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ABSTRACT

***Background*: The rising Caesarean section rate in the developing world implies that the incidence of placenta accreta might be on the increase and this might worsen the maternal mortality burden.**
***Objective*: To draw the attention of Obstetricians and other relevant professionals to this emerging but challenging trend.**
***Data Sources*: Original research findings and reviews published in the English literature. Additional information was obtained from texts and electronic books such as CD ROMS.**
***Data Extraction*: Online searches of electronic database (Medline, Pubmed and Embase), requests for reprints from corresponding authors and institutional/private subscriptions.**
***Data Synthesis*: Information obtained was categorised accordingly.**
***Conclusion*: Optimal treatment of women with placenta accreta requires recognition of the clinical risk factors, accurate pre-operative diagnosis and meticulous planning to ensure safety at the time of delivery. In view of the rising incidence of this condition, and the absence of a highly reliable antenatal diagnostic method especially in developing countries, a high index of suspicion and advanced preparation is required to reduce its associated maternal morbidity and mortality.**

INTRODUCTION

Placenta accreta is a rare and challenging complication of pregnancy associated with increased maternal morbidity and mortality , loss of reproductive organs and high demands on meagre health resources (1 – 5).

The incidence of placenta accreta in the developed world is said to have increased ten-fold in the past 50 years (1, 4 – 5). This remarkable rise in its incidence has been largely attributed to the rising Caesarean section rate (1, 4 – 5).

In Nigeria and other developing countries, an increasing caesarean section rate has been reported, indicating also that the incidence of placenta accreta may be on the increase (6-10). Placenta accreta may therefore further worsen the already bad maternal mortality situation the developing world. The purpose of this review is to draw the attention of Obstetricians, Sonologists, Obstetric Anaesthetists and Haematologists to this emerging but challenging trend.

DEFINITIONS AND PATHOLOGICAL BASIS

Placenta accreta is an abnormal adherence of the placenta to the underlying myometrium or serosa. If the placental villi are attached to, but do not invade the myometrium, the condition is referred to as placenta accreta. If the villi invade the myometrium, the condition is called placenta increta, and if the villi penetrate completely through the myometrium to the serosal surface of the uterus, the term placenta percreta is applied. The term placenta accreta is commonly used as a generic term to refer to all the three categories together (11).

Soon after fertilisation and implantation, the maternal endometrium in response to increased levels of oestrogen and progesterone, undergoes a change in histology forming a thickened soft layer called decidua. This layer has three parts one of which is the decidua basalis, which forms beneath the area of the zygote implantation. Normally, the placenta villi do not invade beyond the deciduas basalis. Placenta accreta therefore occurs as a result of a decidua basalis defect in which the anchoring placental villi

are in direct contact with the myometrium instead of decidual cells. This abnormal adherence leads to none or incomplete separation of the placenta at the time of delivery and massive post-partum haemorrhage. Moreover, placenta percreta may result in invasion of adjacent pelvic organs such as the bladder and the gut (12).

INCIDENCE

The reported incidence of placenta accreta worldwide is extremely variable, ranging from 0.001% to 0.9% (4–5, 12, 13). The variability is due to the definition adopted for accreta (clinical or histopathologic diagnosis), the population studied and the time of the study (4, 13). Some studies based their definition or diagnosis of placenta accreta strictly on the histological criteria and as such reported lower incidence whereas the studies that combined clinical criteria with histology tended to report a higher incidence (1,4,13). The histological method is said to be the classic and more objective method that firmly establishes the minimum incidence of placenta accreta (13).

The histological diagnosis is however not perfect and is fraught with the following pitfalls:

- Post-partum histological examination of the placenta involves only samples of the placental surface and as such small parts that contain myometrial tissue may be missed. Moreover the accuracy of histological diagnosis even on using hysterectomy specimens is said to depend on the number of tissue blocks examined.
- Mild cases of placenta accreta diagnosed histologically might be clinically unnoticed (incidental findings)
- The increasing use of conservative management further makes the incidence harder to define, as no histology is available.

  It has therefore been suggested that strict histological criteria with total disregard of clinical criteria may not be appropriate (1, 4, 13, 14).

The clinical criteria for definition of placenta accreta include:

- Failure to find a cleavage plane for placenta at manual removal or Caesarean section leading to piece meal removal of placenta and / or persistent bleeding.
- Placenta completely replacing a segment or portion of the uterus with or without extension to adjoining pelvic organs (1,4).

