

# New evidence-based diagnostic and management strategies for placenta accreta spectrum disorders

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## **Abstract**

The increasing incidence of caesarean delivery (CD) has resulted in a rise in placenta accreta spectrum (PAS), adversely impacting maternal outcomes globally. Currently, more than 90% of women diagnosed with PAS present with a placenta previa (previa PAS). Previa PAS can be reliably diagnosed antenatally with ultrasound, it is unclear if magnetic resonance imaging improves diagnosis beyond what can be achieved by skilled ultrasound operators. Therefore, any screening programme for PAS will require improved training in diagnosis of placental disorders and development of targeted scanning protocols. Management strategies for previa PAS vary depending on the accuracy of prenatal diagnosis, findings at laparotomy and local surgical expertise. Current epidemiological data for PAS are highly heterogeneous, mainly due to wide variation in the clinical criteria used to diagnose the condition at birth. This significantly impacts research into all aspects of the condition but especially comparison of the efficacy of different management strategies.

**Key Words:** Placenta accreta; increta; percreta; ultrasound imaging; caesarean hysterectomy; prenatal diagnosis.

## Summary

The recent rapid increase in caesarean delivery (CD) rates has changed the epidemiology of placenta accreta spectrum (PAS) worldwide from a rare, serious, pathological condition to an increasingly common major obstetric complication. The risk of placenta previa increases following CD, and women presenting with a low-lying/placenta previa and history of CD are at the highest risk of PAS (previa PAS). Prenatal identification has been shown to improve the outcomes in PAS. In specialist centres, the diagnostic accuracy of ultrasound in identifying previa PAS is over 90% so there is often no need for magnetic resonance imaging (MRI). Exceptions include where the placenta cannot be fully interrogated with ultrasound, for example a posterior previa with extensive fetal shadowing. Ultrasound screening for PAS requires development of targeted training with standardised protocols and reporting tools. A planned preterm caesarean hysterectomy with the placenta left *in situ* is the strategy often used for PAS although conservative management may be considered when the woman wants fertility preservation. Access to specialist centres with multidisciplinary expertise and essential resources such as blood products and neonatal and maternal intensive care is pivotal to improving the management of these complex cases. There are no RCTs or prospective, well-controlled observational studies comparing surgical and conservative management strategies. The evaluation of epidemiological trends and management outcomes has been limited to date by poor quality study design, in particular by the lack of a standardized description of the clinical grade of PAS at birth and histopathologic confirmation of the clinical diagnosis.

## PLACENTA ACCRETA SPECTRUM

### **A. Historical perspective**

Irving and Hertig were the first to publish a case series of placenta accreta in 1937 and included a literature review of the cases published before then. They reported that the first case of “placenta accreta” may have been Mrs. Galla who died at delivery in 1588 and was found at autopsy to have a placenta previa “firmly adherent” to the internal os. Langhans (2) and Hart (3), described the histology of placenta accreta at the end of the 19<sup>th</sup> century, and used the term “adherent placenta,” whereas Baisch (4) was the first author to use the term “placenta accreta” in 1907.

In 1966, Lukes et al (5) proposed a histological classification for placenta accreta based on the depth of the villous penetration of the myometrium. They separated placenta accreta into three categories: *placenta adherenta or creta* (PC) when the villi adhere directly to the myometrium without a decidual interface, *placenta increta* (PI) when the villi invade the myometrium and *placenta percreta* (PP) when the villi invade the full thickness of the uterine wall including the serosa (Figure 1). Percreta villi can also invade organs, tissues and the pelvic vasculature beyond the uterine serosa. This terminology is still used today by most pathologists. Luke et al., also highlighted the fact that villous penetration of the myometrium is rarely uniform and that both adherent and invasive villi may co-exist in the same specimen (Figure 2). The term placenta accreta spectrum (PAS), which includes all grades of abnormal placentation, is now the preferred umbrella term to define this heterogeneous condition, and has been recently endorsed by the FIGO (6), the RCOG (7) the ACOG and the SMFM (8).

