Pro Index | Journal of Science in Medicine and Life
Volume: 3 Issue: 8 Year: 2025
ISSN: 2992-9202 | http://journals.proindex.uz

Placenta Accreta Spectrum Disorder, Risk Factor, Clinical Grading, Histopathology, and Diagnostic Ultrasound

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Abstract: **Background:** Placenta accreta spectrum (PAS) is a serious pregnancy condition that can result in maternal morbidity and mortality due to hemorrhage. Prenatal diagnosis is based on subjective interpretation of sonographic findings, but the definitive diagnosis can only be made clinically at delivery and confirmed by histopathology.

Aim of the study: To elucidate the risk factors, clinical grading, histopathology correlations and diagnostic accuracy of perinatal imaging in pregnancies complicated by PAS disorders.

Patients and methods: A prospective cohort study that was conducted in the department of Obstetrics and Gynecology at Al- Elwiyah Maternity Teaching Hospital during a period of 12 months from 1st of January 2022 to 31st of December 2022. The study included all cases of PAS disorders according to the ultrasonic features presented to our hospital during the study period.

Results: Seventy-three cases were enrolled with finding of ultrasonic features suggestive of PAS disorders. All participants underwent C/S at which only 47 cases were diagnosed as having PAS disorders depending on clinical features, of those 41 cases underwent hysterectomy and histopathological diagnosis showed different grades of PAS in 37 cases only. Cases of PAS disorders had higher mean maternal age, higher gravidity, parity, and higher rate of previous C/S. Placental hypervascularity was significantly associated with clinical PAS diagnosis. The ultrasound features were not sensitive nor specific in diagnosing PAS according to clinical and histological findings, but ultrasonic features associated with high PPV in cases of those who had PAS disorders and required hysterectomy.

Conclusion: Ultrasound had limited sensitivity and specificity but was associated with high PPV making it a good tool for screening for PAS disorders. Advancing maternal age, high parity, high miscarriage rate associated with increased risk of PAS disorders. •The clinical diagnosis associated with high specificity and strongly associated with histopathologic finding.

1. Introduction

1.1 Background:

PAS disorders is one of the most dangerous conditions associated with pregnancy, because hemorrhage associate with multisystem organ failure, disseminated intravascular coagulation, need for admission to an intensive care unit, hysterectomy, and even death[1].

Outcomes are generally improved with antepartum diagnosis and care by a multidisciplinary team with expertise in the condition, though morbidity is still high as more than half of women receive transfusions of blood products, and a third have incidental cystotomy in association with surgical

management. Ureteral injury, vesicovaginal fistula, and the occurrence of reoperation are less frequent complications[2].

PAS disorders is considered a high-risk condition with serious associated morbidities; therefore, ACOG and the Society for Maternal–Fetal Medicine recommend these patients receive level III (subspecialty) or higher care[3].

1.2 Definition:

PAS disorders are the general term applied to abnormal adherence and invasion of the placental trophoblast to the uterine myometrium, it is also referred to as morbidly adherent placenta. The spectrum includes placenta creta (attachment of the placenta to myometrium without intervening decidua), placenta increta (invasion of the trophoblast into the myometrium), and placenta percreta (invasion through the myometrium, serosa, and into surrounding structures) (**Figure 1**). The major clinical problem occurs when the placenta does not detach normally from the uterus after delivery of the fetus, leading to bleeding, which is often severe[4].

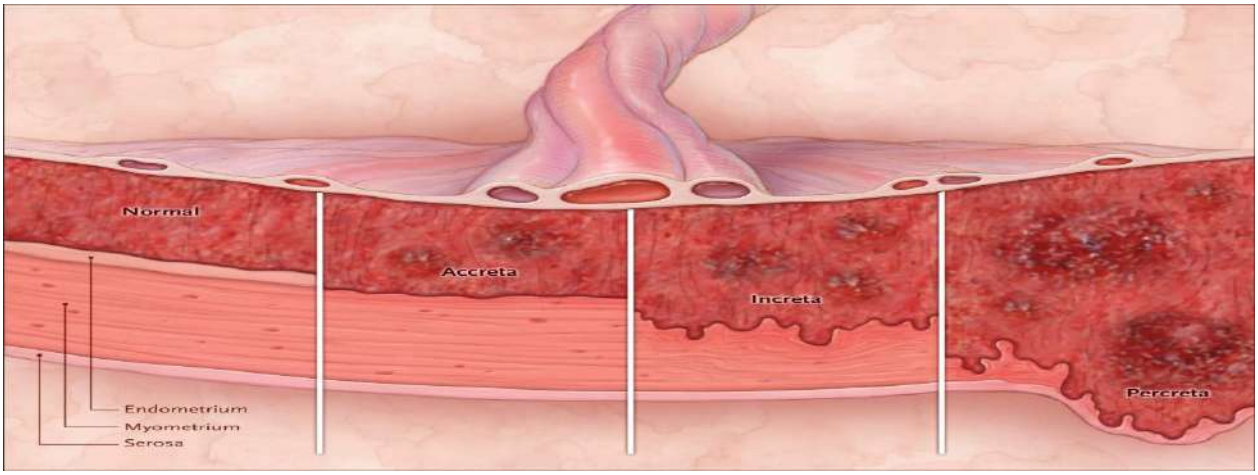

Figure 1: Placenta accreta spectrum[4]

1.3 Epidemiology:

As the rate of caesarean delivery is increasing globally, the rates of placenta accreta spectrum disorders are increasing[5]. A 2016 study conducted using the in-patient sample found that the overall rate of placenta accreta in the United States was 1 in 272 for women who had a birth-related hospital discharge diagnosis, which is higher than any other published study. The increasing rate of placenta accreta over the past four decades is likely due to a change in risk factors, most notably the increased rate of cesarean delivery[6]. In Iraq the rate of CS was (40.7%) according to Ministry of Health[7], in this goes with increasing prevalence PAS disorders in single center in Iraq, as it was 162.4 per 100,000 women in 2014, 266.7 in 2015, 382.3 in 2016, and 191.5 per 100 000 women in 2017[8].

1.4 Pathophysiology:

The pathophysiology of the several concepts has been proposed to explain why and how PAS disorders occur. The oldest concept is based on a theoretical primary defect of trophoblast biology leading to excessive invasion of myometrium. The current prevailing hypothesis is that a secondary defect of the endometrium-myometrial interface leads to a failure of normal decidualization in the area of a uterine scar, allowing abnormally deep placental anchoring villi and trophoblast infiltration. There is no doubt that the decidua normally regulates trophoblast invasion, as evidenced by the aggressive invasion of the muscular and serosal layers seen at sites of ectopic implantation in the fallopian tube or in the abdomen[9].

1.4.1 Scar implantation:

The exact pathogenesis of PAS disorders remains unknown, the most prevailing theory is that prior uterine surgery involving the endometrial-myometrial interface leads to defective decidualization in an area with a uterine scar, allowing the anchoring villi of the placenta to adhere to the myometrium abnormally and further trophoblast invasion. This hypothesis is supported by the finding that the vast majority of PAS disorders patients present a history of disruptions within the uterine cavity such as prior caesarean section, previous operative uterine procedures (myomectomy, operative hysteroscopy, etc.), and/or dilation and curettage of the uterus[10].

Nevertheless, such theory fails to explain the occurrence of PAS disorders in primigravid women without any prior uterine procedure or instrumentation. The potential explanation was reported to be that this rare minority of PAS disorders patients may suffer from one of a series of uterine pathology, such as adenomyosis, submucous fibroids, or bicornuate uterus, which may subsequently result in microscopic endometrial defects that further affect the normal biological functions of the endometrium and thus allow abnormal attachment of the placenta[11].

1.4.2 Scar placentation:

Accreta placentation is the consequence of uterine remodeling after surgery, primarily after cesarean delivery. Large cesarean scar defects in the lower uterine segment are associated with failure of normal decidualization and loss of the sub decidual myometrium. These changes allow the placental anchoring villi to implant, and extra villous trophoblast cells to migrate, close to the serosal surface of the uterus. These microscopic features are central to the misconception that the accreta placental villous tissue is excessively invasive and have led to much confusion and heterogeneity in clinical data[12].

Progressive recruitment of large arteries in the uterine wall, that is, helicine, arcuate, and/or radial arteries, results in high-velocity maternal blood entering the intervillous space from the first trimester of pregnancy and subsequent formation of placental lacunae. Recently, guided sampling of accreta areas at delivery has enabled accurate correlation of prenatal imaging data with intraoperative features and histopathologic findings. In one study more than 70% of samples, there were thick fibrinoid depositions between the tip of most anchoring villi and the underlying uterine wall and around all deeply implanted villi[13].

1.4.3 Vascular remodeling

Development of trophoblastic cell lineage on the surface of the embryo is the initial differentiating event in embryonic development. The inner cell mass that goes on to form an embryo and extra embryonic tissues such as the allantois, amnion, and yolk sac is surrounded by early trophoblast cells called trophectoderm.

Trophoblastic cells are of two types: villous and EVT[14]. Placental villi are covered with cyto and syncytiotrophoblasts, and EVT arises from tips of anchoring villi that make contact with uterine decidua. The EVT are involved in trophoblastic invasion, and they differentiate into interstitial and endovascular subtypes.

The interstitial cells invade the decidual stroma as far as the inner third of uterine myometrium called junctional zone (JZ). They are involved in vascular remodeling, while the endovascular subtypes invade uterine spiral arterioles[15]. At the JZ, endovascular trophoblasts fuse to form multinucleated giant cells (MNGs). Migration of EVT is facilitated by their secretion of a variety of matrix metalloproteinases comprising collagenases, gelatinases, and stromelysins[15].