It is however important not to confuse placenta accreta with simple retention of the placenta after birth, which is quite a common condition that is easily managed by conventional methods (13). It has also been observed that since placenta accreta is a clinical obstetric emergency and its management is based on clinical diagnosis, clinical criteria for definition should not be ignored (4,13).

The combination of histological and clinical criteria is therefore more appropriate (4,13).

The incidence of placenta accreta in the last five decades has been observed to be on the increase (1, 4, 5, 12,15). The placenta accreta variant is much more common than the other more invasive variants accounting for 75 – 78% of all cases. Placenta increta and percreta account for 17% and 5 – 7% of cases respectively (11).

AETIOLOGY AND RISK FACTORS

The aetiology of placenta accreta is not known but many speculations and theories have been proposed during the years. These include lack of progesterone, local inflammation, lack of space for placenta to expand and bleeding in the early pregnancy causing an organisation of blood clot with local fibrosis (12, 13). The contemporary scientific view however is that the pathogenesis leading to the lack of decidua basalis may be due to local trauma, progressive vascular endothelial damage which occurs with aging, inappropriate decidual reaction in the lower segment and genetic factors (2,12,13,16). The possibility of a genetic cause for placenta accreta is supported by the observation that its recurrence rate may be as high as 16% and that a significant number of primiparous women without any known risk factors may be affected (13). The reported risk factors for placenta accreta include placenta praevia, previous Caesarean section, advanced maternal age (≥35 years), previous uterine curettage, previous endometritis, Asherman's syndrome, grandmultiparity, multiple pregnancy, pelvic irradiation, previous trophoblastic disease, previous myomectomy, submucuous fibroid, manual removal of placenta, smoking, female foetus, abnormally elevated second trimester alpha foetal protein and free B-human chorionic gonadotrophin (15 – 17).

Placenta praevia and previous Caesarean section act synergistically to further increase the risk of placenta accreta. When placenta praevia is present without previous uterine surgery, the risk of accreta is 10%. On the other hand the risk of placenta accreta is 12% with a history previous Caesarean section(s) without placenta praevia. However, the risk increases sharply to as high as 25% with a combination of one previous Caesarean section and placenta praevia. The risk further rises proportionately with the number of previous Caesarean sections, hence it increases to 50% after two Caesarean sections and 67% after four Caesarean sections (14).

PRESENTATION

Placenta accreta can be present at any gestation from first trimester to term. It may be discovered during dilatation and curettage when massive bleeding occurs due to placental invasion of the myometrium. Individuals who are at risk of placenta accreta at term are also at risk for it in the first trimester (18).

The most common clinical presentation of placenta accreta is post-partum haemorrhage associated with a retained placenta (11 - 12). It may be observed for the first time at caesarean section (12).

Other modes of presentation include antepartum haemorrhage, acute abdomen and shock from ruptured uterus and painless haematuria if the bladder is involved (11, 12, 14, 18).

ANTENATAL DIAGNOSIS

Antenatal diagnosis of placenta accreta is difficult but very important as it represents a possibility for accurate planning and preparation for delivery. It also creates an opportunity for multidisciplinary input in the management of the condition (12, 14, 19, 20).

If pregnancy is complicated by any of the risk factors earlier mentioned, transabdominal or transvaginal ultrasound, colour flow Doppler ultrasonography and magnetic resonance imaging may be used.

ULTRASOUND FEATURES

Low Lying Gestational Sac: In the first trimester, the ultrasound feature that is suggestive of placenta accreta is a low lying gestational sac that appears to be attached to the anterior wall of the uterus. The usual location of a normal early gestation is in the fundus or very occasionally in the lower segment where it is surrounded by thick myometrium on all sides.

Loss of the clear zone: The usual dark line (sonoluscent space) between the myometrium and the placenta is thought to represent the dilated vessels of the decidua basalis. Since the decidua basalis is absent in placenta accreta, it has been suggested that the absence of this hypoechoic line suggests placenta accreta (11,20–25). Abnormal placental adherence is thus thought to be associated with focal or complete loss of the hypoechoic line, such that the echogenicity of the placenta appears to be contiguous with the bladder wall. This line however said to be absent in many normal patients with anterior placentas. Its sensitivity and positive predictive value is low (20, 23).