### **B. Modern perspective**

The first descriptions of PAS in the international medical literature (9,10) coincided with the first published reports on outcomes of contemporary caesarean delivery (CD) techniques, one century ago (11,12). A CD was rarely performed in the first half of the 20<sup>th</sup> century. Unsurprisingly, only one of the 20 cases personally treated by Irving and Hertig in 1937 occurred after CD (1). CD has now become an essential component of modern maternity care and epidemiological studies have shown a strong association between CD rates, number of prior CDs and the incidence of PAS (13). The steady increase PAS can be directly linked with the increase in CD rates in both low and high-resources countries, with rates rising from less than 7% in 1990s to well over the World Health Organization (WHO) recommendation of 15% in just 2 decades (14). In middle-income countries such as Turkey, Mexico, Brazil and Egypt, more than half of all births are via caesarean, mostly elective. Consequently, in countries with high-birth rates, like Egypt, the prevalence and negative impact of PAS will rapidly outweigh the benefits of improved access to quality obstetric care.

Increased CDs have also increased the incidence of placenta previa (15). The relative risk for placenta previa increases with each prior CD from 4.5% (95% CI 3.6 to 5.5) for one to 7.4 (95% CI 7.1 to 7.7) for two, 6.5 (95% CI 3.6 to 11.6) for three, and 44.9 (95% CI 13.5 to 149.5) for four or more when compared to vaginal delivery (16). Overall, the incidence of placenta previa increases from 10/1000 deliveries after one previous CD to 28/1000 after three or more CDs (17). Similarly, in women with prior CD presenting with a placenta previa, the risk of PAS is 3%, 11%, 40%, 61%, and 67% for first, second, third, fourth, and fifth or more CD, respectively (18). The UK national case-control study reported that the incidence

of PAS increases from 1.7 per 10,000 to 577 per 10,000 births in women presenting with a placenta previa and a prior CD (19).

Currently, more than 90% of women diagnosed with PAS also have a placenta previa (20), the combination of both conditions leads to high maternal morbidity and mortality due to massive haemorrhage at the time of birth (21,22). Maternal mortality of placenta previa with percreta has been reported to be as high as 7% of cases (23). The 2017 report from the UK and Ireland Confidential Enquiries into Maternal Deaths indicated that although there was no significant change in maternal death rates in the UK, between 2010–12 and 2013–15, there has been an increase in the number of deaths of women presenting with PAS (24).

PAS is not exclusively a consequence of CD and has been reported in primiparous women with a history of operative hysteroscopy, suction curettage, surgical termination and endometrial ablation (25,26). In fact, any uterine pathology such as bicornuate uterus, adenomyosis, submucous fibroids and myotonic dystrophy or any procedure causing surgical damage to the uterine wall integrity has been associated with PAS (13,25). Accreta placentation can occur after myomectomy but the risk is relatively low (27). Finally, in vitro fertilization (IVF), especially with cryopreserved embryos increases the risk for PAS from between 4- to 13-fold. PAS is primarily a consequence of modern obstetric and reproductive practices, and is likely to become increasingly common as women delay childbearing, require reproductive assistance and enter pregnancy with medical co-morbidities (25).

## **DIAGNOSING PAS AT BIRTH**

The clinical diagnostic criteria of PAS used since the publication by Irving and Hertig (1) in 1937 have been heterogeneous and vague (29,30). Not surprisingly, the reported prevalence of PAS at delivery has been highly variable ranging between 1 in 1000 and 1 in 40,000 and deliveries (13) and our recent systematic review and meta-analysis on the prevalence of PAS indicates rates ranging between 0.01% and 1% (30). An expert review of literature published between 1977 and 2012 found that the pooled prevalence was 1 in 588 deliveries, however this reflected data from referral centres, which treat more cases than in the general population (28). Histopathologic examination remains the confirmatory gold standard, but most current authors of PAS cohort series do not provide complete and transparent information on *both* clinical and histopathological findings. The clinical and pathologic diagnostic standards have stagnated, with little change since 1937.

