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UTERUS PRESERVING TREATMENT MODALITIES FOR ABNORMAL INVASIVE PLACENTA: A SYSTEMATIC REVIEW

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Abstract

Background: *When a focal accreta is identified, conservative intervention may be considered, such as preserving the uterus and placenta and then enduring methotrexate therapy or pelvic artery embolisation. In spite of this, surgical treatment remains the gold standard for the condition.* ***Methods:*** *By comparing itself to the standards set by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, this study was able to show that it met all of the requirements. So, the experts were able to make sure that the study was as up-to-date as it was possible to be. For this search approach, publications that came out between 2013 and 2023 were taken into account. Several different online reference sources, like Pubmed and SagePub, were used to do this. It was decided not to take into account review pieces, works that had already been published, or works that were only half done.* ***Result:*** *In the PubMed database, the results of our search brought up 401 articles, whereas the results of our search on SagePub brought up 289 articles. The results of the search conducted for the last year of 2013 yielded a total 43 articles for PubMed and 31 articles for SagePub. In the end, we compiled a total of 20 papers, 12 of which came from PubMed and 8 of which came from SagePub. We included seven research that met the criteria.* ***Conclusion:*** *Due to the intricacy of surgery, conservative management should be reserved for individuals who are interested in preserving their fertility as well as those who have major disease.*

Keyword: *abnormal invasive placenta; conservative management; surgery; uterus preserving treatment*

INTRODUCTION

A placenta that exhibits aberrant adhesion to the uterine wall and does not separate on its own naturally upon birth is referred to as having an abnormally invasive placenta (AIP). This is a significant clinical condition that, if left untreated, can result in major bleeding and possibly the death of the mother. Aberrant placentation involves placental villi directly attaching to the myometrium, which can invade the uterine wall or neighbouring organs and cause postpartum haemorrhage. Placenta accreta risk factors include caesarean section, dilatation and curettage, and myomectomy.[1]

The placenta often adheres to the decidua, which is the uterus' outer layer. The placenta must be robust enough to remain attached to this layer for the whole pregnancy, but it must separate as soon as the baby is delivered. The decidua is crucial to attaining this equilibrium because it regulates the placenta's level of invasion and coordinates its capacity to release when the baby is delivered. Therefore, an invasive placenta may form if the decidua is injured or aberrant. This most frequently occurs if the uterine wall bears a scar from a prior Caesarean section or other uterine surgery.[2]

The difficulty in diagnosing this illness explains why the frequency of placenta accreta varies between 1 in 300 and 1 in 2000 pregnancies.[3,4] In women who have had a prior single caesarean delivery, the presence of placenta previa is related with an increased risk of placental abruption syndrome (PAS), whereas the absence of placenta previa is associated with a decreased risk of PAS (0.03%).[5] Patients diagnosed with AIP have an estimated mean blood loss anywhere from 2,000 to 7,800 ml, and they require an average of five units of blood to be transfused due to their condition.[6,7]

The prevalence of PAS fluctuates anywhere from 0.01% to 1%, according to the meta-analysis that was conducted by Jauniaux et allatest. This risk differential is substantially more severe among female patients who have had more than one caesarean section. Women who were older than 35 years old and who had a personal history of pelvic irradiation, manual placenta removal, endometritis, or infertility had a greater likelihood of developing PAS compared to control groups. This increased risk was also seen in women who had a family history of PAS.[8]

Typically, gray-scale ultrasound is used to make the diagnosis, which is then confirmed by magnetic resonance imaging, which may better clarify the degree of placental invasion.[9] Planning ahead for the surgery can significantly cut down on the amount of blood lost and help minimise serious morbidity that is linked with placenta accreta. As a result, getting a diagnosis before giving birth is really necessary. It is possible to preserve these people's lives by administering severe treatment for their bleeding, which may include uterotonics, fluid resuscitation, blood products, planned hysterectomy, and surgical hemostatic medicines.[10,11]

When a focal accreta is identified, conservative intervention, such as preserving the uterus and placenta and then undergoing methotrexate therapy or pelvic artery embolisation, may be considered. Despite this, surgical management is still the gold standard for treating the condition.[10,11] It has been shown in recent research that there is an interest in conserving the uterus and avoiding hysterectomy by leaving a piece or the complete attached placenta in the uterus. This would maintain fertility and possibly reduce difficulties.[12,13] The goal of this study is to discover different therapeutic options that will preserve the uterus in cases with aberrant invasive placenta.

