

Placenta Accreta Spectrum (PAS) Disorders

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Received: October 19, 2023; **Published:** October 27, 2023

The last 30 years have witnessed the dramatic increase in the incidence of placenta accreta spectrum (PAS) disorders from 0.12% to 0.31%. The spectrum of abnormal placental invasion ranges from the subclinical findings of adherent placental basal plate with the myometrial fibres to the substantial presentation of placenta percreta. Irving in 1937, first described placenta accreta as the failure of separation of the placenta from uterine wall following delivery of the fetus leading to the often used term morbid placental adherence. Various terminologies has been applied to this condition, however, recent guidelines suggested the adoption of term "Placenta accrete spectrum (PAS)", including accreta, increta and percreta. Invasive placentation is associated with catastrophic hemorrhage and having approximately 7.0% mortality rate. PAS refers to a spectrum of abnormal placental invasion which ranges from the subclinical (mostly microscopic) findings of adherent placental basal plate with the myometrial fibres to the substantial presentation of placenta percreta, where the placental tissues invades through the uterine wall and its serosa into the peritoneal cavity including the bladder most often. PAS is traditionally considered to occur as the consequence of localized uterine injury (previous caesarean section) which leads to locally defective decidualization or scarring and abnormal placental adherence in a subsequent pregnancy. The rising trends of PAS disorder is attributed to advancing maternal age (≥ 35 years) and increasing number of cesarean sections globally. Women having prior myomectomy, vigorous curettage resulting in Asherman syndrome, submucous leiomyomas, thermal ablation and uterine artery embolization is at risk for PAS disorders. Optimal and timely management of women with PAS will help reducing the maternal and perinatal morbidity and mortality. It involves early antenatal diagnosis and recognition of high-risk pregnancy based on clinical risk factors, accurate preoperative diagnosis with dedicated ultrasound and MRI if necessary, proper maternal counselling and multidisciplinary approach at the time of delivery.

Following sonographic and color doppler findings suggested the diagnosis of PAS:

- Multiple linear, irregular vascular spaces within the placenta (Swiss cheese appearance).
- Marked thinning or obliteration of the retroplacental hypoechoic zone.
- Interruption of the hyperechoic border between the uterine serosa and bladder.
- Remarkably thin or even non visualized lower uterine segment.
- On color doppler, marked peri-placental vascularity and vascular lakes with turbulent flow (PSV > 15 cm/s).

Abnormal adherence of the placenta to the myometrium is established very early in pregnancy and it's been classified into 3 types, placenta accreta where chorionic villi gets implanted directly on the myometrium, placenta increta where chorionic villi invades inside

the myometrium and placenta percreta where chorionic villi invades through the entirety of myometrium and involves the surrounding organs. Most common type is placenta accreta accounting for 75% of cases. The widely accepted hypotheses regarding the etiology for PAS is the underlying defect at the endometrial-myometrial interface at the scar of previous cesarean section or any other uterine surgery which injures the endometrium, which leads to abnormal decidualization in the scar area and causes deep anchoring of chorionic villi and trophoblast infiltration. But this could not justify the rare occurrence of PAS in nulliparous women without any previous uterine surgery. A probable explanation for this can be obtained from the recent article by Helena, *et al.* which describes the similarities between the molecular biology of PAS and 8 hallmarks of carcinogenesis. The increasing incidence in the placenta accreta spectrum is quite evident from the observational studies across the past decades. It's been observed that the prevalence of PAS described in studies from 1970 to 1980 were between 1 in 2,510 and 1 in 4,017 compared to which the rate reported was 1 in 533 from 1982 to 2002. In the United States overall incidence of PAS in 2016 study using National Inpatient Sample was 1 in 272, which is strikingly high when compared to any other published study. The increasing trend is also observed in the incidence of cesarean section from 39.6% in 2010 to 44.9% in 2019. Several risk factors have been implicated for the PAS. The most common is previous cesarean delivery and the incidence rises with the higher order of prior cesarean deliveries. Another significant risk factor is placenta previa but there is dramatic increase in the PAS incidence in the cases of previa with prior cesarean section as reported by Silver, *et al.* Recent studies in literature demonstrate that the abnormal levels of placental biomarkers increase the risk of PAS. Elevated levels of pregnancy associated plasma protein A (PAPP-A), low hCG and β -hCG in first trimester (11 - 12 weeks) have been observed in women with PAS disorders. During second trimester (14 - 22 weeks) women having placenta previa are at greater risk of PAS disorders if serum β -hCG and α -fetoprotein (AFP) are > 2.5 MoM. No difference was noted in the level of cell free fetal DNA (cff-DNA) in the serum of women having PAS disorders compared with normal controls. By contrast, the level of cell free placental mRNA was significantly greater in patients having PAS disorders than in those without it. The level of cell-free placental mRNA is found to be associated with the degree of placental invasion and having high negative predictive value that increases the accuracy of USG and color Doppler in prediction of PAS. It is essential to diagnose PAS as early as possible in the pregnancy and to strategize its management in order to reduce its high maternal morbidity and mortality. Features of PAS visible in ultrasonogram may be present as early in the I trimester as low implantation of gestational sac in cases of prior cesarean section.