#### **A. Clinical diagnosis**

The clinical signs of PAS disorders, in particular in cases of a partially adherent placenta, can be very similar to those of placental retention, i.e. difficult manual or piecemeal removal of the placenta; absence of spontaneous placental separation 20-30 min after birth, despite active management including bimanual massage of the uterus, use of oxytocin and controlled traction of the umbilical cord; retained placental fragments requiring curettage after vaginal birth and; heavy bleeding from the placental bed after placental removal during CD (33-38). Some authors include sonographic evidence of retained placenta tissue requiring curettage (33). These various criteria are used by many authors and explain the wide heterogeneity in the evaluation of the prevalence of PAS in the general obstetric population (30). A retained placenta, which is merely entrapped inside the uterine

cavity owing to constriction of the cervix, should not be included in the category of PAS nor should cases where a retained placenta is removed whole or spontaneously delivered within 24h after birth.

Macroscopic changes detected upon entry to the abdomen can also raise suspicion to the presence of accreta placentation such as tortuous large varicosities seen on the serosal surface, distended bulging lower uterine segment, or direct extension of placenta onto the uterine surface, bladder, or pelvic sidewalls (38). Most of these gross changes are common in multiparous and thus at the other end of the spectrum it is pivotal to make the differential diagnosis between a scar dehiscence and a placenta percreta. Women with a history of multiple lower-segment CDs may have an anterior myometrial wall largely consisting of fibrotic scar tissue (31,32). Myofibre loss and the excessive accumulation of collagen impairs the function of muscular tissue, which loses elasticity and becomes more prone to dehiscence and rupture in subsequent pregnancies. Lower-segment dehiscence becomes more pronounced as pregnancy advances due to the pressure of the fetus and uterine contractions, both of which increase the disruption of the fibrotic tissue. This can create a large uterine “window” made only of serosa, and through which a portion of the placenta is visible without any villous tissue truly invading the serosa and/or the surrounding myometrium (Figure 3). The high prevalence of PAS in some population studies (33-37) and rates of successful conservative surgical management (39-42) in recent cohort studies may reflect inclusion of a large proportion of cases of non-accreta placental retention and/or uterine dehiscence in their data.

Several authors have also report using the World Health Organization (WHO) international statistical classification of diseases (ICD-10) and related health



problems to describe the clinical diagnosis of PAS (43-45). WHO ICDs are designed for health information managers, coders, policy-makers, insurers and patient organizations to classify diseases ([www.who.int/classifications/icd](http://www.who.int/classifications/icd)). This classification provides no clinical description of the condition, makes no distinction between adherent and invasive accreta placentation, and relies upon accurate coding. In 2016, Collins et al proposed a grading system to clearly assess the severity of PAS using clinical findings at birth (46). This system has been developed into the 2019 FIGO classification (Table 1) for PAS disorders (47).

### ***B. Histopathologic***

Until the 1970s, the diagnosis of PAS was almost exclusively histological (48,49). The main histopathological criterion used in recent clinical cohorts to confirm the diagnosis of PAS is the absence of decidual/Nitabuch layer the between the tip of anchoring villi and superficial myometrium as originally described by Irving and Hertig (1). This is an elusive and simplistic histological criterion for the diagnosis of PAS as such areas are found with increasing incidence with advancing gestation in pregnancies without evidence of PAS (50). It is also important to highlight that Irving and Hertig (1) did not have cases of invasive PAS in their series and thus their definition would only apply to abnormally adherent placenta, not to placenta increta or percreta.

Confirmation of the depth of villous invasion of the uterine myometrium in cases of PAS is essential to improve prenatal detection and clinical management strategies. However, most recent studies lack clear descriptions of the histological criteria used to define the different grades of PAS (29,30). This is surprising considering the high rates of caesarean hysterectomy in many studies and may reflect limited access to experienced perinatal pathologists. A summary of the few

studies that do provide PAS grading indicate that the prevalence of both adherent and invasive PAS is not as high as previously reported (Table 2).

Dannheim et al. (52) recently proposed methods for gross dissection, microscopic examination and reporting of hysterectomy specimens containing PAS. Histopathologic diagnosis of PAS however, can be very difficult if the surgeon has attempted to remove the placenta, or impossible in cases of conservative management where the whole placenta is left *in situ*. Therefore, collaboration between the surgical team and pathologists to guide the sampling of the hysterectomy specimen is paramount to obtain accurate grading and extent of the villous invasion.

