countries where interventional radiology is unavailable. Successful management of MAP with uterine conservation has been reported to retain desired fertility and reduce surgery-related morbidity. Hysterectomy is considered the definitive treatment for ongoing, life-threatening PPH of any etiology, however should be weighed against the costs of permanent sterility and potential surgical complications. Patients treated at institutions with in-hospital obstetric and anaesthesia physicians, immediately available gynaecology/oncology specialists, a blood bank and interventional radiology services encounter less morbidity. Early and active involvement of the anaesthesiologist (including prenatal evaluation, admissions planning “huddles”, call-team hand-offs and postpartum rounds) reduces patient risk and improves quality of clinical care.

ANAESTHETIC MANAGEMENT

All patients with antepartum vaginal bleeding should undergo anaesthesia evaluation, including:

- physical examination of the patient and airway
- assessment of intravascular volume status
- establishment of large-gauge, intravenous cannulas for rapid volume resuscitation, and
- collection of a complete medical, surgical and obstetric history.

Patients with placental pathology face increased risk of peripartum blood loss, possibly indicating a preoperative measurement of haemoglobin concentration and blood-type and screen or crossmatch. If the parturient requires transfusion before blood is crossmatched, type-specific or type-O, Rh-negative blood should be administered. International guidelines recommend estimation of blood loss, possibly indicating a preoperative measurement of haemoglobin concentration and blood-type and screen or crossmatch. If the parturient requires transfusion before blood is crossmatched, type-specific or type-O, Rh-negative blood should be administered. International guidelines recommend estimation of blood loss by clinical signs and symptoms (i.e., tachycardia, tachypnea or hypotension) instead of visual approximation. A readily-available, regularly-serviced receptacle containing PPH emergency equipment is also recommended.

Anaesthetic technique will depend on several factors, notably, the indication and urgency for delivery. Expert consensus supports
neuraxial technique for scheduled CD of placenta previa. Parturients with severe placental pathology have also been reported to tolerate complex surgery of prolonged duration under neuraxial technique. The sympathetic block induced by neuraxial anaesthesia (and consequent low arterial pressures) may beneficially decrease blood loss and blood transfusion requirement. Hong et al\textsuperscript{43} found lumbar epidural anaesthesia to be associated with more stable blood pressures after delivery, lower transfusion rates and lower transfusion volumes without significant differences in haematocrit concentrations, operative times, intraoperative blood loss or neonatal Apgar scores compared to those for patients under GA. Combined spinal-epidural technique to accommodate prolonged surgical duration may be acceptable for parturients without active bleeding or coagulopathy; however, the possibility of rapid fluid or blood resuscitation should be discussed preoperatively to prepare the awake patient. When neuraxial anaesthesia is planned, precautions should be taken to address obstacles in conversion to general anaesthesia (GA) (e.g., difficult airway, undiagnosed placenta accreta). International literature reports a conversion to GA risk of 8 - 45%: the higher rates occur in situations without prior suspicion of placental pathology and in low-income countries.\textsuperscript{42} Reasons for intraoperative conversion of neuraxial to GA after delivery include rapid volume resuscitation, patient pain and improved surgical exposure.\textsuperscript{45} Conversion of neuraxial to GA during caesarean-hysterectomy is associated with a history of > 2CDs, longer surgical durations, and > 3 units of PRBCs transfused.\textsuperscript{49} Reported times from the obstetrician decision to the caesarean delivery of the newborn are shortest for induction of general versus epidural or spinal anaesthesia\textsuperscript{44,45}; however, neonatal respiratory complications appear to improve using neuraxial technique, likely by avoiding placental transfer of volatile agents.\textsuperscript{42}

For haemodynamically unstable, actively bleeding and/or coagulopathic patients, rapid sequence induction of GA with endotracheal tube has been the traditionally preferred technique. Ketamine – or etomidate, where available—is an appropriate alternative to low dose propofol for patients with uncorrected hypovolemia.\textsuperscript{46} Placental abruption presents increased risk for persistent haemorrhage due to uterine atony or coagulopathy, requiring aggressive monitoring and repletion of coagulation factors, especially fibrinogen.\textsuperscript{27} Oxytocin is the first choice uterotonic agent for prevention of PPH. Dosing regimens vary broadly from slow intravenous (IV) bolus up to 10 IU to infusion of up to 40 IU over 4 hours\textsuperscript{48}, or 10 IU intramuscular (IM) injection. Side-effects of oxytocin include hypotension, tachycardia and myocardial ischemia, and receptor desensitization during prolonged exposure is associated with increased risk of PPH and transfusion. Carbetocin – the long-acting, heat-stable, oxytocin analogue -given 100mcg IM was found to be noninferior to oxytocin in preventing PPH.\textsuperscript{49} Randomized controlled trials comparing different dose regimens for each agent are needed. Administration of antifibrinolytic agent tranexamic acid (TXA) within 3 hours of recognizing postpartum haemorrhage (e.g., 1 gram IV at a rate of 100mg/min), has been found to significantly reduce maternal mortality due to bleeding of any etiology.\textsuperscript{50,51} Although supported by little evidence\textsuperscript{52}, prophylactic administration of TXA where blood product availability is limited is an area of recent focus to reduce global maternal mortality.\textsuperscript{53}

**CONCLUSION**

Although relatively rare, placental pathology presents significant risk of maternal and perinatal morbidity and mortality. Awareness of increasing trends in risk factors associated with abnormal placental implantation and separation is critical to the anaesthesiologist’s management of these conditions in order to improve obstetric outcomes worldwide.

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SUGGESTED READING (from references)


