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Review Article

# Challenges and Risks Facing Conservative Management of Placenta Accreta Spectrum in Low Resources Countries

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#### **Abstract**

Placenta accrerta spectrum comprises a group of disorders that are considered a nightmare for both patients and obstetricians. PAS is associated with catastrophic complications and mortality rates. The main treatment is cesarean hysterectomy; however, some obstacles exist in performing this procedure. Patient age, desire for future fertility, and psychological aspects are the main obstacles in the decision-making process. Conservative treatment is not an easy road with roses on its sides; it is associated with many challenges and risks. In this review, we discuss the challenges and risks associated with conservative treatment of PAS.

Keywords: PAS; Placenta; Cesarean Section; Challenges; Hysterectomy

#### Introduction

The placenta accreta spectrum (PAS) encompasses placenta accreta, increta, and percreta. In placenta accreta, the placental villi attach directly to the myometrium; in placenta increta, the villi penetrate the myometrium; and in placenta percreta, the villi extend through the myometrium into the serosa. A meta-analysis conducted in 2019 revealed that among patients diagnosed with PAS, 63% presented with placenta accreta, 15% with placenta increta, and 22% with placenta previa [1].

Placenta accreta is classified into total, partial, or focal types based on the extent of placental tissue that adheres to the myometrium. The exact cause of the placental accreta spectrum (PAS) is not well understood. The leading hypothesis suggests that after uterine surgery, irregular blood vessel formation during the healing process results in localized hypoxia, which, in turn, causes inadequate decidualization, permitting an abnormal invasion of trophoblastic cells during placentation [2,3].

The occurrence of placenta accreta spectrum (PAS) is on the rise, currently estimated at approximately three cases per 1000 deliveries, primarily due to the increasing frequency of cesarean sections. This upward trend in PAS cases is significantly linked to the higher rates of cesarean deliveries observed in recent decades. In developed nations, PAS has become the leading cause of cesarean hysterectomy. Several factors heighten the risk of developing PAS, with previous cesarean deliveries and placenta previa being the most significant. Additionally, the likelihood of PAS increases with the number of prior cesarean sections, reaching a staggering 67% in individuals who have had four cesarean deliveries along with placenta previa. Notably, even among those without any history of cesarean delivery, the presence of placenta previa carries a 3% risk of developing PAS. In the absence of placenta previa, a systematic review demonstrated that the rate of PAS increased from 0.3% in women with 1 previous cesarean delivery to 6.74% for women with 5 or more cesarean deliveries [8].

This review highlights the challenges and risks of PAS management in low-resource countries, medico-legal aspects, reproductive outcomes, and psychological impacts of placenta accrete spectrum.

# Preoperative challenges in PAS Challenges in diagnosis of PAS

Ultrasound is typically used for the prenatal diagnosis of the placenta accreta spectrum (PAS) because many patients do not exhibit symptoms. While some may experience vaginal bleeding and cramping, these symptoms often arise in conjunction with placenta previa, which is common in PAS. Intraoperative diagnosis is frequently encountered, especially in patients with notable risk factors. Therefore, it is crucial to uphold a heightened clinical awareness, particularly in individuals with significant risk factors [9,10].

Ultrasound is the primary imaging technique used to diagnose PAS. It showed a sensitivity of 90.72% (95% CI, 87.2–93.6) and a specificity of 96.94% (95% CI, 96.3%–97.5%) in identifying PAS. It is crucial to understand that no ultrasound characteristics of PAS or any combination of these features can consistently predict the extent of PAS invasion, except for the indication of placental tissue penetrating adjacent pelvic organs. Patients who are at risk for PAS should be directed to specialized centers due to significant interobserver variability and lower diagnostic sensitivities reported in certain studies [11,12].

Utilizing a transvaginal sonographic method to evaluate the placenta provides improved resolution and better visualization. This technique facilitates the confirmation of placenta previa, examination of the posterior bladder wall, and evaluation of the degree of placental invasion into the cervical tissue. Over 80% of placenta accreta spectrum (PAS) cases are linked to placenta previa. The vascularization of the placenta and lower segment can be further analyzed using color Doppler in low-velocity scenarios [13].

Magnetic resonance imaging (MRI) also aids in the diagnosis of PAS, especially when the posterior placenta is encountered or there is lateral extension to the broad ligament. It is not superior to ultrasound in ordinary cases and expensive for patients in low resources countries [14].