## **PRENATAL DIAGNOSIS**

Prenatally unsuspected PAS is often associated with massive obstetric haemorrhage (MOH) due to attempts by the surgical team to remove the placenta manually from the uterine wall (52). In these cases, the total blood loss is increased two-fold and the need to give blood products is 86% compared to 57% when the placenta is left undisturbed (53). The risk of MOH is particularly high in invasive PAS due to involvement of the main branches of uterine arteries and the possible invasion of the bladder wall and surrounding pelvic vessels (41,54). A recent systematic review and meta-analysis confirmed that antenatal diagnosis of PAS reduces perioperative complication rates, particularly the risk of surgical bleeding (55). Imaging by a skilled operator using the modality of their choice (usually ultrasound) enables precise localization of the placenta and has become crucial in improving the management of PAS (56). However, recent population studies have shown that PAS remains undetected before delivery in half (53,57) to two-third of

the cases (44). While antenatal diagnostic precision nears 90% in series from expert centres, recent series show that up to a third of cases of PAS are not diagnosed during pregnancy (58).

The first case of prenatal identification of a placenta accreta was performed by Sadovsky et al in 1967 using placentography with radioactive isotopes (59). Tabsh et al were the first to report in 1982 on prenatal grey scale ultrasound diagnosis of placenta increta (60). Since then more than 1200 cases of prenatal ultrasound diagnosis have been described in the international literature (29) and ultrasound imaging is considered as highly accurate when performed by a skilled operator (7). The absence of ultrasound findings does not preclude the diagnosis of PAS (especially abnormally adherent placenta) and clinical factors (CDs and placenta previa) remain important in identifying women at high-risk (7,8).

Numerous techniques have been added to grey-scale imaging over the years, including colour Doppler imaging (CDI) and three-dimensional (3-D) power Doppler sonography raising the sensitivity of ultrasound (20,56). However, the results of well conducted prospective cohort studies have shown that the sensitivity and specificity of grey-scale imaging alone in diagnosing for PAS are as high as 90% when performed by experienced operators (61,62). As with clinical studies, there has been wide heterogeneity in terminology and study designs used in the published reports on the prenatal ultrasound diagnosis of PAS (29). Standardized descriptions of ultrasound signs associated with PAS were recently proposed by the European Working Group on Abnormally Invasive Placenta (AIP) (63) and a reporting pro forma based on these was suggested by an AIP international expert group (64). Although there is good to excellent agreement between expert observers for the diagnostic accuracy of the individual signs (65), some artefacts

are the consequence of myometrial damage due to prior CD and some signs are extremely rare. Use of a combination of signs increases the detection rate of ultrasound for PAS, in particular for placenta percreta (66).

Magnetic resonance imaging (MRI) has been used increasingly for the antenatal detection of PAS and has been reported to be useful in assessing the depth of myometrial and parametrial invasion (7,56). Recent systematic reviews have found that prenatal MRI is highly accurate in identifying disorders of invasive placentation and that ultrasound and MRI have comparable predictive parameters (67,68). However, a recent study found that MRI resulted in a change in diagnosis that could alter clinical management of PAS disorders in more than one third of cases, but when changed, the diagnosis was often incorrect (69).

Overall it is unclear if MRI improves the diagnosis of PAS beyond what can be achieved by trained ultrasound operators (7,8). MRI may be less operator-dependent but the cost and limited access to equipment and expert radiologists makes it impractical as a screening tool for PAS, in particular in early pregnancy (70). The implementation of standardized prenatal targeted ultrasound protocols in specialist centres for pregnant women with risk factors for PAS is associated with improved maternal and neonatal outcomes (71). However, placental imaging is not routinely taught during ultrasound and radiology training courses. The rise in the rates of CD and PAS highlights the need to develop training programs for sonographers and other operators providing mid-pregnancy ultrasound examination and to use targeted scanning protocols at national and international levels.

## **MANAGEMENT STRATEGIES**

For the majority of specialists, the principal management strategy to prevent excessive bleeding is to leave the placenta *in situ* and perform a primary hysterectomy (PH) at delivery (71-74). In cases where suspicion of PAS is high during CD, most US obstetricians proceed with PH, with less than a third attempting conservative management (72-73). Similarly, a recent international survey of experts found that 61% opt for a primary PH with the placenta left *in situ* as their first-choice management approach (74). Controversies still exist among experts regarding optimal timing of delivery, use of adjunctive measures, and conservative (uterine-sparing) methods. Overall, there are no RCTs nor prospective well-controlled observational studies comparing surgical and conservative approaches for the same grade of PAS. Management strategies for PAS will vary depending on prenatal diagnosis, local surgical expertise and, more recently, access to a specialist multidisciplinary team (MDT). The different management strategies and supporting evidence have been recently reviewed by the RCOG (7), FIGO (76), ACOG and SMFM (8).