In cases of invasive placentation, an unusual uteroplacental vasculature was observed in which physiological changes were present in large arteries deep in the myometrium. Invasion of larger vessels beyond the level of the JZ is probably determined by access rather than a preexisting defect in trophoblastic differentiation that would produce uncontrolled invasion of EVT through the entire depth of the myometrium. Prenatal imaging and macroscopic observation at delivery of the

hypervascularity of the placental bed in most cases of invasive placentation suggest a phenomenon of neovascularization around the scar area in addition to the vasodilatation of the radial and/or arcuate uterine vasculature in the accreta area[10].

1.5 Risk factors:

PAS disorders have been attributed to abnormal or deficient areas of decidua, allowing chorionic villi to adhere to the underlying myometrium. Such damage may result from previous procedures or inflammation. Correspondingly, most of the risk factors studied involve some degree of uterine trauma or scarring (Table 1). The role of the hormonal environment or the trophoblast itself has been less well addressed but offers ongoing opportunities for discovery [16].

1.5.1 Primary and secondary uterine pathologies:

Given that cesarean deliveries are a common source of scarring in the myometrium and endometrium, this common procedure has been associated with the development of PAS disorders in subsequent pregnancies[16].

Uterine curettage is likely the most commonly encountered uterine procedure in a patient's surgical history, but its role as an independent PAS disorders risk factor has been unclear[17].

A relatively large study (n=854) done in Australia, between 2003 and 2012, found a dose-dependent relationship between the number of previous uterine procedures and development of abnormally invasive placenta. These procedures included laparoscopic uterine procedures, hysteroscopy, and uterine curettage[18].

Including in vitro fertilization and intracytoplasmic sperm injection, are linked to PAS disorders development. This outcome has been further linked to specific ART practices, including transfer of >1 embryo and use of cryopreserved embryos[19]. Though other studies have showed an independent relationship between transfer of cryopreserved embryos and PAS disorders even after controlling for maternal factors and placenta previa[20]. Development of a thin endometrium during uterine preparation has been linked to both previa and PAS disorders development and provides a biologically plausible explanation for this association[21].

Asherman syndrome, in which fibrotic scars obliterate the normal endometrium and potentially obstruct the uterine cavity[22]. Adenomyosis and current fibroids may distort the normal endometrium, but have not been well studied with regard to adherent placentation[23].

Table 1: Primary and secondary uterine pathologies reported to be associated with PAS disorders[23]:

Classification	Type of uterine pathologies
Direct surgical scar	➢ Cesarean delivery ➢ Myomectomy ➢ Surgical termination of pregnancy ➢ Endometrial resection ➢ Dilatation and curettage ➢ Asherman's syndrome
Non-surgical scar	➢ IVF procedures ➢ Intra-uterine device ➢ Uterine artery embolization ➢ Manual removal of ➢ Chemotherapy and radiation placenta ➢ Endometritis ➢ Previous accreta
Uterine anomalies	➢ Bicornuate uterus ➢ Submucous fibroids

	➢ Adenomyosis ➢ Myotonic dystrophy

1.5.2 Placenta previa:

Placenta previa is the most important risk factor for PAS disorders, and at one time was considered necessary for the diagnosis. Insufficient decidua in the lower uterine segment and cervix may predispose to placental adherence with low implantations[24].

1.5.3 Maternal age:

Advanced maternal age, usually defined as 35 years or greater, has been implicated in PAS disorders development. This relationship may be confounded by higher parity and previa risk, as well as a higher probability of previous uterine procedures or fertility treatments, but also may represent an altered hormonal or implantation environment[25].

1.5.4 Previous placenta accreta:

While previous cesarean section is the most commonly encountered risk factor from a previous pregnancy, a previous history of accreta or adherent placenta will confer the highest absolute risk. Previous PAS disorders are a novel risk factor, as cases of PAS disorders historically ended in hysterectomy. However, uterine conservation is increasingly described in management of this condition. For patients who have experienced a subsequent pregnancy, PAS disorders rates will be of 4.7% in the second pregnancy and 7.6% in the third pregnancy[26].

1.6 Presentation:

1.6.1 Clinical presentation:

- Placenta accreta may not present any symptoms, but some cases may lead to bleeding or pelvic pain in the third trimester.
- Attempting to manually remove the placenta may lead to heavy bleeding and high maternal morbidity and mortality.
- Clinical symptoms of placenta accreta disorders can be similar to those of placental retention, but retained placenta should not be included in the category of placenta accreta spectrum (PAS) disorders.

1.6.2 Ultrasound changes seen in PAS disorders:

In 2016, The European Working Group on Abnormally Invasive Placenta proposed standardized descriptions of ultrasound signs used for the prenatal diagnosis of PAS disorders [27].

1.6.2.1 Types of ultrasound changes:

A. Loss of the clear zone:

Loss of the clear zone is used when the normal hypoechoic retroplacental zone in the myometrium under the placental bed is not visible on ultrasound. It was one of the first signs identified by grayscale ultrasound imaging in cases of PAS disorders. This sign is supposed to represent an abnormal extension of the placental villi through the decidua basalis into the myometrium and was used by many authors as a marker of PAS disorders on gray-scale ultrasound. Loss of the clear zone has been reported in around 70% of cases in those series that included data on the depth of villous myometrial invasion[28].Absence of clear zone Shown in **Figure 2** A.

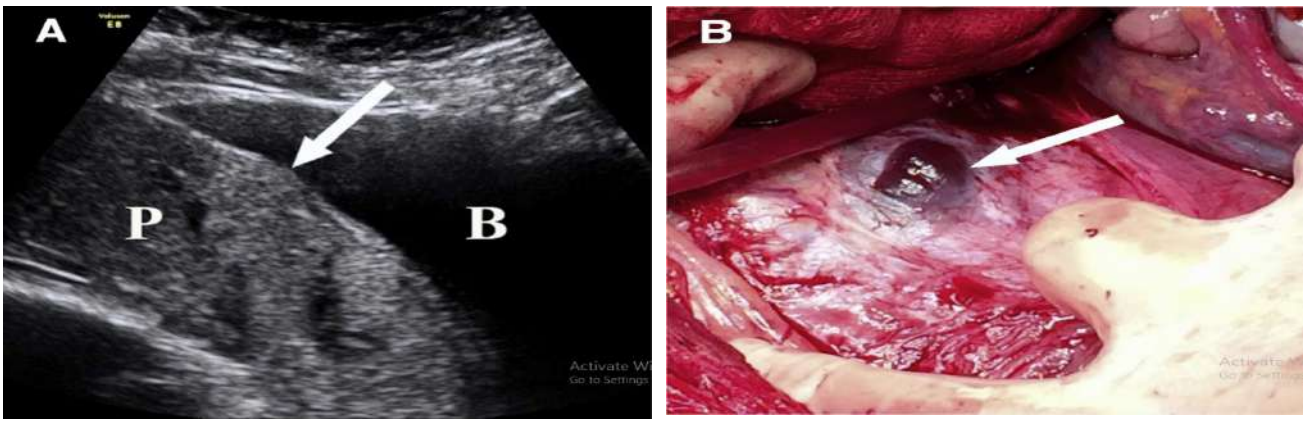

Figure 2: Myometrial thinning secondary to uterine thinning at scar defect[10].

- A: Transabdominal ultrasound longitudinal view of placenta (P) previa at 36 weeks showing myometrium defect (arrow) under bladder (B). Note absence of clear zone and myometrium in area.
- B: Findings at surgery later same day of "uterine window" (arrow)

B. Myometrial thinning:

Myometrial thinning to 32-34 weeks when the lower uterine segment is further stretched by the combined action of fetal presentation and Braxton-Hicks uterine contractions. This may contribute to false-positive diagnoses where extreme myometrial thinning is incorrectly diagnosed as abnormal invasion. Occasionally, the myometrium may partly dehisce or become so thin that the placenta can be seen through it at delivery; this phenomenon should be described as a "uterine window" (**Figure 2** B) as it represents deficient myometrium rather than abnormal placentation. In true PAS disorders, especially PP, the myometrium appears excessively thin or undetectable due to villous invasion. This not only results in the loss of the clear zone but also changes the echogenicity of the myometrium itself, resulting in a loss of visual contrast between placental tissue and myometrium. In invasive placentation, as the villi breaches the serosa, the myometrial echogenicity becomes indistinguishable from that of the placental tissue. The sonographer must take care with this sign as, like the clear zone, myometrial thickness will be influenced by direct pressure of ultrasound probes and fullness of the maternal bladder[29].

C. Placental lacunae:

Placental lacunae are numerous, large, irregular sonolucent intra-placental spaces often described on ultrasound giving the placenta a "moth-eaten" appearance in PAS disorders in both transabdominal (**Figure 3**) and trans-vaginal (**Figure 4**) ultrasound. It is the most common ultrasound sign described in PAS disorders with around 80% of the authors reporting them antenatally, independently of the depth of invasion[28]. Other terms have been used to describe these spaces including "placental lakes" and "Swiss cheese." Placental lakes are seen as echo lucent areas often in the center of a lobule or cotyledon, under the chorionic plate or in the marginal zone. These lakes are a common finding in normal pregnancies from the end of the first trimester but changes in their peripheral echogenicity (resulting in the term echogenic cystic lesions) have been associated with the development of intervillous thrombosis and uteroplacental insufficiency.