METHODS

Protocol

By following the rules provided by Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, the author of this study made certain that it was up to par with the requirements. This is done to ensure that the conclusions drawn from the inquiry are accurate.

Criteria for Eligibility

In this literature review, we investigate the various alternatives for maintaining the uterus in the treatment of atypical invasive placenta. This may be performed by reviewing or examining the prior research that has been done on the subject. The relevance of the challenges that have been highlighted will be demonstrated throughout this paper as its primary objective.

The following requirements were met by researchers in order for them to participate in the study: 1) The paper needs to be written in English and should centre on the topic of safeguarding the uterus through the use of abnormal invasive placenta treatment procedures in order for it to be considered for publication. 2) The analysed literature includes publications that were published after 2013 but before the time period that this systematic review considers. Editorials, submissions that do not have a DOI, review articles that have already been published, and entries that are virtually similar to already published journal papers are examples of types of research that are not allowed.

Search Strategy

We used "uterus preserving treatment" and "abnormal invasive placenta" as keywords.The search for studies to be included in the systematic review was carried out from July, 6th 2023 using the PubMed and SagePub databases by inputting the words: *("uterus"[MeSH Terms] OR "uterus"[All Fields] OR "uteri"[All Fields]) AND ("preservation, biological"[MeSH Terms] OR ("preservation"[All Fields] AND "biological"[All Fields]) OR "biological preservation"[All Fields] OR "preservation"[All Fields] OR "preserved"[All Fields] OR "preservations"[All Fields] OR "preserve"[All Fields] OR "preserves"[All Fields] OR "preserving"[All Fields]) AND ("therapeutics"[MeSH Terms] OR "therapeutics"[All Fields] OR "treatments"[All Fields] OR "therapy"[MeSH Subheading] OR "therapy"[All Fields] OR "treatment"[All Fields] OR "treatment s"[All Fields]) AND ("abnormal"[All Fields] OR "abnormalities"[MeSH Subheading] OR "abnormalities"[All Fields] OR "congenital abnormalities"[MeSH Terms] OR ("congenital"[All Fields] AND "abnormalities"[All Fields]) OR "congenital abnormalities"[All Fields] OR "abnormality"[All Fields] OR "abnormally"[All Fields] OR "abnormals"[All Fields] OR "abnormities"[All Fields] OR "abnormity"[All Fields]) AND*

("invasibility"[All Fields] OR "invasible"[All Fields] OR "invasion"[All Fields] OR "invasions"[All Fields] OR "invasive"[All Fields] OR "invasively"[All Fields] OR "invasiveness"[All Fields] OR "invasives"[All Fields] OR "invasivity"[All Fields]) AND ("placenta"[MeSH Terms] OR "placenta"[All Fields] OR "placentas"[All Fields] OR "placenta s"[All Fields] OR "placentae"[All Fields]) used in searching the literature.