#### **A. Surgical management**

Planned preterm (34-35 weeks) caesarean hysterectomy with the placenta left *in situ* is the recommended management strategy for PAS by ACOG (8). Both general and regional anaesthetic techniques have been shown to be safe for surgical procedures required for the delivery of PAS (7). The choice of anaesthetic technique for CD for placenta praevia and PAS should therefore be made by the anaesthetist conducting the procedure and the woman should be informed of the possible need to convert from regional to general anaesthesia (76).

If the placenta is anterior and extending towards the level of the umbilicus, a midline skin incision is often needed to allow for a high upper-segment transverse

uterine incision above the upper border of the placenta (76). A large extended transverse incision (Cherney or Maylard) can be used to avoid a vertical incision but there is limited data available on their use in the management of PAS (76).

Total PH is the preferred method of due to the potential risk of malignancy developing in the cervical stump, the need for regular cervical cytology and other associated problems such as bleeding or discharge (76). This is always necessary if invasive placental tissue has been seen within the cervix on prenatal imaging. Devascularization of the uterus laterally on both sides and clamping the uterus at the lowest possible point just below the edge of the placenta while sparing the ureters has been recently shown to reduce maternal bleeding morbidity (77). Unless there are significant concerns regarding the risk of malignancy the ovaries should always be left. However, oophorectomy is always a risk for example due to adhesions precluding safe separation or bleeding occurring proximal to the ovary.

Planned delayed or secondary hysterectomy is an alternative “definitive” surgical management strategy for PAS (7). Delayed hysterectomy may be necessary where extensive invasion (percreta) of surrounding structures would render immediate cesarean hysterectomy extremely difficult or if the diagnosis of PAS is made at the time of birth and the operating team has limited surgical experience in performing complex surgical procedures.

### ***B. Conservative management***

Planned PH may be unacceptable to women desiring to preserve their fertility, and conservative management techniques for uterine preservation for both adherent and invasive placenta accreta have been used increasingly in many centres around the world. These techniques include leaving the placenta *in situ*, partial myometrial resection of the accreta area with myometrial repair, and suturing

around the accreta area (78). These methods have been used alone or in combination with additional procedures such as uterine artery devascularisation techniques either surgical or with interventional radiology (IR).

When the extent of the PAS area is limited in depth and can be entirely visualized (i.e. completely anterior, fundal or posterior without deep pelvic or cervical invasion) and is accessible a conservative uterus-preserving surgery may be appropriate. Partial myometrial resection can be attempted to allow a conservative management of the uterus (7,78). However, this should only be attempted by teams with experience and appropriate expertise to manage such cases conservatively (78).

There are no RCTs comparing the different conservative management techniques. Uterus-preserving surgical techniques are associated with a 16% unintentional urinary tract injury rate compared to 57% for standard hysterectomy and that use of ureteric stents reduces the risk of urologic injury (79). An increasing number of authors claim to have high success rates, sometime 100%, for uterine preservation surgery for PAS using compressive suture, intra-uterine balloon, uterine devascularization etc. (80-82). Although the retrospective design, small number of cases, lack of controls, absence of histopathological evidence and lack of standardized clinical or photographic evidence of PAS at birth considerably limits the value of their data (30). Specifically, it is impossible to reproduce such results in other centers or populations, or carry out meaningful meta-analysis unless a clear, clinical definition of the severity of PAS encountered is described. For these reasons, FIGO have developed a standardized clinical classification for PAS that clearly defines features of any given case (Table 1) and can be corroborated with histopathology where available.

### ***C. Additional therapeutic techniques***

There are no RCTs on the use of ureteral stents in PAS. Ureteral stents or catheters are more commonly used in the US where 26% of ACOG fellows are using them in the management of PAS (74) but there are currently insufficient data to recommend the routine use of ureteric stents in PAS.