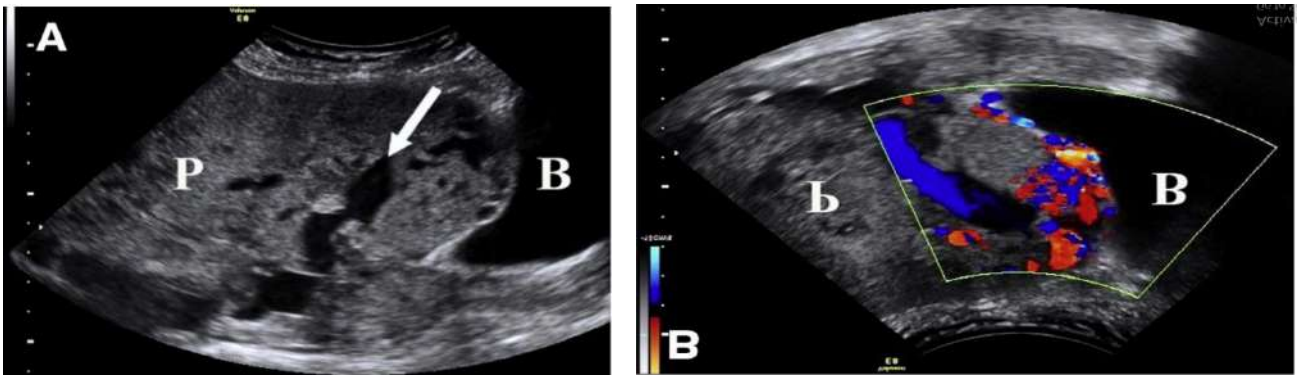

Figure 3: Transabdominal ultrasound longitudinal views of placenta (P) previa accreta at 36 weeks.

- A, "Motheaten" area with numerous lacunae of different size and shape secondary; and B, high-velocity, turbulent blood flow within lacunae on color Doppler imaging next to bladder (B).

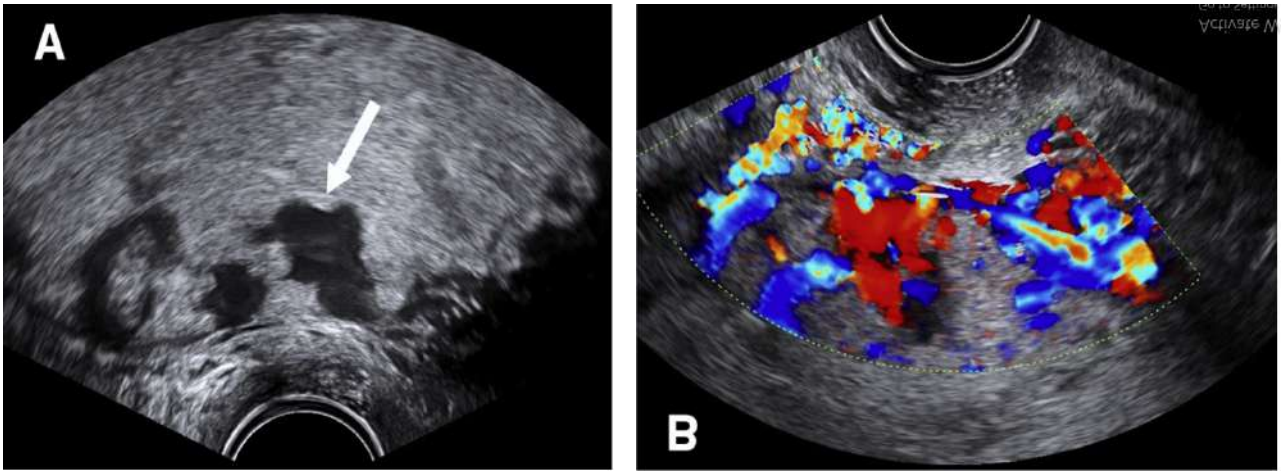

Figure 4: Transvaginal ultrasound views of placenta previa increta at 20 weeks.

- A, "Moth-eaten" appearance of placenta with numerous lacunae of different size and shape secondary (arrow);
- B, highvelocity, turbulent blood flow within lacunae on color Doppler imaging.

The shape and number of lakes will vary with gestational age, with the location of the placenta inside the uterine cavity, and with direct pressure of the ultrasound probes. The difference between the lacunae associated with abnormal invasion and placental lakes is not clear cut, but relates to number, shape, location, and velocity of the blood flow inside the space[10].

D. Bladder wall interruption:

This is often described on gray-scale ultrasound as an interruption, loss, or irregularity of the bladder wall or of the hyperechoic line between uterine serosa and bladder lumen. This sign may arise as a direct result of villous invasion into the muscle of the posterior wall of the bladder, thereby changing its echogenicity, but is most likely an ultrasound artefact arising from the massive neovascularity found within the peritoneal fold between the anterior wall of the uterus and the posterior wall of the bladder[30].

E. Placental bulge:

Placental bulge describes the ballooning of the uterus containing the placenta away from its expected plane into the surrounding tissue, usually the bladder. This sign is seen on ultrasound and

MRI. It most likely represents villous invasion deep into and/or through the myometrium resulting in loss of structural integrity of the surrounding uterine muscle[31].

F. Exophytic mass:

Exophytic mass describes the invasion of the villous tissue through the myometrium and the serosa into adjacent extrauterine organs, usually the bladder. This focal exophytic mass of placental tissue, extending beyond the uterine serosa, should only occur in cases of PP[32].

G. Sub placental and/or uterovesical hypervascularity:

This results from excessive dilatation of the uteroplacental circulation beyond the spiral arteries, i.e., including the radial and arcuate arteries, and is a prominent feature of PAS disorders on prenatal ultrasound. This is often accompanied by extensive neovascularization within the peritoneum, especially between the anterior wall of the uterus and the posterior wall of the bladder[33].

H. Placental lacunae feeder vessels:

These are seen as vessels with high velocity blood flow arising from the deep arterial vasculature of the myometrium, i.e., radial, or arcuate arteries, and feeding the lacunae. An ultrasound study found that the total area occupied by vessels in normal and PI placental beds is similar, but that vessels are significantly sparser and larger in invasive placentation. This could explain the abnormal hemodynamics underlying the development of the lacunae in invasive placentation[34].

I. Bridging vessels:

Bridging vessels are seen as CD signals arising in the myometrium and appearing to travel beyond the uterine serosa and into the bladder before disappearing. This bridging is an ultrasound artefact as these vessels do not traverse between the myometrium and bladder but are actually the contorted vessels of the neovascularity within the peritoneum caught in cross-section in a 2-dimensional image. They have been referred to as “bladder varicosities” in cases of placenta previa accreta. Collectively, these CDI features have been reported in 66% of the cases of abnormally invasive placenta diagnosed prenatally, and are due to the dilatation of large and deeper myometrial vessels below the JZ of normal implantation[35].

1.6.2.2 Ultrasound accuracy:

Irrespective of the imaging modality used, prenatal diagnosis of PAS disorders remains subjective, with accuracy depending on the experience of the operator. The definitive diagnosis, however, can only be made clinically at delivery and should be confirmed by histopathology wherever possible. There is wide variation in prenatal detection rates depending on the ultrasound signs used, operator’s experience, scanning conditions, equipment used, and gestational age[36]. In particular, color Doppler imaging is more susceptible to operator error than grey-scale imaging[37].

In an attempt to reduce errors due to the subjectivity involved in making this diagnosis and ensure that all operators are using the same description for the same sign, the European Working Group on Abnormally Invasive Placenta (EW-AIP) recently proposed a standardized description and name for all the ultrasound signs used for the prenatal diagnosis of placenta accreta[38].

A systematic review using this new standardized description for ultrasound examination of PAS disorders found that the loss of the clear zone (62.1%) and the presence of bridging vessels (71.4%) were the most common ultrasound signs found in cases of placenta creta. For placenta increta, a loss of the clear zone (84.6%) and sub-placental hypervascularity (60%) were the most common ultrasound signs, whereas placental lacunae (82.4%) and sub-placental hypervascularity (54.5%) were the most common ultrasound signs in placenta percreta. Due to wide heterogeneity in terminology used to describe the grades of PAS disorders and differences in study design, no

ultrasound sign or combination of ultrasound signs is specific for the depth of accreta placentation[39].

1.6.2.3 Technical issues in the diagnosis of PAS disorders:

A. Transducer selection:

TVS is often recommended to identify the cervical canal, internal o s, and the relationship between the leading placental edge and the internal os; it can also be used for a focused evaluation of the lower uterine wall and the bladder interface. Transabdominal scans can be improved by selecting a higher frequency (5–9 MHz) transducer (linear if possible), and carefully "walking" the scar from one end to the other, keeping the transducer perpendicular to the uterine wall[40].

B. Bladder filling:

Ultrasound examination must be conducted with a full bladder (approximately 200–300 mL). The bladder outline is vital to identify the lower uterine segment, which is the presumed location of the previous cesarean delivery scar, thereby making the assessment of the placental position in relation to the presumed site of the scar possible. Without a full bladder, such signs as bladder wall interruption, placental bulge, and uterovesical hypervascularity cannot be appropriately assessed[23].

C: Probe pressure:

Excessive probe pressure during transabdominal scanning can lead to the apparent loss of the retroplacental clear zone—one of the signs of invasive placentation. Therefore, this should be avoided. The loss of the retroplacental clear zone should be assessed with light probe pressure. This pitfall is also much less likely to occur with TVS[10].