## Controversy between FIGO and ISUOG classifications

Many attempts have been made to classify PAS disorders. The first and most popular classification is the histologic classification, which includes accreta, increta, and percreta. This was based on histopathological examination of the degree of invasion. Recently FIGO classified PAS disorders into 6 grades according to surgical findings intra-operatively [15].

This was not accepted because we did not want to wait to open the case and classify the disorders intraoperatively. ISUOG classified PAS disorders into 4 grades only and this was done preoperatively. This is important and beneficial for both patients and clinicians. This helps in preoperative preparation and prediction of surgical outcomes [16].

The PAS classifications according to FIGO and ISUOG categorize placenta accreta spectrum (PAS) into three stages based on ultrasound findings, histopathology, and FIGO grading. PAS 0 is identified by placenta previa with no ultrasound signs of invasion, corresponding to placenta previa without PAS and a FIGO grade of 1-2. PAS 1 is characterized by the presence of at least two ultrasound signs, such as placental lacunae, loss of clear zone, or bladder wall interruption, and is linked to placenta accreta/increta with a FIGO grade of 3. PAS 2 involves PAS 1 findings plus uterovesical hypervascularity, associated with placenta percreta focal or diffuse, and a FIGO grade of 4-5. PAS 3 includes PAS 1 or 2 with hypervascularity in the inferior part of the lower uterine segment extending into the parametrial region, corresponding to placenta percreta invading the uterine segment and lateral pelvic walls or parametria, with a FIGO grade of 6 [15,16].

PAS encompasses all classifications of abnormal placentation and serves as the foundation for a novel clinical classification suggested by FIGO [15].

- Grade 1: Abnormally adherent placenta (PC) occurs when the villi attach directly to the myometrium and lack a decidual interface.
- Grade 2: Abnormally invasive placentation (PI) occurs when the villi penetrate the myometrium of the uterus.

- Grade 3: Abnormally invasive placentation (PP) occurs when
  the villi penetrate the entire thickness of the uterine wall,
  reaching either the serosa or extending further. This category
  is further divided into the following.
  - Grade 3a: Confined to and encompassing the uterine serosa
  - Grade 3b: Invasion of the urinary bladder.
  - Grade 3c: Infiltration into additional pelvic tissues or organs is observed.

#### Prediction of PAS and its severity

Clinical risk factors and imaging are helpful for the early identification of PAS. Ultrasound was the first-level imaging modality, with a reported good accuracy using specific findings suggestive of PAS [17].

According to Cali., et al. (2020), an early sonographic evaluation during the first trimester of pregnancies with a history of cesarean delivery can accurately predict the ultrasound stage of placental accreta spectrum (PAS) disorder. By integrating the findings from first-trimester ultrasounds with those from second- and third-trimester examinations, it is possible to assess the surgical risk in women diagnosed with a PAS disorder. This information was similarly presented by Dar., et al. (2024).

According to Maurea., et al. (2023), a nomogram-based model that integrates clinical risk factors along with ultrasound and MRI indicators could assist in predicting PAS in patients with PP, with MRI playing a more significant role than ultrasound imaging assessment [20].

Greenberg., et al. (2022) assessed the effectiveness of ultrasound in forecasting placenta accreta spectrum (PAS). They determined that ultrasound demonstrates a greater predictive capacity for more severe PAS conditions, although its overall sensitivity and specificity are still low [21]. Similarly, Eid., et al. (2022) discovered that prenatal ultrasound serves as the most effective screening method for PAS, with the presence of abnormal lacunae and the absence of the retro-placental clear zone being reliable indicators for surgical outcomes and histopathological assessments [22].

Various scoring systems have been introduced to assess PAS severity [23]. Luo., *et al.* (2019) discovered that 95.44% of individu-

als in the low-score category (score < 2.25) had PAS, whereas in the high-score category (8.95–10), 81.81% of patients were diagnosed with percreta. In the moderate-score categories (2.25–6.2 and 6.2–8.95), histopathological evaluations confirmed that 80.26% and 75.47% of women had accreta and increta, respectively. They indicated that this scoring system could effectively predict PAS severity in women with placenta previa, aiding in the identification of genuinely high-risk patients and enhancing their treatment options [24]. A comparable scoring system was suggested by Abd-Elrouf., *et al.* (2025), who found that their severity prediction scoring system is a straightforward and practical method for determining the presence of PAS in women with placenta previa [25].