Interventional radiology (IR) including intraoperative internal iliac artery and/or postoperative uterine artery embolisation and internal iliac artery or abdominal balloon occlusion has been proposed to reduce bleeding in women at high risk of perioperative and post-partum hemorrhage. A systematic review has reported success rates of around 90% for arterial embolisation in PAS, with secondary PH being necessary in 11.3% (78). Arterial balloon occlusion catheters have been associated with a success rate of nearly 70% but the use of prophylactic placement of balloon catheters in the iliac arteries in cases of PAS is still controversial, mainly because of the high risks of complications. A more recent systematic review and meta-analysis has shown that IR reduces the risks of bleeding during surgery but the studies were heterogenous and of very low quality (84). A small RCT preoperative prophylactic balloon catheters versus controls of women presenting with a prenatal diagnosis of PAS found no difference in blood loss >2500 ml, number of plasma products transfused, duration of surgery, peripartum complications and hospital stay (85). Some argue that the vast collateral blood supply to the gravid uterus, and particularly to the invasive placenta may require higher vascular occlusion, such as at the infra-renal aorta, to significantly reduce blood loss during surgery for PAS. Larger, higher quality studies are necessary to determine the safety and efficacy of IR before this technique can be advised in the routine management of PAS (7).



Internal iliac artery ligation was first described by surgeons at the beginning of the 20<sup>th</sup> century and used in obstetrics to reduce the risks of post-partum hemorrhage before the advent of IR. In low-resources countries, where IR is not available it has remained in use in particular in the context of uterine preservation in PAS. A recent RCT of bilateral internal iliac artery ligation (n= 29 cases) versus controls (n= 28 cases) reported no significant difference between the two groups regarding the intraoperative estimated blood loss (86).

#### ***D. Multi-Disciplinary Team (MDT) approach***

A recent observational study of obstetric-led units in England found that 70% manage their PAS cases "in-house", despite one third of these units reporting that they only treat one or fewer cases each year (87). However, there is mounting evidence that women with PAS diagnosed prenatally and managed by an MDT in a centre of excellence are less likely to require emergency surgery, large-volume blood transfusion and reoperation within 7 days of delivery for bleeding complications compared with women managed by standard obstetric care without a specific protocol (38,88,89). In addition, women with PAS admitted at 34 weeks of gestation and delivered between 34 and 35 weeks of gestation by a specialist MDT have a significantly lower emergency surgery rate than those not cared for by such a team despite a similar median gestational age at delivery. These studies have also shown that maternal outcomes are improved over time with increasing experience within a well-established MDT performing 2–3 cases per month. A recent systematic review and meta-analysis has confirmed these findings but has also highlighted that all the studies included in the review are retrospective (90). Furthermore, these studies provide no data on the differential clinical diagnosis between abnormally adherent and abnormally invasive PAS nor

detailed pathologic confirmation of the depth and lateral extension of villous myometrial invasion. There is therefore a need for more prospective studies with detailed clinical and histopathologic data.

## **CONCLUSION**

Accreta placentation is a potentially life-threatening condition. The incidence of PAS will predictably increase further over time, if modern obstetric caesarean delivery trends continue. It is therefore, incumbent on all healthcare providers to systematically improve upon the recognition of risk factors, the accuracy of antenatal diagnosis, and the intrapartum management for women with PAS.

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**Table 1:** FIGO clinical classification for the diagnosis of PAS disorders at delivery.<sup>47</sup>