D: Use of color flow mapping and power Doppler:

Excessive vascularity of the lower uterine segment is associated with abnormal invasion but is an inherently subjective sign. The normal uteroplacental interface is quite vascular but color Doppler imaging evaluation of this area is not part of a routine examination. Even experienced operators often do not have a baseline understanding of normal flow; it is, therefore, difficult to assess increased flow[23].

1.6.3 MRI

Clinicians should be aware that the diagnostic value of MRI and ultrasound imaging in detecting placenta accreta spectrum is similar when performed by experts. MRI may be used to complement ultrasound imaging to assess the depth of invasion and lateral extension of myometrial invasion, especially with posterior placentation and/or in women with ultrasound signs suggesting parametrial invasion[28].

1.6.4 Histopathology:

The histopathologic findings are essential and often provide a gold standard for the definition of the condition. However, myometrial fibers can sometimes be found in the basal plate of normal placentas[41], the decidua is not a continuous layer and it becomes thinner with advancing gestation, and in many cases of placenta percreta the extended damage to the uterine wall, with no decidual and myometrial tissue left at the site of placentation, makes histopathologic examination impossible[41].

1.6.5 Biomarkers of PAS disorders

Several placental and fetal hormones routinely used in the screening of Down syndrome have been found to have different concentrations in the serum of women with placenta previa accreta compared with those with a non-accreta previa[42]. At 11–12 weeks of pregnancy, human chorionic gonadotropin (hCG) and its free beta-subunit (β-hCG) are lower and pregnancy-associated plasma protein A (PAPP-A) is higher in the maternal serum of women with PAS disorders. By contrast, at

14–22 weeks, women presenting with a placenta previa are at higher risk of PAS disorders if serum β-hCG and alpha-fetoprotein (AFP) are above 2.5 multiples of the median (MoM) (OR 3.9, 95% CI 1.5–9.9; and OR 8.3, 95% CI 1.8–39.3, respectively)[23].

By contrast, no difference has been found in the amount of cell-free fetal DNA (cffDNA) in the maternal serum of women presenting with PAS disorders compared with normal controls. Overall, biomarkers could be used with ultrasound imaging to screen for PAS disorders prenatally in a model similar to that used for aneuploidy screening; however, the benefit of this remains unknown until more prospective data are available[43].

1.7 General classification of placenta accreta spectrum:

The process of clarifying the reporting data on PAS disorders in the international literature started in the previous years with the development of the new grading system for the clinical diagnosis of PAS disorders that have been adopted by the International Federation of Gynecology and Obstetrics (FIGO). Adherence to this new FIGO classification should improve future systematic reviews and meta-analysis and provide more accurate epidemiologic data which are essential to develop new management strategies[44].

According to FIGO classification (2018) for the clinical diagnosis of placenta accreta spectrum disorders three grades of PAS disorders were identified, each grade diagnosed by either clinical, or histological criteria (**Table 2**)[44].

Table 2: FIGO classification (2018) for the clinical diagnosis of placenta accreta spectrum disorders[44]:

Clinical criteria	Histologic criteria
Grade 1: Abnormally adherent placenta (placenta adherenta or creta)	
At vaginal delivery ➢ No separation with synthetic oxytocin and gentle controlled cord traction ➢ Attempts at manual removal of the placenta result in heavy bleeding from the placenta implantation site requiring mechanical or surgical procedures. **At laparotomy** ➢ 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	➢ 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. ➢ The diagnosis cannot be made on just delivered placental tissue nor on random biopsies of the placental bed.
Grade 2: Abnormally invasive placenta (Increta)	
➢ Abnormal macroscopic findings over the placental bed: bluish/purple coloring, distension (placental "bulge") ➢ Significant amounts of hypervascularity (dense tangled bed of vessels or multiple vessels running parallel craniocaudally in the uterine serosa) ➢ No placental tissue is seen to be invading through the uterine serosa. ➢ Gentle cord traction results in the uterus being pulled inwards without separation of the placenta (so-called the dimple sign)	➢ Hysterectomy specimen or partial myometrial resection of the increta area shows placental villi within the muscular fibers and sometimes in the lumen of the deep uterine vasculature (radial or arcuate arteries)

Grade 3: Percreta **Grade 3a:** Limited to the uterine serosa	
➢ Abnormal macroscopic findings on uterine serosal surface (as above) and placental tissue seen to be invading through the surface of the uterus. ➢ 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)	➢ Hysterectomy specimen showing villous tissue within or breaching the uterine serosa
Grade 3b: With urinary bladder invasion	
➢ Placental villi are seen to be invading into the bladder but no other organs. ➢ Clear surgical planes cannot be identified between the bladders and uterus.	➢ Hysterectomy specimen showing villous tissue breaching the uterine serosa and invading the bladder wall tissue or urothelium
Grade 3c: With invasion of other pelvic tissue/organs	
➢ Placental villi are seen to be invading into the broad ligament, vaginal wall, pelvic sidewall, or any other pelvic organ (with or without invasion of the bladder)	➢ Villous tissue breaching the uterine serosa and invading pelvic tissues/organs (with or without invasion of the bladder)

1.8 Management of PAS disorders:

Clinical management of patients with PAS disorders varies worldwide. Although the harmful consequences of PAS disorders have been well recognized, few randomized controlled trials or prospective studies have investigated the optimal management of accreta placentation[45].

1.8.1 General management:

The management for the three different types of PAS disorders is essentially the same, except for some special conditions, such as placenta percreta extending to extra-uterine tissue. Management lines are:

- Given the potential hemorrhage, optimizing pre-delivery hemoglobin values and correcting anemia, especially iron deficiency anemia, are desirable.
- For women with antepartum bleeding, the option of antenatal corticosteroids may be considered between 23 and 34 weeks of gestation[46]. Notably, the risks of using antenatal corticosteroids should be fully informed to the patients and their family members, especially to those with lower gestational ages.
- Hospitalization in late period of pregnancy can be considered, particularly on the occasions when vaginal bleeding or contractions occur, or when living far away from a tertiary care center; outpatient follow-ups can be implemented in asymptomatic women with appropriate counsels and rapid access to the hospital[47].
- Notably, management by a multidisciplinary team, including obstetrician-gynecologists with expertise in placenta accreta spectrum, experienced anesthesiologists, neonatologists, interventional radiologists, urologist, nursing panel and blood bank, is desirable given its ability to improve maternal and neonatal outcomes. If such a multidisciplinary team is not available, transferal to a large tertiary center, which has the capability to handle massive obstetric hemorrhage and provide intensive care, should be recommended[48].
- Some recommendations, such as avoiding rigorous activity and pelvic examination, have not been proven to generate any benefit and thus should be provided with caution[6].

- There is clearly demonstrated the ability of preoperative tranexamic acid to minimize intraoperative blood loss
- The routine strategy for the delivery of women with PAS disorders is planned caesarean section. The optimum timing of such planned delivery, which needs to balance between maternal risks and neonatal benefits, remains unclear. Generally speaking, given the ability to deal with maternal and neonatal complications in most large tertiary care centers at this gestational age and potentially higher risk of hemorrhage beyond 36 weeks in women with PAS disorders, delivery planned at 34 weeks of gestation was considered reasonable and close to optimal[48]. As for those stable patients with favorable systematic conditions, the ideal gestational age for scheduled CS or hysterectomy is suggested to be around 36 weeks of gestation. However, for patients with pre-eclampsia, rupture of membranes, lasting bleeding, fetal compromise, or progressive maternal comorbidities, delivery should be planned in advance and sometimes unscheduled delivery becomes possible.
- Notably, the recommendations on the timing of pregnancy termination are various in different counrties and associations, necessitating further studies on the optimum timing of pregnancy termination[48].

1.8.2 Non-conservative management:

- The choice of skin incision is mainly dependent on the area that needs to be exposed, the elective or emergency nature of the operation, and the surgeon's personal preference. However, this type of incision may have a profound influence on the occurrence of postoperative wound complications. Major incision types commonly used in obstetrical surgery are the Pfannenstiel incision, a vertical incision, and a Maylard incision. The most commonly preferred skin incision method in surgery of cases with PAS is a vertical incision. This preference aims to reach the uterine fundus and pelvic retroperitoneal natural spaces more easily[49].
- Whenever possible the incision in the uterus should avoid the placenta which sometime makes a nontraditional incision necessary, Caesarean hysterectomy, with the placenta left undisturbed in situ after delivery of the fetus, is the most universally accepted procedure in the non-conservative management of PAS disorders [50]. It is noted that prenatal diagnosis of PAS disorders, made by clinical risk assessment and ultrasound imaging, is essential to this approach. Prophylactic antibiotics before surgery are also of great importance and should be one of the standard managements for PAS disorders[51].
- Cystoscopy or intentional cystotomy should be considered in cases of suspected bladder invasion to evaluate the degree of bladder, and potential ureteral involvement. Further, partial cystectomy may be an option of placenta percreta with confirmed bladder invasion[52].
- In addition to these mentioned nonconservative approaches, to further deal with massive hemorrhage and prevent potential pelvic hemorrhage, several procedural strategies have been proposed. Nevertheless, further discussions are needed to adopt these supplementary procedures. Internal iliac artery ligation is thought to have capability to reduce blood loss, but its time-consuming feature and unproven efficacy for handling pelvic hemorrhage preclude the possibility of using this procedure more widely[50].
- Interventional radiologic techniques, such as endovascular intervention with a balloon catheter and embolizing the internal iliac arteries or uterine artery, are not routine considerations, because these procedures are difficult to perform and specialist-dependent, with controversial effectiveness.
- Other approaches like aortic compression or clamping and damage control are not supported by high-quality data; therefore, the practical use of them should be cautious. Overall, large prospective studies are still required for these adjuvant methods to decrease blood loss[53].