Placental Lakes (Lacunae): Placental lacunae are multiple linear, irregular vascular spaces within the placenta. Such lacunae need not be near the area of invasion for the diagnosis to be made (20,23). The likelihood of placenta accreta increases with the number of the lacunae. The lacunae give a 'moth-eaten' appearance to the placenta (11,20-25). Not all large sinuses or vessels are associated with placenta accreta. Those not associated with abnormal adherence are smooth in contour and quite round (20, 23). The presence of placenta lacunae is said to be more sensitive for diagnosis than the loss of the hypoechoic space (20, 23, 25).

Bladder border: The border between the bladder and myometrium is normally highly echogenic and smooth. In placenta accreta interruption of the posterior bladder wall-uterine interface occurs such that a continuous echoluscent line appears instead of the echogenic border. This feature is said to be highly specific. It is however poorly sensitive as interruptions are not present in many patients with placenta accreta (21 – 25).

Generally speaking, ultrasonography has a variable sensitivity of 35–93% for diagnosing placenta accreta. It is limited in obese women and in evaluating extra uterine extent and fundal or posterior placenta accreta (20, 19 – 24).

The role of colour doppler: Colour Doppler will not only show the placental sinuses but their transversing through the uterine wall. It will also demonstrate turbulent blood flow extending from the placenta into the surrounding tissues (20, 23).

The sensitivity and specificity of colour Doppler imaging for diagnosing placenta accreta are reported to be 82.4 – 100% and 92 – 96.8%, respectively (3, 20, 23-24). The advantages of colour Doppler compared to gray-scale ultrasonography are improved specificity and better assessment of the depth of myometrial and serosal invasion.

Magnetic Resonance Imaging (MRI): The role of magnetic resonance imaging in the diagnosis of placenta accreta remains controversial. It may however be utilised if gray scale ultrasonography and colour Doppler are not satisfactory and the placenta is posteriorly located (20, 23).

It has been suggested that the use of gadolinium-based contrast enhancement will add to the specificity of MRI in the diagnosis of placenta accreta because it more clearly delineates the outer placental surface relative to the myometrium and eliminates the confusion between heterogeneous signals thought to be within the placenta from those caused by maternal blood vessels (24).

Biochemical Markers: It has been reported that many

women with placenta accreta will have an otherwise unexplained elevation of the maternal serum alpha-fetoprotein, free B-human chorionic gonadotrophin and creatine kinase (5, 12). Accordingly, elevation of these biochemical markers in the second trimester co-existing with placenta praevia and/or previous caesarean section should raise concerns about the possibility of placenta accreta.

There is as yet no diagnostic technique that affords the clinician 100% assurance of either ruling in or ruling out the presence of placenta accreta (5, 20,23). A high index of suspicion is still required in the diagnosis of the condition. In settings where the above-mentioned imaging and biochemical modalities are not available, all cases of placenta praevia in women with one or more previous caesarean sections should be managed as placenta accreta until proven otherwise.

MANAGEMENT

If an antenatal diagnosis or strong suspicion of placenta accreta is made;

- The patient should be counselled about the likelihood of hysterectomy and blood transfusion.
- At least 8 – 12 units of cross-matched blood should be made available.
- If the personnel and equipment required for the management of such cases are lacking, referral to centres with such capacity should be made,
- A preoperative anaesthesia assessment should be obtained, specific preoperative preparations such as autologous blood donation, arterial and central line insertion or hypogastric artery balloon placement can be undertaken in preparation of surgery.
- The Senior Obstetrician with vast experience in obstetric hysterectomy must be present at surgery. (A case of placenta accreta is not the one to be left to the Senior Registrar or junior Residents).
- Cell saver technology should be considered if available.

Treatment options for placenta accreta include surgical removal of the uterus (and the involved structures in some cases of placenta percreta) and conservative therapy (3-5,12,14,26).

SURGICAL REMOVAL OF THE UTERUS (HYSTERECTOMY)

Hysterectomy is the conventional treatment for placenta accreta. Placenta accreta has become the most common indication for emergency peripartum hysterectomy in developed countries (30-32). With rising caesarean section rates in Nigeria and other developing countries, placenta accreta may become superimposed on the preventable indications for peripartum hysterectomy such as ruptured uterus and uterine atony (8-10). Peripartum hysterectomy may be total or subtotal. A subtotal hysterectomy may be acceptable where maternal instability mandates a more expeditious procedure (26). It may be however associated with continued bleeding from the cervical branch of the uterine artery which supplies the lower uterine segment and cervix. Some authorities therefore favour total abdominal hysterectomy especially in cases of placenta praevia accreta.