Ultimately, Quiner., *et al.* assessed the predictive accuracy of nine systems for PAS during the first trimester. Their findings indicated that all the scoring systems evaluated exhibited low diagnostic accuracy, with none demonstrating any enhancement in diagnostic precision compared to the others [26].

#### **Prediction of PAS surgical outcomes**

It is important to predict surgical outcomes before high-risk surgeries to prepare the resources and implement a management plan. Several studies and scores have been proposed to predict the surgical outcomes. Shazly, *et al.* (2021) proposed a machine learning model for predicting surgical outcomes in patients with PAS. The primary outcome was massive PAS-associated perioperative blood loss (intraoperative blood loss ≥2500 ml, triggering a massive transfusion protocol, or complicated by disseminated intravascular coagulopathy). Other outcomes included prolonged hospitalization (> 7 days) and admission to the intensive care unit (ICU). They reported that their model could calculate the individualized risk of morbidity in women with PAS. Model-based risk assessment facilitates *the a priori* delineation of management strategies for these patients [27].

Taşkum., et al. (2025) aimed to forecast the likelihood of cesarean hysterectomy (CH) in patients with placenta accreta spectrum disorders (PASD). Their model integrated factors such as maternal age, gestational age, history of uterine surgeries, ultrasound results, and placental position. The study revealed that the existence of multiple placental lacunae and an anterior placental position were the findings most strongly linked to CH in individuals with PAS [28].

According to Elbasuiny, *et al.* (2024), timely identification of PAS enables both the patient and obstetrician to adequately prepare for optimal management while minimizing complications. Early prediction of PAS can be achieved using clinical risk factors, early imaging during pregnancy, and biomarkers. The study indicated that ultrasound markers are not only more precise and easier to monitor but also show a positive correlation with surgical outcomes related to PAS, including blood loss and the need for peripartum hysterectomy [29].

Similarly, Chong., *et al.* (2018) proposed a self-made ultrasonic scoring system to predict surgical outcomes in patients with PAS. They reported that their model was an effective diagnostic tool for assessing the types of placenta accreta, and predicted the associated bleeding risk, indicating the possibility of hysterectomy [30].

#### **Preoperative preparation of patients**

The availability of at least four units of cross-matched blood and blood products is crucial before surgery. Some cases may require more and more units of blood and its products [31,32].

ICU bed availability is also mandatory for blood transfusions. The availability of human resources is not inferior to that of other resources. Human resources should include senior obstetrician, senior urologist, senior anesthesiologist, and vascular surgeon [32,33].

Signing preoperative consent is also a great challenge, where surgeons must explain all aspects of the surgery, including the complications and mortality. In emergencies, consent was obtained retrospectively [34].

# Operative challenges in PAS Massive hemorrhage

The main risks associated with PAS are coagulopathy, multiorgan system failure and death. A dangerous scenario arises when PAS is unsuspected at the time of delivery and the surgeon attempts to remove the invasive villous tissue [35]. Women diagnosed with PAS, especially those with placenta increta or percreta who have not attempted any removal of their placenta, exhibit lower levels of hemorrhage and a decreased requirement for blood transfusion. Women suspected of having PAS who give birth prior to their scheduled delivery date are considerably more prone to experi-

ence vaginal bleeding and uterine contractions than those with a planned delivery. Each instance of antenatal vaginal bleeding correlated with a heightened risk of unscheduled delivery (adjusted OR, 3.8; 95% CI, 1.8–7.8), and this risk escalated with the preterm rupture of membranes. Furthermore, the majority of women with PAS also present with placenta previa, which places them at an increased risk for antenatal bleeding and preterm delivery associated with this condition. Placenta percreta may lead to significant prenatal complications early in pregnancy, such as uterine rupture and symptoms indicating bladder invasion, including severe hemorrhage that necessitates urological intervention.