Due to the significant impacts of the above non-conservative operations on the maternal hemodynamic homeostasis, postoperative monitor of hemodynamic is necessary and can be conducted in the intensive care unit. On some occasions, interventional radiology and reoperation may be necessary, in order to address some severe issues related to maternal complications after surgery[50].

1.8.3 Conservative management:

The key to conservative management for PAS disorders is uterine conservation to preserve the fertility of women especially those with strong intention. In addition, another merit of this approach is thought to have potential to reduce major complications associated with hysterectomy, such as massive obstetric hemorrhage, and injury to adjacent pelvic organs. The decision on conservative management should balance between fertility and associated risks with uterine preservation, such as infection, hemorrhage, potential need for hysterectomy, recurrence or hemorrhage in future pregnancies, and even death[54].

1.8.4 Expectant management:

Realizing uterine conservation with the placenta left in situ is known as expectant management of PAS disorders. In this strategy, the placenta is left undisturbed in situ after delivery of the new-born; a series of procedures to manage postpartum hemorrhage, such as compression sutures, intrauterine balloon catheter, and uterine artery ligation or embolization, can be employed as needed. Notably, postpartum prophylactic oxytocin is not routinely used, for its administration associated with increased risk of bleeding by resulting in potential placental separation. Nevertheless, uterotonic drugs may be considered when the placenta has been mostly or even completely removed or major bleeding has already occurred[47].

Up to now, very limited data have been reported regarding other approaches to treat bleeding in the setting of expectant management, such as methotrexate therapy, high-intensity focused ultrasound (HIFU), delayed hysteroscopic resection of placental remnants and delayed-interval hysterectomy; therefore, their utilization was not routinely recommended[55].

The immediate complications and long-term outcomes of patients who underwent expectant management can be very severe, indicating that this strategy should be attempted only in fully informed women, or only as part of approved clinical trials[56].

1.8.5 Uterine preservation with placental removal:

For women with focal accreta and posterior or fundal placenta accreta, uterine preservation with placental removal, through manual removal or surgical excision followed by repair of the corresponding defect, may be successful in cases without excessive risk. Sonographic findings are of vital importance to determine focal accreta and specific area of accrete[47].

An emerging technique to preserve uterus by removing placenta has already been introduced, called triple P procedure (perioperative localization of the placenta, pelvic devascularization and placental non-separation). The main process of this approach involves pelvic devascularization as well as partial removal of the uterus, where the invasive placentation occurred. The aim is to achieve the maximum preservation of uterine and its physiologic function. Before its safety and efficacy are demonstrated in larger clinical studies, triple P procedure cannot become the mainstream in the conservative management of placenta accreta spectrum[11].

Finally, PAS disorders still a challenging topic, due to the heterogeneity in defining the condition and about half of the cohort studies published over the last three decades were not provide evidences of correlation between prenatal ultrasound signs, clinical symptoms, and detailed pathologic findings at delivery, so it was pivotal to improve the accuracy of PAS diagnosis in the international literature, and for that purpose the FIGO proposed reporting guidelines on 2018, which

include a standardized basic dataset for future clinical research, to allow comparison between centers with different management strategies.

1.9 Aim of Study

To elucidate the risk factors, clinical grading, histopathology correlations and diagnostic accuracy of perinatal imaging in pregnancies complicated by PAS disorders.

2. Patients & methods

2.1 Study Design, Setting and Data Collection Time:

A prospective cohort study that was conducted in the Department of Obstetrics and Gynecology at Al- Elwiyah Maternity Teaching Hospital during a period extending from the 1st of January 2022 to the 31st of December 2022.

2.2 Study patients and sample size:

The study included 73 cases of PAS disorders suspected by ultrasound presented to Al- Elwiyah Maternity Teaching Hospital.

Intraoperative 26 cases show Non PAS while 47 cases show PAS , 6 cases of them treated by conservative managment while 41 cases undergo hysterectomy and sent for histopathology , by histopathology 37 cases show PAS and 4 cases Non PAS as shown as (Figure 5).

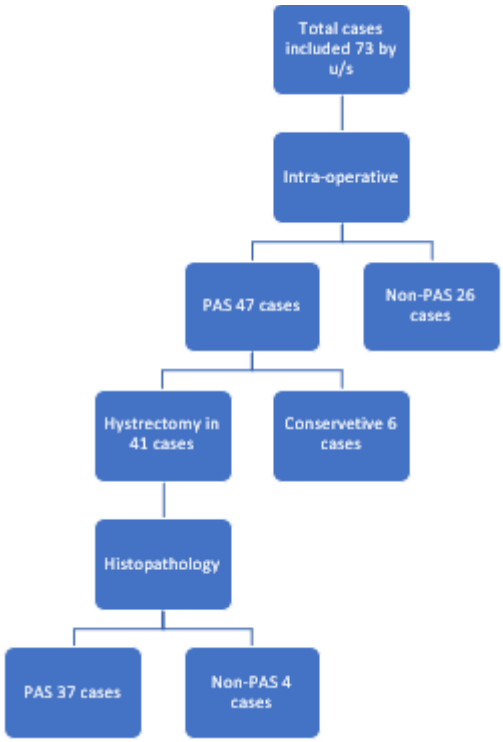

Figure 5: Distribution of the cases.

2.3 Inclusion criteria:

Pregnant women with clinical diagnosis of PAS disorders that would undergo hysterectomy.

2.4 Data collection:

Participants were interviewed with pre-designed questionnaire that informed about the demographical data patient age, weight and height, gravidity, parity and miscarriage, educational level, occupation, and residency.

Information on the current pregnancy obtained that include antenatal care visit (ANC) adequacy, last menstrual period, expected date of delivery, and estimation of the gestational age (GA). The presenting complaints (vaginal discharge, bleeding, and decreased fetal movements).

Previous surgical history, number of CS, and previous uterine surgery.

Examination in the form of vital signs and abdominal examination.

All cases undergo trans-abdominal ultrasound by the same experienced radiologist using (Philips HD11 XE Germany) with assessment of the diagnostic criteria, with reporting the ultrasonic features of PAS disorders.

The surgery was done by expert specialist Obstetrician who identified the clinical criteria of PAS disorders and perform either conservative or non-conservative procedure.

All cases of caesarean hysterectomies have undergone histopathological study at Al- Elwiyah Maternity Teaching Hospital and final histopathological grade obtained.

Interventions applied such as the need for blood and blood products and ICU admission were also recorded.

2.5 Ethical considerations and official approvals

Informed consent was obtained from each patient prior to collecting data, and information was anonymous. Names were removed and replaced by identification codes. All information kept confidential in a password secured laptop and data used exclusively for the research purposes."

Administrative approvals were granted from the following bodies:

1. The Council of Iraqi Board of Medical Specialization.
2. Approval and agreement of the Department of Obstetrics and Gynecology at Al- Elwiyah Maternity Teaching Hospital.

2.6 Statistical analysis

The ultrasound features of PAS disorders were compared to clinical grade, and histopathological grade. Also, estimation of the rate of each risk factor was done using Statistical Package for Social Sciences (SPSS) version 26. The data presented as mean, standard deviation and ranges. Categorical data presented by frequencies and percentages. Normality of the distribution of the continuous variables evaluated by Shapiro–Wilk test. The independent t-test (two tailed) was used to compare the parametrical continuous variables while, Mann-Whitney U test for non-parametrical continuous variables. The Chi square test and Fisher-Freeman-Halton exact test were used for estimation of the significance of categorical data. A level of P – value less than 0.05 was considered statesticaly significant.

3. Results

Seventy-three cases were enrolled after finding an ultrasonic feature suggestive of PAS disorders. All participants underwent C/S, at which only 47 cases were diagnosed as having PAS disorders on clinical ground during surgery. 41 of the 47 cases were underwent hysterectomy and histopathological diagnosis showed different grades of PAS disorders in 37 cases only, as further illustrated in **Figure 6**.