| <b>GRADE 1</b>      | <b>Abnormally adherent placenta (PLACENTA ADHERENTA OR CRETA)</b>  |
|---------------------|--|
| Clinical criteria   | <p>At vaginal delivery</p> <ul style="list-style-type: none"> <li>- No separation with synthetic oxytocin and gentle controlled cord traction.</li> <li>- Attempts at manual removal of the placenta results in heavy bleeding from the placenta implantation site requiring mechanical or surgical procedures.</li> </ul> <p>If laparotomy is required</p> <ul style="list-style-type: none"> <li>- Same as above.</li> <li>- 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.</li> </ul> |
| Histologic criteria | <ul style="list-style-type: none"> <li>- Microscopic examination of the placental bed samples from hysterectomy specimen shows extended areas of absent decidua between villous tissue and myometrium with placental villi attached directly to the superficial myometrium.</li> <li>- The diagnosis cannot be made on just delivered placental tissue nor on random biopsies of the placental bed.</li> </ul>   |
| <b>GRADE 2</b>      | <b>Abnormally invasive placentation (PLACENTA INCRETA)</b>   |
| Clinical criteria   | <p>At laparotomy</p> <ul style="list-style-type: none"> <li>- Abnormal macroscopic findings over the placental bed: bluish/purple colouring, distension (placental 'bulge').</li> <li>- Significant amounts of neovascularity (dense tangled bed of vessels or multiple vessels running parallel cranio-caudally in the uterine serosa).</li> <li>- No placental tissue seen to be invading through the surface of the uterus.</li> <li>- Gentle cord traction results in the uterus being pulled inwards without separation of the placenta (the 'dimple' sign).</li> </ul>   |
| Histologic criteria | 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.   |
| <b>GRADE 3</b>      | <b>Abnormally invasive placentation (PLACENTA PERCRETA)</b>  |
| <b>GRADE 3a</b>     | <b>Limited to the uterine serosa</b>   |
| Clinical criteria   | <p>At laparotomy</p> <ul style="list-style-type: none"> <li>- Abnormal macroscopic findings on uterine surface (as above) and placental tissue seen to be invading through the surface of the uterus (serosa).</li> <li>- 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).</li> </ul>  |
| Histologic criteria | Hysterectomy specimen showing villous tissue within or breaching the uterine serosa  |

|                     |   |
|---------------------|---|
| <b>GRADE 3b</b>     | <b>With urinary bladder invasion</b>  |
| Clinical criteria   | At laparotomy <ul style="list-style-type: none"> <li>- Same as 3a.</li> <li>- Placental villi are seen to be invading into the bladder but no other organs.</li> <li>- Clear surgical plane cannot be identified between the bladder and uterus.</li> </ul> |
| Histologic criteria | hysterectomy specimen showing villous tissue breaching the uterine serosa and invading the bladder wall tissue or urothelium.   |
| <b>GRADE 3c</b>     | <b>With invasion of other pelvic tissue/organs</b>  |
| Clinical criteria   | At laparotomy <ul style="list-style-type: none"> <li>- Same as 3a.</li> <li>- Placental villi are seen to be invading into the broad ligament, vaginal wall, pelvic sidewall or any other pelvic organ (+/- invasion of bladder).</li> </ul>                |
| Histologic criteria | Hysterectomy specimen showing villous tissue breaching the uterine serosa and invading pelvic tissues/organs.   |

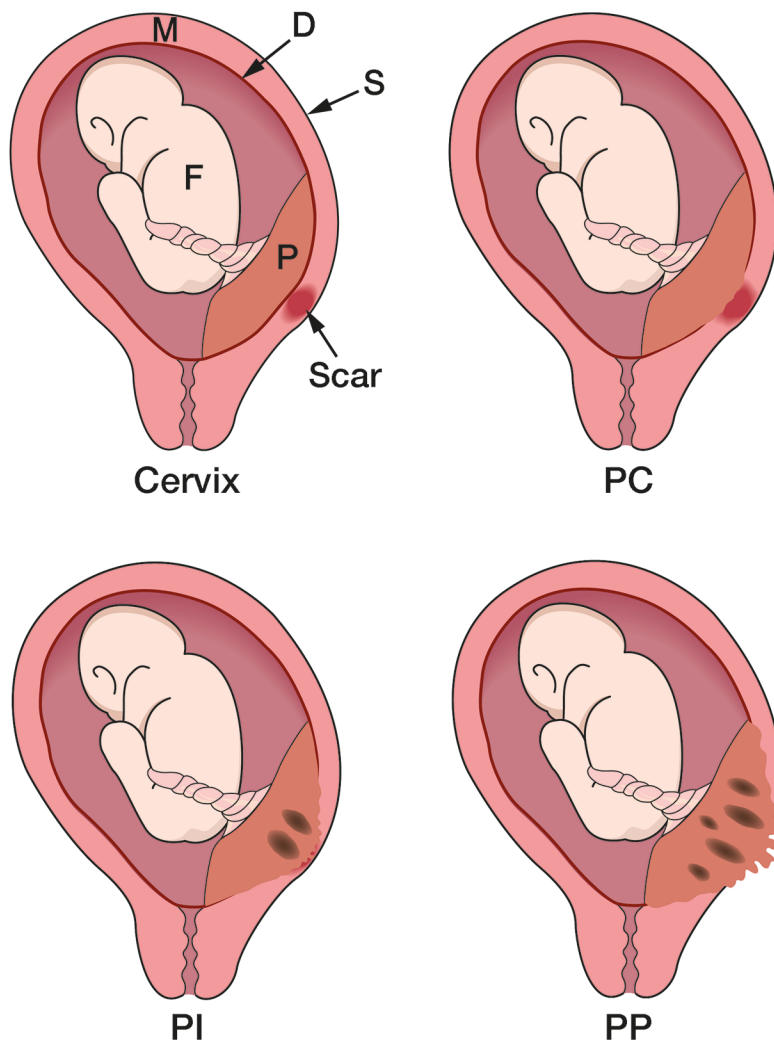
**Table 2.** Distribution and prevalence of the different grades of PAS disorders in histopathology and prenatal diagnosis series (13) and population studies (30).