When the decision has been made prior to caesarean section to perform hysterectomy, the intact placenta should be left in place following delivery of the foetus through a classical uterine incision. The uterine incision should be closed or over sewn circumferentially before proceeding to hysterectomy. This reduces blood loss associated with separation of the adherent placenta.

Other measures that help to prevent massive blood loss during hysterectomy and as such keep the operative site sufficiently dry to carry out a careful dissection include balloon occlusion of the aorta or hypogastric vessels, and application of tourniquet around the uterine cervix (33).

Caesarean hysterectomy is associated with significant maternal morbidity due to urological injury, fistula formation, sepsis, adnexal removal, massive blood transfusion and devastating psychological consequences (28). Nevertheless, it remains the mainstay of treatment for severe intractable postpartum bleeding and should not be delayed until the patient has deteriorated to a moribund state (3,12,14,28).

In cases of placenta percreta with extension to contiguous structures, surgery may involve resection of such structures such as the bladder or bowel and this may further worsen the morbidity (34).

Conservative Treatment: Conservative treatment has the advantage of preserving fertility and menstrual function, and reducing blood loss (3, 12,26, 35-37). It is however only possible in the presence of a stable haemodynamic condition and adequate technical support (12, 26). This treatment modality should be considered whenever feasible in environments such as ours where there is a strong desire for large family size and aversion to hysterectomy (41). Conservative treatment may however be complicated by sepsis, secondary haemorrhage and treatment failure (26).

Conservative approaches include:

Uterine Packing: This involves tight packing of the uterus with gauze after removing the placenta.

Following good and uniform packing of the uterine cavity, the abdomen is closed up under careful monitoring with adequate fresh blood and broad-spectrum antibiotic cover. The pack can then be removed 24 to 36 hours later. This treatment modality for the treatment of post-partum haemorrhage was previously abandoned because it was considered as an unphysiological procedure and was associated with concealed haemorrhage (28). New interest has been however aroused recently in its favour (28).

Uterine and internal iliac arteries ligation: Uterine artery ligation may be used to control bleeding from the uterus as the uterine arteries supply 90% of the uterine blood flow. The technique of its ligation has been described as a potentially easier alternative to hypogastric artery ligation (28). A stitch is passed into the myometrium 2 – 3 centi metre medial to the artery at the same level as a transverse lower segment incision would be made for caesarean section. The suture is brought out through the posterior aspect of the uterus and then brought anteriorly again through the broad ligament at the same level before tying. Care must be taken to exclude the ureter in the stitch. If this procedure proves time consuming and the patient's condition is deteriorating, it should be abandoned in favour of hysterectomy.

The use of bilateral internal iliac artery ligation for arresting active placental bed haemorrhage is becoming less popular because it does not result in the complete cessation of bleeding due of the extensive pelvic collateral circulation. Moreover, the technical problems encountered in the procedure are enormous (28).

LEAVING THE PLACENTA *IN SITU* WITH OR WITHOUT ADJUVANT TREATMENT

The placenta may be left *in situ* with adjuvant treatment such as methotrexate, uterine artery embolisation, or sulprostone (26,35,38-39).

Methotrexate is a cytotoxic drug, which affects the placental tissue by decreasing its vascularity thereby leading to its necrosis. The sensitivity of trophoblastic tissue to methotrexate is well documented by its use in gestational trophoblastic disease. It can be administered intramuscularly at a dose of 50mg/m^2 per week x 6 doses (35). The use of methotrexate requires serial ultrasound and serum BHCG assays as well as frequent blood counts, liver and renal function tests to monitor its effectiveness and safety (38).

Some reports have shown the success of uterine artery embolisation as an adjuvant procedure (28). Sulprostone is well known uterotonic agent used in case of post-partum haemorrhage (26).

In contrast to the use of adjuvant treatment, some cases have had no additional treatment after leaving the placenta *in situ* and still had successful outcomes. Published reports do not currently prove the superiority of the adjuvant treatment (3, 26).