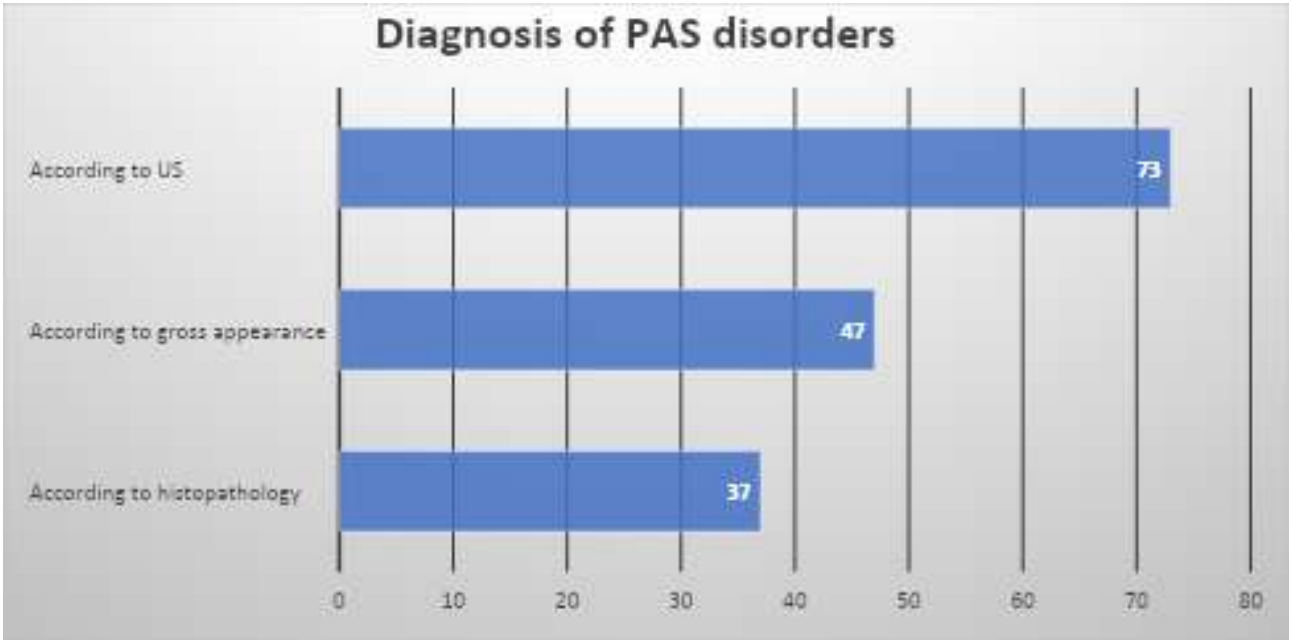

Figure 6: Distribution of cases of PAS disorders in accordance with diagnostic criteria

According to intraoperative findings 47 cases were diagnosed as having PAS disorders, while the remaining 26 cases had false ultrasound diagnosis (false positive rate =35.6%) and considered as non-PAS group.

Regarding patient characteristics, cases of PAS had higher mean maternal age, higher gravidity, parity, and higher rate of previous C/S. while rate of previous miscarriage, past surgical (previous myomectomy or dilatation and curettage) and past medical history were not different statistically, as shown in **Table 3** and **Table 4**.

Table 3: Participants characteristics:

Variables	PAS		Non-PAS		P value
	Mean	SD	Mean	SD	
Maternal age (years)	34.62	4.35	29.23	4.47	**<0.0001**
Gravidity	7.74	1.45	5.5	1.73	**<0.0001**
Parity	5.68	1.64	3.42	2.06	**<0.0001**
Previous miscarriage	1.06	0.79	1.08	0.8	0.947
BMI	28.06	2.58	27.83	3.01	0.747
Gestational age	37.57	1.19	37.21	0.95	0.174
No. of previous C/S	5.15	1.81	3.65	1.23	**<0.0001**

Table 4: Participants previous surgical and medical history:

Variables		PAS		Non-PAS		P value
		No.	%	No.	%	
Previous uterine surgery	**Yes**	12	25.5	4	15.4	0.316
	No	35	74.5	22	84.6	
DM	**Yes**	9	19.1	10	38.5	0.072
	No	38	80.9	16	61.5	
HT	**Yes**	9	19.1	5	19.2	0.993
	No	38	80.9	21	80.8	

The anteriorly placed placenta was significantly higher in cases of PAS disorders than those with non-PAS diagnosis. Similarly placental hypervascularity was significantly associated with clinical PAS diagnosis. The other ultrasonic features were not different between cases of PAS and non-PAS as shown in **Table 5**.

Table 5: Ultrasonic features of the participants:

Variables		PAS		Non-PAS		P value
		No.	%	No.	%	
Placental position	**Low**	5	10.6	0	0	**0.017**
	Anterior	42	89.4	23	88.5	
	Posterior	0	0	3	11.5	
Disappearance uteroplacental clear zone	**Yes**	28	59.6	17	65.4	0.625
	No	19	40.4	9	34.6	
Thinning of myometrium	**Yes**	27	57.4	15	57.7	0.984
	No	20	42.6	11	42.3	
Vascular changes within the placenta	**Yes**	22	46.8	11	42.3	0.711
	No	25	53.2	15	57.7	
Placental bed hypervascularity	**Yes**	32	68.1	9	34.6	**0.006**
	No	15	31.9	17	65.4	

The most common clinical features in PAS disorders cases that presented in our study was bleeding after trial of removal of placenta, as illustrated in **Figure 7**.

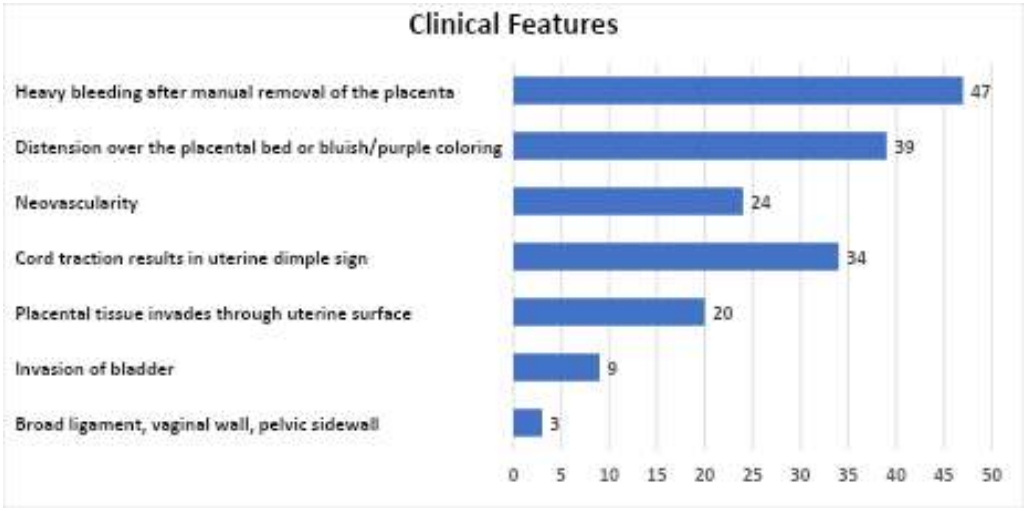

Figure 7: Distribution of clinical features in PAS disorders cases.

According to these clinical features the cases were graded according to FIGO grading system into five grades as shown in **Figure 8**.

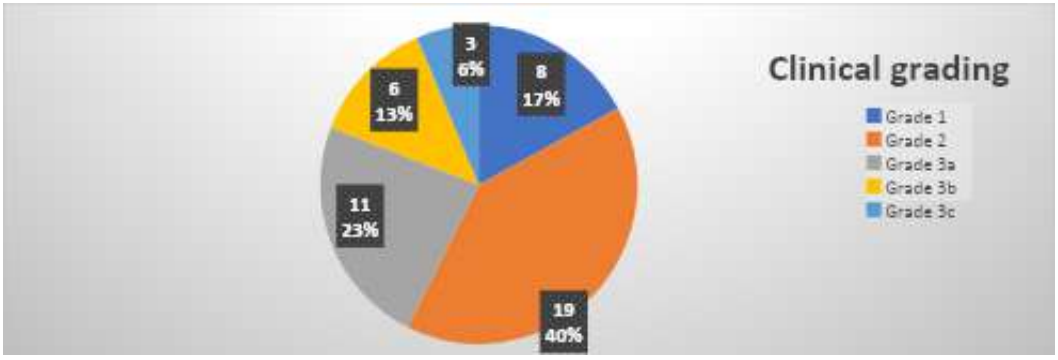

Figure 8: Clinical grading of PAS disorders cases

When correlating risk factors of PAS disorders case with the clinical grading, it has been found that there was a significant association with previous miscarriage and BMI mainly up to grade 3a, while other risk factors didn't show that, as shown in Table 6.

Table 6: Correlation of risk factors and clinical grading in PAS disorders cases:

Variables	Grade 1	Grade 2	Grade 3a	Grade 3b	Grade 3c	P Value
	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD	
Maternal age (years)	33.13 ±4.52	36.37 ±4	34 ±3.44	32.33 ±5.2	34.33 ±6.03	0.205
Gravidity	7.38 ±1.6	7.95 ±1.61	7.64 ±1.21	7.83 ±1.72	7.67 ±0.58	0.921
Parity	5.75 ±1.98	5.74 ±1.82	5.64 ±1.43	5.17 ±1.6	6.33 ±0.58	0.903
Previous miscarriage	0.63 ±0.74	1.21 ±0.71	1 ±0.89	1.67 ±0.52	0.33 ±0.58	**0.047**
BMI	25.86 ±0.92	28.67 ±2.53	29.46 ±2.89	26.25 ±1.25	28.53 ±1.82	**0.006**
Gestational age	37.77 ±1.3	37.68 ±1.02	37.44 ±1.39	37.02 ±1.44	37.86 ±0.99	0.762
No. of previous C/S	5.88 ±1.55	5.05 ±2.2	4.73 ±1.35	5.17 ±2.04	5.33 ±0.58	0.756

The past surgical and medical histories were not different across the clinical grades of PAS disorders, as shown in **Table 7**.

Table 7: Correlation of past surgical and medical history with clinical grading in PAS disorders cases.