| Author (year)                          | Total No. of cases of PAS | No. of PC (%) | No. of PI (%) | No. of PP (%) |
|--|---------------------------|---------------|---------------|---------------|
| Histopathology studies (1966-1978)     | 118                       | 82 (69.5%)    | 28 (23.7%)    | 8 (6.8%)      |
| Prenatal diagnosis studies (2000-2016) | 203                       | 103 (50.7%)   | 49 (24.2%)    | 51 (25.1%)    |
| Population studies (1982-2018)         | 757                       | 473 (62.5%)   | 117 (15.4%)   | 167 (22.1%)   |
| Prevalence (PAS/births)                | 1/2415                    | 1/3865        | 1/15628       | 1/10949       |

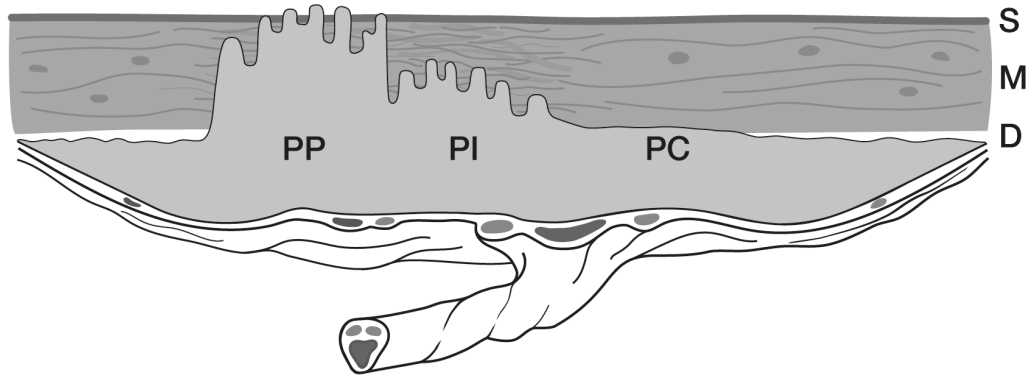
PC= Placenta Creta (abnormally adherent); PI= Placenta Increta (abnormally invasive); PP= Placenta Percreta (abnormally invasive).

## Figure legends

**Fig 1:** Diagram showing an anterior placenta previa on a caesarean scar and the different grades of placenta previa accreta: Creta (PC) where placental (P) villi adhere to the myometrium (M), Increta (PI) where the villi invade the myometrium and Percreta (PP) where the villi invade the entire myometrium and cross the uterine serosa (S). From reference 50.



**Fig 2:** Diagram showing an anterior placenta previa accreta combining areas of abnormal adherence and invasion: Creta (PC), Increta (PI) and Percreta (PP). D= Decidua; M= myometrium; S= Serosa. From reference 50.



**Fig 3:** Large myometrial dehiscence at 35 weeks (arrow) due to multiple prior CDs creating a “uterine window” where part of the underlying placenta tissue is visible through the serosa mimicking a placenta percreta.