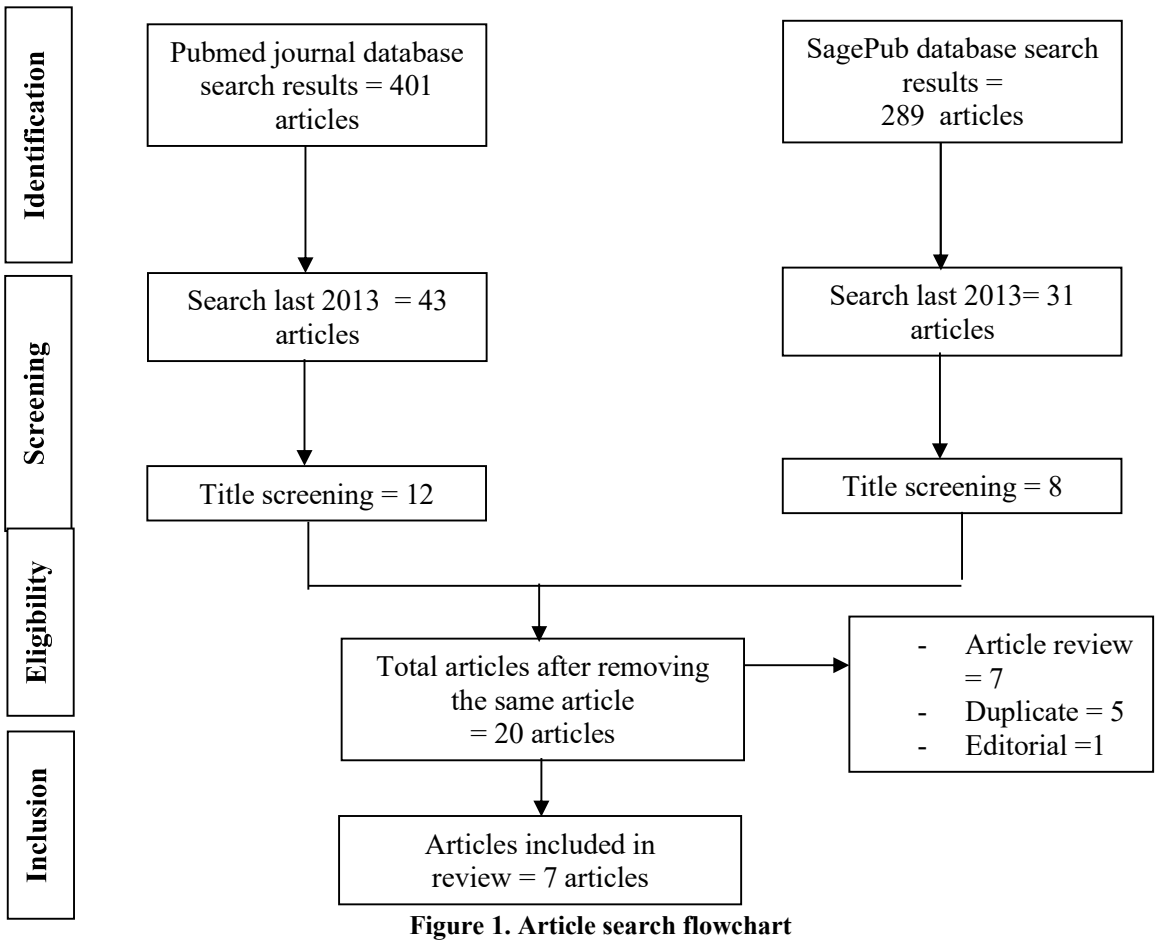

Figure 1. Article search flowchart

Data retrieval

After reading the abstract and the title of each study, the writers performed an examination to determine whether or not the study satisfied the inclusion criteria. The writers then decided which previous research they wanted to utilise as sources for their article and selected those studies. After looking at a number of different research, which all seemed to point to the same trend, this conclusion was drawn. All submissions need to be written in English and can't have been seen anywhere else.

Only those papers that were able to satisfy all of the inclusion criteria were taken into consideration for the systematic review. This reduces the number of results to only those that are pertinent to the search. We do not take into consideration the conclusions of any study that does not satisfy our requirements. After this, the findings of the research will be analysed in great detail. The following pieces of information were uncovered as a result of the inquiry that was carried out for the purpose of this study: names, authors, publication dates, location, study activities, and parameters.

Quality Assessment and Data Synthesis

Each author did their own study on the research that was included in the publication's title and abstract before making a decision about which publications to explore further. The next step will be to evaluate all of the articles that are suitable for inclusion in the review because they match the criteria set forth for that purpose in the review. After that, we'll determine which articles to include in the review depending on the findings that we've uncovered. This criteria is utilised in the process of selecting papers for further assessment. in order to simplify the process as much as feasible when selecting papers to evaluate. Which earlier investigations were carried out, and what elements of those studies made it appropriate to include them in the review, are being discussed here.

RESULT

In the PubMed database, the results of our search brought up 401 articles, whereas the results of our search on SagePub brought up 289 articles. The results of the search conducted for the last year of 2013 yielded a total 43 articles for PubMed and 31 articles for SagePub. In the end, we compiled a total of 20 papers, 12 of which came from PubMed and 8 of which came from SagePub. We included seven research that met the criteria.

Yongzhong, et al (2022)[14] showed that inflated Cook Cervical Ripening Balloon (ICRB) reduced surgical time and duration of infrarenal abdominal aorta balloon occlusion (IAABO) (mean = 172.7 min vs 206.6 min, p = 0.017; median = 30 min vs 40 min, p <0.001) and peripartum hysterectomy (2.9% vs 30.4%). ICRB significantly reduced blood loss (median 2500 ml vs 4000 ml, p <0.001), packed red blood cell (PRC) and fresh-frozen plasma (FFP) transfusion (median = 6 U vs 13.5 U, p <0.001; median 450 ml vs 1200 ml, p <0.001), postoperative hospital stay, and oligomenorrhea. The two groups had similar rates of deep vein thrombosis (DVT), femoral thrombosis, puerperal morbidity, intrauterine infection, surgical site infection, and deep tissue infection, cryo and platelet (PLT) use, urinary system injury, relaparotomy, intensive care unit (ICU) admission, postpartum hematocele in the uterine cavity, and postoperative complications.[14]