Variables		Grade 1	Grade 2	Grade 3a	Grade 3b	Grade 3c	P value
		No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	
Previous uterine surgery	**Yes**	1 (12.5)	7 (36.8)	0 (0)	3 (50)	1 (33.3)	0.101
	No	7 (87.5)	12 (63.2)	11 (100)	3 (50)	2 (66.7)	
Previous history of PAS	**Yes**	2 (25)	4 (21.1)	4 (36.4)	1 (16.7)	0 (0)	0.705
	No	6 (75)	15 (78.9)	7 (63.6)	5 (83.3)	3 (100)	
Diabetes Miletus	**Yes**	1 (12.5)	4 (21.1)	1 (9.1)	2 (33.3)	1 (33.3)	0.706
	No	7 (87.5)	15 (78.9)	10 (90.9)	4 (66.7)	2 (66.7)	
Hypertension	**Yes**	1 (12.5)	4 (21.1)	2 (18.2)	2 (33.3)	0 (0)	0.778
	No	7 (87.5)	15 (78.9)	9 (81.8)	4 (66.7)	3 (100)	

The ultrasound features were not different according to clinical grade, as shown in **Table 8**.

Table 8: Ultrasound parameters distribution according to clinical grade.

Variables		Grade 1	Grade 2	Grade 3a	Grade 3b	Grade 3c	P value
		No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	
Placental position	**Low**	0 (0)	1 (5.3)	2 (18.2)	1 (16.7)	1 (33.3)	0.400
	Anterior	8 (100)	18 (94.7)	9 (81.8)	5 (83.3)	2 (66.7)	
	Posterior	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
Disappearance uteroplacental clear zone	**Yes**	3 (37.5)	12 (63.2)	7 (63.6)	4 (66.7)	2 (66.7)	0.739
	No	5 (62.5)	7 (36.8)	4 (36.4)	2 (33.3)	1 (33.3)	
Thinning of myometrium	**Yes**	4 (50)	10 (52.6)	7 (63.6)	3 (50)	3 (100)	0.576
	No	4 (50)	9 (47.4)	4 (36.4)	3 (50)	0 (0)	
Vascular changes within the placenta	**Yes**	3 (37.5)	11 (57.9)	6 (54.5)	1 (16.7)	1 (33.3)	0.421
	No	5 (62.5)	8 (42.1)	5 (45.5)	5 (83.3)	2 (66.7)	
Placental bed hypervascularity	**Yes**	7 (87.5)	10 (52.6)	9 (81.8)	3 (50)	3 (100)	0.150
	No	1 (12.5)	9 (47.4)	2 (18.2)	3 (50)	0 (0)	

Regarding histopathological features results, placental villi attached directly to the superficial myometrium was the most common histopathological feature that shown to be present in all cases that had been diagnosed as having PAS disorders, as shown in **Figure 9**.

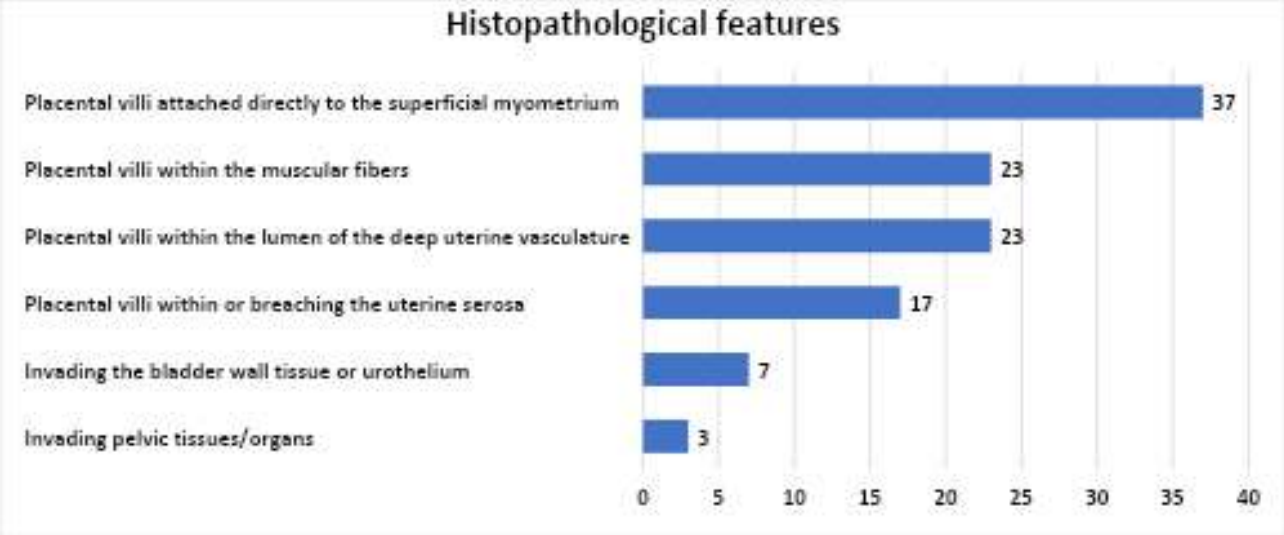

Figure 9: Histopathological features in PAS disorders.

Regarding the histopathological grade the most common grade was grade 1, as illustrated in **Figure 10**

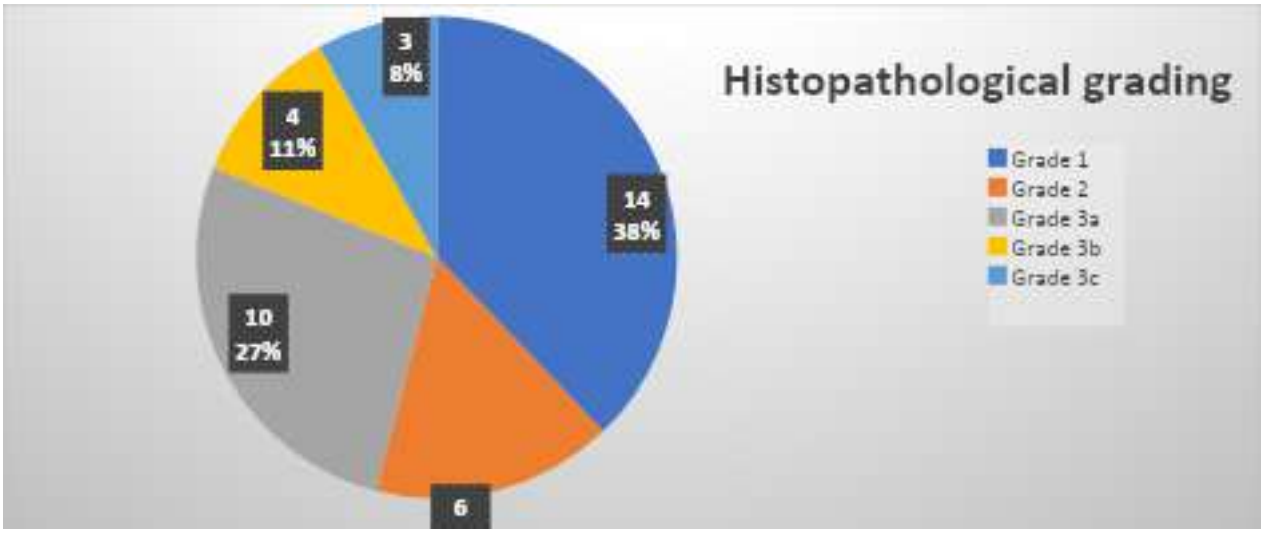

Figure 10: Histopathological grading of hysterectomized cases

The histopathological features were correlate positively with the clinical grading to certain extent but to note that some of cases diagnosed to have grade 2 PAS were over diagnosed and histopathology showed that they were grade 1, the more level of invasion of the placenta by histopathology the higher the clinical grade was found, as shown in **Table 9**.

Table 9: Distribution of histopathological features according to clinical grading.

Variables		Grade 1	Grade 2	Grade 3a	Grade 3b	Grade 3c	P value
		No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	
Placental villi attached directly to the superficial myometrium	**Yes**	0 (0)	17 (89.5)	11 (100)	6 (100)	3 (100)	**<0.0001**
	No	8 (100)	2 (10.5)	0 (0)	0 (0)	0 (0)	
Placental villi within the muscular fibers	**Yes**	0 (0)	3 (15.8)	11 (100)	6 (100)	3 (100)	**<0.0001**
	No	8 (100)	16 (84.2)	0 (0)	0 (0)	0 (0)	
Placental villi within the lumen of the deep uterine vasculature	**Yes**	0 (0)	3 (15.8)	11 (100)	6 (100)	3 (100)	**<0.0001**
	No	8 (100)	16 (84.2)	0 (0)	0 (0)	0 (0)	

Placental villi within or breaching the uterine serosa	**Yes**	0 (0)	0 (0)	8 (72.7)	6 (100)	3 (100)	**<0.0001**
	No	8 (100)	19 (100)	3 (27.3)	0 (0)	0 (0)	
Invading the bladder wall tissue or urothelium	**Yes**	0 (0)	0 (0)	0 (0)	4 (66.7)	3 (100)	**<0.0001**
	No	8 (100)	19 (100)	11 (100)	2 (33.3)	0 (0)	
Invading pelvic tissues/organs	**Yes**	0 (0)	0 (0)	0 (0)	0 (0)	3 (100)	**<0.0001**
	No	8 (100)	19 (100)	11 (100)	6 (100)	0 (0)	

The ultrasound features were not sensitive nor specific in the diagnosing PAS disorders when compared with the clinical and histopathological findings, but they were associated with high positive predictive value in cases of those who had PAS disorders and required hysterectomy as shown in **Table 10**

Table 10: Diagnostic ability of ultrasound features versus clinical and histopathological grading.