Women diagnosed with placental accreta spectrum (PAS) who receive care from a multidisciplinary team (MDT) have a reduced risk of requiring extensive blood transfusions and undergoing reoperation for bleeding complications within a week after delivery. Additionally, these women are less likely to face extended stays in the intensive care unit (ICU), require large blood transfusions, suffer from coagulopathy, experience urinary tract injuries, or require early reoperations. Those with PAS who delivered between 34 and 35 weeks under the care of an MDT had a notably lower rate of emergency surgeries compared to those not managed by an MDT (23% versus 64%; P < .001), even though the median gestational age at delivery was similar (34 [16-39]. versus 34 [19-40]., P < .50). This evidence strongly advocates for the planned delivery of women with accreta placentation at specialized centers that possess multidisciplinary expertise and resources for managing PAS, along with access to adult and neonatal ICUs and blood products for transfusion.

#### **Massive blood transfusion**

For conservative management of PAS, it is advisable to have packed red blood cells (10–20 units), fresh frozen plasma (10–20 units), and platelets (12 units) on hand. Women diagnosed with placenta percreta are at a higher risk of requiring extra blood products, experiencing urologic injuries, and requiring admission to the ICU than those with uncomplicated placenta accreta [39].

Before making the skin incision, it is crucial to have blood products, such as red blood cells, fresh frozen plasma, and platelets, on hand. Prompt replacement of blood products, considering volume, oxygen-carrying capacity, and coagulation factors, can help de-

crease perioperative complications and enhance patient outcomes. In women undergoing cesarean hysterectomy, autologous transfusion of salvaged red cells can reduce the need for banked blood transfusion. When transfusions are necessary, administering sufficient platelets and fresh frozen plasma in relation to red blood cells, typically at a 1:1 ratio, has been linked to better outcomes in trauma-related bleeding. Regional anesthesia might restrict the ability to adjust the abdominal contents for retractor placement; therefore, general anesthesia may be more suitable in high-risk cases that may require a hysterectomy or in instances of placenta percreta affecting the bladder. Establishing adequate vascular access, which often involves central venous access and arterial line placement, is essential before starting the surgical procedure. Additionally, having a rapid infusion device ready to quickly replace blood products is vital in the event of a significant blood loss.

Performing cesarean hysterectomy in the context of the placenta accreta spectrum (PAS) presents significant challenges. Patients with multiple cesarean deliveries frequently exhibit pelvic adhesions, a lower uterine segment that is both thin and highly vascularized, a large in situ placenta, pronounced pelvic hypervascularity, and potential invasion of the placenta into surrounding structures such as the bladder, bowel, cervix, and parametrium, particularly in cases of placenta percreta. Upon accessing the abdominal cavity, a thorough examination of the pelvis was conducted [41].

The anterior wall of the uterus is the most frequent location for placental invasion; however, villous tissue can extend laterally, encroaching on the parametric area. This lateral invasion of the placenta can complicate the identification of the ureters and pose challenges in isolating uterine blood vessels. The myometrium beneath and adjacent to the improperly implanted villous tissue is generally thin and fragile, surrounded by enlarged vascular channels.

Once the position of the placenta has been determined, it is crucial to choose a site for the uterine incision (hysterotomy) in an area that is free from the placenta. This may necessitate an incision at the fundus or even the posterior wall of the uterus, which can be technically demanding and may lead to delays in delivering the fetus, potentially causing fetal or neonatal distress. This underscores the significance of precise prenatal diagnosis of Placenta Accreta

Spectrum (PAS) to prevent subjecting mothers and newborns without PAS to surgical interventions that carry a higher risk of perioperative complications [42].

#### The need for adjuvant procedures

The management of PAS requires a multidisciplinary approach. We sometimes require ureteric catheters to delineate ureters and prevent their injury or unintended ligation [43].

The B-Lynch suture may be required in cases where the uterus is preserved and atonic. This can help reduce the incidence of postpartum hemorrhage. The need for hysterectomy is another challenge in the management of PAS. It leads to loss of fertility and many psychological problems and usually refused by many patients even those completed their families [44].

The use of balloon catheters for prophylactic placement in the iliac arteries of women with PAS remains a topic of debate, primarily because of the increased risk of complications compared to uterine artery embolization (UAE) and the absence of direct comparative studies [45].