THE USE OF VASOPRESSIN

Vasopressin is a nano-peptide produced by the supraoptic and paraventricular nuclei of the hypothalamus. It has a potent vasoconstrictor effect on the arterioles throughout the human body. This effect has been widely used by gastroenterologists to arrest massive bleeding from oesophageal varices (28). It can be diluted with saline and injected at the bleeding sites of the placental bed. It should be used before massive haemorrhage has occurred since uterine vasculature in massive obstetric haemorrhage is non-responsive to vasoconstrictor agents (28). The use of vasopressin, if effective, is superior to other conservative measures since bleeding stops almost immediately (28).

OTHER CONSERVATIVE APPROACHES

Other conservative treatment modalities include localised resection and uterine repair, B-Lynch uterine compression suture, over sewing the uterine defect, blunt curettage of the uterine cavity and argon beam coagulation of the placental site (12, 14,39,44,45).

COMPLICATIONS OF PLACENTA ACCRETA

The most important complication of placenta accreta is haemorrhage (3-4, 12,33,43). It can be massive and life threatening except in conditions of small focal placenta accreta. The massive haemorrhage can lead to cardiovascular collapse and shock, acute renal failure, Sheehan's syndrome, disseminated intravascular coagulopathy, massive blood transfusion, loss of reproductive organs and maternal death (12, 14,33). Maternal death associated with placenta accreta is put at 7% (12, 33). This may be even higher in developing countries. The complications related to treatment of the condition include injury to the bladder; ligation or injury to the ureters, fistula formation, sepsis, treatment failure and complications from massive blood transfusion (12,14,33). Other complications related to degree of uterine wall invasion include uterine rupture and extension to adjoining structures such as the bladder and bowel (12,34).

The reported perinatal complications of placenta accreta include prematurity, small for gestational age and increased perinatal mortality (43). The adverse perinatal outcomes are thought to result from pathological implantation of the placenta that

interferes with normal placental function and leads to abnormal fetal growth (43).

The average number of units of blood required for transfusion in cases of placenta accreta is put at 6.6 units with some cases requiring over 20 units of blood (33). This massive transfusion classically illustrates the high demand this condition may have on the meagre health resources of developing countries where homologous blood is often not available due to difficulties in recruiting and screening donors and in the collection and storage of blood (42).

PRACTICE POINTS

- In the presence of risks factors; Sonologists should look for and report the presence or absence of the ultrasound features discussed.
- In the absence of reliable ultrasound diagnosis placenta praevia in women with one or more previous caesarean sections should be managed as if they have placenta accreta until proven otherwise.
- Placenta accreta is a long term complication of multiple caesarean sections and as such women undergoing such procedure should be counselled about the complication and the need for prevention through family planning.
- If the personnel and materials required for the management of suspected or diagnosed cases are lacking, referral to centres with such capacity should be made.
- A senior obstetrician with experience in obstetric hysterectomy must be present at surgery for suspected placenta accreta.
- The incidence of placenta accreta may increase further in the coming decades and as such residents in obstetrics must be trained to be able to carry out such a life saving procedure as caesarean hysterectomy.
- The average number of units of blood transfused in cases of accreta is 6.6 units with some cases requiring over 20 units of blood. At least 8 – 12 units of blood must be made available in suspected cases of placenta accreta. There is need to improve the blood transfusion services of many obstetric centres in order to meet up with this challenge.
- When a decision has been made prior to caesarean section to carry out hysterectomy, the intact placenta should be left *in situ* following the delivery of the foetus through a classical uterine incision.

RESEARCH POINTS

- There is generally a need for a large study on placenta accreta in the developing countries especially its trend with rising caesarean section rates and advanced maternal age.
- There is need for a large multicentre trial comparing the conventional extirpative with conservative management. Although there are several cases reports of successful conservative treatment, they cannot be used to evaluate benefits and disadvantages of each therapeutic strategy in a comparative manner.
- A similar study is also required to demonstrate if adjuvant therapy in cases where placenta is left in situ has any advantages over those without adjuvant treatment. This is particularly important, as a cytotoxic drug such as methotrexate with toxic side effects should not be used if it confers no benefit.

In conclusion, optimal treatment of women with placenta accreta requires recognition of the clinical risk factors, accurate pre-operative diagnosis and meticulous planning to ensure safety at the time of delivery.

In view of the rising incidence of this condition, and the absence of a highly reliable antenatal diagnostic method especially in developing countries, a high index of suspicion and advance preparation is required to reduce its associated maternal morbidity and mortality. Moreover, the need for peripartum hysterectomy might be on the increase and as such Residents in obstetrics who carry out most of the caesarean sections should be adequately trained to perform peripartum hysterectomy.

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