Variable	**Clinical**				
	SN	**SP**	**PPV**	**NPV**	**ACC**
Disappearance uteroplacental clear zone	59.6	34.6	62.2	32.1	50.7
Thinning of myometrium	57.4	42.3	64.3	35.5	46.6
Vascular changes within the placenta	46.8	57.7	66.7	37.5	52.1
Placental bed hypervascularity	68.1	65.4	78	53.1	67.1
	Histopathology				
Disappearance uteroplacental clear zone	63.4	66.7	96.3	11.8	68.2
Thinning of myometrium	56.1	33.3	92	5.3	51.2
Vascular changes within the placenta	48.8	66.7	95.2	8.7	53.7
Placental bed hypervascularity	65.9	0	90	0	65.9

Regarding clinical features, Distension over the placental bed or bluish/purple coloring and Cord traction results in uterine dimple sign were had the highest accuracy rate and were the most sensitive and specific features in diagnosing PAS disorders depending on clinical ground, as shown in **Table 11**.

Table 11: Diagnostic ability of PAS disorders depending on clinical features.

Variable	**Histopathology**				
	SN	**SP**	**PPV**	**NPV**	**ACC**
Heavy bleeding after manual removal of the placenta	100	0	78.7	0	78.7
Distension over the placental bed or bluish/purple coloring	100	80	94.9	100	95.7
Neovascularity	64.9	100	100	43.5	72.3
Cord traction results in uterine dimple sign	91.9	100	100	76.9	93.6
Placental tissue invades through uterine surface	54.1	100	100	37	63.8
Invasion of bladder	24.3	100	100	26.3	40.4
Broad ligament, vaginal wall, pelvic sidewall	8.1	100	100	22.7	27.7

4. Discussion

Placenta accreta spectrum (PAS) disorders are a potentially life-threatening complication of pregnancy that demand coordinated interdisciplinary care to achieve safer outcomes. The rising incidence of this disease is due to a growing number of uterine surgical procedures, including the rising incidence of pregnancy following C/S[57].

According to our knowledge this is first paperwork that examine the new FIGO classification in Iraq.

The maternal age was significantly higher in cases of PAS, similar result found by systematic reviews done by Piñas et al[58], and Silver et al[59]. Kyozuka et al[60] (n=136) also found similar results. This may be attributed to the associated multiparity and increased number of previous C/S.

Gravidity and parity were found to be higher in cases of PAS disorders than non-PAS, this could be attributed to the altered endometrial–myometrial interface that could leads to a failure of normal decidualization, which allows abnormally deep placental anchoring villi and trophoblast infiltration as suggested by Jauniaux et al[10] (n=142).

The rate of previous miscarriage was not different between the two clinical diagnoses (PAS and non-PAS). Ogawa et al[61] (n=2253) found that the rate of PAS disorders increased in cases of high previous miscarriage rate, this difference may be attributed to the small sample size used in our study.

Cases of PAS disorders had higher mean number of previous C/S than Non-PAS cases, similar result found by previous studies (Piñas et al[58], Silver et al[59], and Kyozuka et al[60]).

The previous uterine surgery in the form of myomectomy, correction of uterine anomalies and dilatation and curettage were not different between the two groups. This was also found to be significantly higher in cases of PAS disorders by the previous studies (e.g., Piñas et al[58], Silver et al[59], and Kyozuka et al[60]) again this attributed to both small number of cases of previous uterine surgery and the sample size used in the current study which associated with higher rate of type II error.

The past medical history in the form of diabetes was not different regarding clinical PAS disorders diagnosis. Matsuzaki et al[62] found that cases of gestational diabetes had higher rate of PAS disorders as it is associated with abnormal function of endometrium with associated increased local inflammation at placentation site as found by Ehlers et al[63] (n=849). This difference in result may be attributed to two factors. First, the small sample size used in this study, secondly this study included only cases diagnosed by ultrasound as having PAS disorders.

The history of hypertension was not different between the two groups, Ehlers et al[63] again found that there is increased rate of PAS disorders in cases of preeclampsia suggesting a common pathology of inflammation and abnormal placentation, as suggested by Jing et al[64] (n= 2,786,871).

The anterior placental position was the most common position in cases of PAS disorders, this could be attributed to the effect of presence of uterine scar of previous C/S that had altered endometrial-myometrial interface making abnormal decidualization common finding as suggested by Do QN et al[65] (n=145).

The our study included only cases diagnosed by ultrasound as PAS disorders. Thus, the sensitivity and specificity of ultrasound were not calculated. But worth noting that of seventy-three cases diagnosed by ultrasound as having PAS disorders, only thirty-seven cases were proved to be that by histopathology. Riteau et al[66] (n=412) found that the sensitivity of the ultrasound was 100% but the specificity was rather low which is only 37.5%, and from 26 cases diagnosed to have PAS disorders only 16 cases had proved by histopathology to have that.

In our study the false positive rate of the ultrasound was 49.3% according to histopathology and 35.6% according to clinical diagnosis of PAS disorders. Bowman et al[67] (n=349) found that the rate of false positive ultrasound was 5.9%, with sensitivity and specificity of 53.5% and 88% respectively. On the other hand, Maher et al[68] (n=134) found the false positive rate to be 23.3%. These conflicting results of ultrasound may be attributed to the fact that ultrasound is an operator dependent investigation that needs to be taken into consideration. To note that in our hospital the reports of ultrasound did not describe all ultrasonic features of PAS in all reports, and many reports

had been tailed by the sentence "placenta accreta cannot be excluded". to overcome this limitation, we examined each parameter of ultrasound separately and compare it to FIGO ultrasound findings that done by Jauniaux et al[10].

The ultrasonic feature of disappearance of uteroplacental clear zone was not different between the two groups. In other words, it could not differentiate cases of PAS disorders and non-PAS that are diagnosed based on clinical findings. This means that the rate of false positive cases of this ultrasonic feature was 23.3% (17/73). Similarly, Jauniaux et al[10] found that this feature to be inaccurate as it is affected by the location of the placenta, the degree of pressure by ultrasound probe, the amount of scar tissue of previous pregnancy and by fullness of urinary bladder.

Thinning of myometrium could not differentiate between the clinical diagnosis of PAS disorders and non-PAS, Haba et al[69] in their systematic review found that myometrial thinning of less than 1 mm associated with high sensitivity and specificity in the prediction of grade 1 and 2 but it was not sensitive in detecting grade 3 cases. This difference in the accuracy level may be attributed to the fact that the ultrasound is an operator dependent and thin myometrium could be due to uterine dehiscence or thinning of myometrium in third trimester which falsely estimated as PAS disorder, as suggested by Jauniaux et al[10].

Vascular changes within placenta also were not different between cases of PAS disorders and non-PAS based on clinical findings. Florrie et al[33] found that these vascular changes associated with 77% sensitivity, Garofalo et al[70] found that this feature associated with 60% sensitivity and high specificity. This result is associated with varying degree of sensitivity and specificity in previous studies as the vascular changes in the placenta is influenced by the placental position, and its distance from the main uterine arteries, and the remodeling of the myometrial circulation around the scar area.

Placental bed hypervascularity was significantly higher in cases of PAS disorders than cases of non-PAS. The sensitivity found in the current study is 68.1% based on clinical diagnosis and 65.9% based on histopathological diagnosis (the highest sensitivity and specificity achieved from ultrasound features) yet this level associate with high rate of false positive and negative ratios. Florrie et al[33] found that sensitivity of 40.7% in regard to placental bed hypervascularity.

It is very important to note that all of these ultrasound features of PAS disorders associated with high positive predictive value, and therefore these ultrasound features had very important role in prediction of PAS disorders preoperatively, in other words, based on positive predictive value ultrasound is a good screening tool for PAS disorders (as PPV is more important than sensitivity in choosing screening tools as suggested by Trevethan et al[71]).

The clinical features used to diagnosis PAS disorders during operation were further analyzed using histopathological result as gold standard and we found that heavy bleeding after manual removal of the placenta happened in all cases that underwent hysterectomy thus sensitivity was 100%, and calculation of specificity was shown zero (as no cases that did have true negative were included i.e., cases without heavy bleeding).

The distention over the placental bed or blush discoloration of placental bed associated with 100% and 80% sensitivity and specificity respectively with the highest accuracy rate 95.7%. FIGO classification considered this sign to be grade 1 PAS disorder [44].

Neovascularization, placental tissue invasion through uterine surface, bladder or other structures associated with low sensitivity of PAS disorders but 100% specific to PAS disorders.

On the other hand, cord traction results in uterine dimple signs associated with both high sensitivity and specificity and accuracy.

The histopathological features were accurately correlated with clinical findings, but the clinical features associated with high specificity thus their presence could replace the need for histopathology in the diagnosis of PAS disorders.

5. Conclusion & Recommendations

Conclusions:

Ultrasound had limited sensitivity and specificity but associated with high ppv making it a good tool for screening for PAS disorders. Advancing maternal age, high parity, high miscarriage rate associated with increased risk of PAS disorders. The clinical diagnosis associated with high specificity and strongly associated with histopathologic finding.

Recommendations:

- We recommend the use of ultrasound as a screening tool for PAS disorders.
- The need for better training of ultrasound operators about the advances in ultrasonic features of PAS disorders using the standardized protocols.
- The need to train the medical staff who are working in the field about the last FIGO classification.
- This study could open the road for future studies that involve larger sample sizes for better correlation of the different parameters used in the diagnosis of PAS disorders.
- Maternal and community education regarding the risk of high parity on women health and subsequent risk of PAS disorders.

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