However, the impact of this approach on blood loss has not been fully established. One randomized controlled trial found no differences in the number of women with blood loss greater than 2500 mL, number of plasma products transfused, duration of surgery, peripartum complications, and hospitalization length using prophylactic placement of balloon catheters in the iliac arteries compared with a conventional approach. Nonetheless, various studies have indicated the advantages of decreased blood loss. Furthermore, only 50% of women who received prophylactic balloon catheter placement in the internal iliac arteries for PAS disorders experienced balloon inflation during delivery in cases of significant bleeding. Numerous complications associated with the use of balloon catheters in the internal iliac arteries have been documented, with an incidence rate of 16%. Balloon-related complications include rupture of the left iliac artery, dissection of the internal iliac artery, leg ischemia, and permanent claudication of the limb. Even with the implementation of low-radiation-dose techniques, fetal exposure to radiation remains a significant concern when evaluating internal iliac artery balloon occlusion. Although it varies, the average fetal radiation exposure is 4.4 mGy [45].

#### **Urologic injuries**

Women diagnosed with placenta percreta are at a higher risk of requiring extra blood products, experiencing urologic injuries, and requiring admission to the ICU than those with simple placenta accreta [43].

The genitourinary system is at significant risk of damage during these procedures. Injuries to the bladder and ureters are common in laparoscopic surgeries. However, locating the ureter can be difficult if the villous tissue encroaches on the parametrial area. To aid in ureter identification, retrograde ureteral stents can be inserted via cystoscopy. These stents can be placed following the induction of anesthesia and prior to making the abdominal incision. There is limited data regarding the effectiveness of ureteral stents in minimizing the risk of ureteral injury, and further assessment is necessary before considering their routine application for all women with PAS [46].

#### Diversity of conservative surgical techniques

Several techniques have been described for the management of PAS. Both radical and conservative techniques have been described by several surgeons. Each technique has its advantages and disadvantages, with no single technique proven superior [47].

Among the techniques described for uterine conservation are triple-P procedures, Shehata's technique, Assar's technique, leaving the placenta in situ, different devascularization techniques, different compressive sutures, resection and reconstruction of the uterus, and tamponade techniques [47].

# Postoperative challenges Consumptive coagulopathy and DIC

Mojahed., *et al.* (2025) in their systematic review reported that coagulopathy was found in a total of 50 cases in the conservative cohort and 64 cases in the CS hysterectomy cohort [48].

Shamshirsaz., *et al.* (2019) found that 37 PAS cases (30.1%; 95%CI 22.1–39.0) developed coagulopathy and 86 (69.9%; 95%CI 61.0–77.9) did not. The initial demographic characteristics of the patients showed no significant differences between the groups. The median estimated <u>blood loss</u> (along with the interquartile range) was 2100cc (1800, 400) in the presence of coagulopathy and 1400 (1000, 2500) in its absence (P < 0.01). Univariate regres-

sion analysis validated the link between coagulopathy and (i) the number of RBC units transfused and (ii) estimated blood loss. The ROC curves indicated that an estimated blood loss of  $\geq 1500\,\mathrm{mL}$  provided the most effective discrimination. The depth and/or severity of placental invasion did not correlate with coagulopathy in patients diagnosed with PAS [49].

According to Biele., *et al.* (2021), 11 studies have indicated the presence of disseminated intravascular coagulation-like symptoms during conservative treatment of PAS. In the majority of instances, an emergency hysterectomy was carried out, resulting in a nearly instant restoration of coagulation status, although it was associated with significant maternal blood loss [50].

#### **Thromboembolism**

Thromboembolic events have been observed in the management of PAS. A total of 87 patients were treated conservatively, including 28 with coagulopathy. The onset of coagulopathy was documented in 11 cases. The median duration until coagulopathy occurred was 58 days, with an interquartile range of 50–67 days post-delivery. The presence of significant placental lakes may serve as a potential marker for the onset of coagulopathy.

#### Reoperations

Up to one-third of women who undergo peripartum hysterectomy may require reoperation. Approximately 75% of re-exploration cases involve the management of persistent bleeding. The remaining procedures are conducted to address surgical injuries, primarily affecting the genitourinary system [52].

## **Infectious morbidity**

In patients with PAS, conservative treatment increases the risk of developing endometritis. Postoperative febrile complications and bowel dysfunction are common. Febrile conditions are primarily caused by endometritis. Surgical site infection may complicate these surgeries due to excessive blood loss and anemia [53].

#### Prolonged hospital stay

The duration of hospital stay was reported to be prolonged in PAS management. The mean preoperative duration of stay was 9.5 days ( $\pm$  8.3) and the mean postoperative duration of stay was 8.8 days ( $\pm$  8). Total hospital stays ranged from 6 to 48 days (mean 19.5,  $\pm$  11.4) [54,55].