The pregnant women at high risk for PAS such placenta previa and scarred uterus, should be evaluated with experienced sonologist having expertise in this field to establish early diagnosis. In the II or III trimester, the most important USG finding to suspect the PAS is the presence of placenta previa which is reported to be in association with more than 80% of accreta in major studies. A systematic review, including 23 studies and 3,707 pregnancies, noted an average sensitivity of 90.72% and specificity of 96.94%. In cases of unexpected and unplanned intraoperative diagnosis of PAS disorder, avoid placental removal and proceed to hysterectomy as judiciously as possible. The clinical risk factors should be considered equally important as a predictor of PAS disorder even in the absence of USG findings. Other major modality to diagnose PAS is magnetic resonance imaging (MRI). The reported sensitivities of MRI in various studies are 75 - 100% and specificities 65 - 100%. In difficult cases such as posterior placenta previa, MRI comes in very handy to assess the depth of placental invasion in PAS suspect. According to ACOG, MRI is not recommended as an initial evaluation of PAS disorders. As the estimates of perioperative blood loss in cases of PAS is higher, prior notification to blood bank is essential for the readiness of cross-matched blood for the frequent need for multiple blood products transfusion in every elective cesarean delivery. Pre-operative maximization of hemoglobin is advisable. The dynamic traction of invaded myometrial tissue may activate coagulation cascade system- active fibrinolysis and considerable hypofibrinogenemia (between 100 and 200 mg/dl) resulting capillary and continuous hemorrhage after removing the placenta or performing the hysterectomy. If pre-operative level of plasma fibrinogen < 250 mg/dl, cryoprecipitate (1U/10 kg body weight) must be infused before surgery begins. There are conflicts in opinion regarding the ideal gestational age for elective cesarean section. An analytical study suggests that 34 weeks of gestation is minimum given that most large centers are competent to tackle the neonatal complications at this maturity and tops the gestation age at 36 weeks in view of increased risk of bleeding after 36 weeks. During the cesarean hysterectomy in PAS cases, the most accepted approach is transverse fundal incision or classical incision on uterus to deliver

the fetus, not to attempt removing the placenta as manual removal of placenta involves vulnerable risks of torrential hemorrhage and it is strongly discouraged. However, in cases of PAS disorders with deep invasion up to serosa and presence of cervical involvement, subtotal hysterectomy may not be an effective option. In cases of PAS disorders, subtotal hysterectomy has not been found protective against urologic injury in comparison to total hysterectomy. The survey conducted by SMFM specialists reported that 55% surgeons performed total hysterectomy and 45% surgeons performed supracervical hysterectomy for PAS disorders. In 2007, POBC (prophylactic occlusion balloon catheter) program was introduced which advocated the insertion of balloon catheter into both internal iliac arteries before elective cesarean section in PAS, which aimed to reduce blood flow to uterus after cesarean, preventing hysterectomy and massive hemorrhage by allowing timely progression to arterial embolization if necessary. A modified surgical technique- Triple-P procedure was introduced in 2010 which involves 3 steps:

1. Preoperative localization of the placenta and delivering fetus by incision above the upper border of placenta.
2. Pelvic devascularization by inflating balloon catheter in both internal iliac arteries.
3. Placental non-separation with myometrial excision and uterine wall reconstruction.

The systematic review by Tam., *et al.* regarding surgical techniques opted for Placenta accrete spectrum disorders, reported 29% (83/285) unintentional urologic injury during cesarean hysterectomy. Out of them 78% had urinary bladder and 17% ureter injury which is remarkably higher than hysterectomies for gynecological pathology. Study by Norris., *et al.* which reported bladder injury in 36.1% and ureteric injury in 4%. Pre-operative placement of ureteric stent decreased the risk of urologic injury from 33% to 6%. Adequate sharp bladder dissection before keeping uterine incision reduces bladder injury, as it provides enough time to identify vesico-uterine plane in clear field and facilitates the identification of the different tissues. Massive hemorrhage hampers visibility and necessitates urgency for urinary bladder dissection and in pool of blood it is difficult to get vesico-uterine plane. In some cases of PAS, abundant neovascularization makes bladder dissection difficult. Smulian., *et al.* found greater incidence of urinary tract injuries when massive hemorrhage during surgery. Scheduled delayed hysterectomy is another option to avoid massive hemorrhage during primary surgery and it also reduces the chances of urological injuries. During cesarean section the cord is tied and the placenta is kept in situ and hysterectomy is planned after 4 - 6 weeks.

Conclusion

Placenta accreta and its variants, placenta increta and placenta percreta, are rare complications of human placentation. It may threaten maternal life due principally to their potential for torrential hemorrhage. Its incidence is rising due to the increasing caesarean rates worldwide and hence aim should be to cut down the rates of primary cesarean section. Early preoperative diagnosis in the suspected women is the key to save the woman's life and adherent placenta should be suspected even in first trimester in women with known high-risk factors. Favorable outcome can only be achieved with preoperative multidisciplinary input and perioperative measures require adequate time in order to be instituted.

Volume 12 Issue 11 November 2023

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