#### **Mortality**

Although there has been a 38% reduction in global maternal mortality over the past ten years, the figures are still alarmingly high, with over 800 maternal deaths occurring each day. There are notable differences in the rates and causes of maternal mortality across regions, with most cases occurring in low- and middle-income countries (LMICs). The primary contributors to direct maternal mortality are hemorrhage, hypertensive disorders during pregnancy, sepsis, complications from abortion, and thromboembolism. To eradicate preventable maternal deaths, it is essential to enhance the clinical management of these critical obstetric conditions and tackle the intricate social and economic obstacles that hinder pregnant women from obtaining quality care.

The primary contributors to direct maternal mortality include hemorrhage (27.1%), hypertensive disorders of pregnancy (HDP; 14.0%), sepsis (10.7%), abortion complications (7.9%), and thromboembolism (3.2%). This article examines each of these causes of maternal mortality in the context of low- and middle-income countries (LMICs), emphasizing clinical diagnosis and management during the intrapartum phase. It is crucial to note that the majority of maternal deaths are preventable. Reducing preventable maternal mortality relies on enhancing the clinical management of these critical obstetric conditions and addressing the intricate social and economic challenges that hinder pregnant women from accessing quality healthcare.

## Psychological aspects related to PAS

Experiencing the placenta accreta spectrum during pregnancy represents a significant life challenge that may lead to the emergence of psychiatric issues, such as post-traumatic stress disorder, depression, and anxiety disorders. It is advisable to identify psychological distress and associated symptoms at every phase of perinatal care for this uncommon range of conditions. Disorders related to PAS are associated with post-traumatic stress disorder, anxiety, or postpartum depression [58].

Currently, no guidelines exist for mental health interventions for women with a placenta accreta spectrum (PAS). Many health-care facilities utilize the Edinburgh Postpartum Depression Scale to evaluate symptoms of depression and anxiety during pregnancy

and in the postpartum phase. It is advisable for women diagnosed with PAS to undergo screening at the time of diagnosis, monthly until delivery, and at various intervals throughout the first year postpartum. Additionally, it is suggested that PTSD screening be conducted both prior to and following childbirth. Effective interventions for the PAS demographic include the formation of a multidisciplinary team, ensuring patient access to a support person or care coordinator, and the creation of a postpartum care team along with a comprehensive care plan [59,60].

Michelet., *et al.* discovered that 64% of women who underwent unplanned hysterectomy subsequently developed PTSD. Additionally, among those who retained their uterus, the memories and perceptions associated with postpartum hemorrhage led to ongoing fears of death, sexual difficulties, severe anxiety, depression, and negative effects on their marriages [61].

Reports indicate that the psychological effects of hemorrhagic complications are not linked to the amount of bleeding or the occurrence of hysterectomy but rather to whether the procedures were emergency or elective. These findings underscore the importance of developing appropriate and timely psychological support to enhance mental well-being and resilience in women experiencing AIP. Healthcare systems focused on PAS care should establish frameworks and processes that effectively address the social, psychological, and emotional requirements of these patients and their families from the point of diagnosis until complete recovery [62,63].

## Reproductive outcomes following conservative surgery for PAS

Although the available data are limited, effective conservative management of PAS does not seem to negatively impact future fertility or obstetric outcomes. Nonetheless, conceiving after a prior PAS carries a heightened risk of negative maternal outcomes such as recurrent PAS, uterine rupture, postpartum hemorrhage (PPH), and peripartum hysterectomy. In general, the likelihood of recurrent PAS in subsequent pregnancies is between 22% and 29%, with early PPH at 8.6%, uterine rupture at 3.3%, peripartum hysterectomy at 3.3%, and the need for blood transfusions at 16.7%. Additionally, long-term issues may include intrauterine synechiae leading to secondary amenorrhea [64].

#### **Conclusions**

Nonetheless, PAS encounters numerous obstacles that must be resolved prior to surgery. The management of these cases should take place in tertiary care centers and hospitals equipped with comprehensive resources. The difficulties associated with PAS impose strain on both patients and healthcare institutions. Financial implications and legal considerations are often undervalued and should be regarded as equally significant as the other challenges encountered.

#### **Disclosure**

The authors declare no conflicts of interest and have nothing to disclose.

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