Gulucu, et al (2022)[15] showed PPH was performed in 35 (3.2/1000) patients who gave birth during the study period. The most prevalent rationale for hysterectomy was placental invasion abnormality (57.1%, n = 20), and complete hysterectomy was the most often done procedure (68.6%, n = 24). The most frequent alternative treatment done prior to hysterectomy was bilateral hypogastric artery ligation (14.3%, n = 5), and the most common consequence was bladder damage (22.9%, n = 8). Due to acute blood loss, blood transfusions were conducted on 94.3% (n = 33) of the patients. The mean newborn weight was 2788.79 ± 913.37 g, and the 1st and 5th-minute APGAR scores were 6.71 ± 2.25 and 7.56 ± 2.35, respectively.

Table 1. The litelature include in this study

Author	Origin	Method	Sample Size	Result
Yongzhong, 2022[14]	China	Retrospective cohort study	74 patients suffering with previa PAS	In conjunction with IAABO and compression suture, ICRB was a simple and effective technique for postpartum haemorrhage (PPH) management and fertility preservation in some previa PAS cases in which abnormally invasive placenta reached the cervical internal ostium and upper cervical canal.
Gulucu, 2022[15]	Turkey	Retrospective analysis	35 patients who underwent PPH	It is advised that pharmaceutical and surgical methods be employed in an effort to preserve the uterine cavity prior to PPH; nevertheless, in the case that this is not effective, a hysterectomy is the ultimate life-saving option that can be considered. PPH may be required in people who have anaemia and increased gravidity since the risk of bleeding is likely to be significant in the first twenty-four hours after birth in such patients, and it is essential to keep in mind that this fact. PPH may be required in people who have anaemia and increased gravidity.
Varlas, 2021[7]	Romania	Retrospective analysis	12 patients	The use of conservative care is the method that should be taken in situations in which it is desirable to maintain fertility or in which serious disease makes surgery challenging. When risk factors are recognised and treated strategically at an earlier stage, there is a greater chance that the results for both the mother and the unborn child will be improved.
Babaei, 2019[16]	Iran	Case series	Twenty-six patients were identified who had the diagnosis of abnormal placenta implantation	There is still a possibility that the treatment will not be successful despite the fact that this surgical method has a high success rate when it comes to maintaining the uterus. Patients who have a strong desire to save their uterus and their fertility should not be candidates for this technique. Instead, it should be saved for situations in which performing a hysterectomy would be technically challenging owing to the amount of the invasion. This treatment need to be reserved for patients who have a strong desire to keep their uterus and their fertility, as there are too little data about its efficacy and safety. Patients should have a strong desire to keep their uterus and their fertility.
Kilicci, 2018[17]	Turkey	Single-center retrospective study	29 patients and segmental resection in 22	Patients who have severe invasive placentation have the option of undergoing an initial fertility saving surgical operation as opposed to having a caesarean hysterectomy done on them. This treatment can preserve the patient's ability to have children in the future. Because of this therapy, the patient will need fewer blood transfusions, and the procedure will take less time overall.
Chung, 2013[18]	Hong Kong	Single-center retrospective study	25 cases of abnormally invasive placenta	There is an option to having an elective caesarean hysterectomy that involves not removing an unusually invasive placenta during a caesarean section and undergoing preventive postoperative uterine artery embolisation.
Hwang, 2013[19]	Republic of Korea	Single-center retrospective study	40 patients	Pelvic artery embolisation (PAE) can be carried out in patients with PPH and PA in a way that is both safe and successful, and it has the potential to save the uterus in many of these patients.

Varlas, et al (2021)[7] conducted a study with 12 patients. At 37 weeks gestation, one woman was conservatively treated for uterine preservation. Placenta previa and past caesarean delivery were risk factors for an exceptionally invasive

placenta in all women. Most women had planned caesareans at 36.40.9 weeks. One patient (8.33%) received a uterus-preserving surgery, while the others underwent ovaries-preserving hysterectomy. Operative maternal blood loss averaged 2,1751,450 millilitres. One (8.33%) had serious maternal effects. They found poor uterine preservation and good perinatal outcomes.

Babaei, et al (2019)[16] showed abnormal placenta implantation diagnosis was determined to be present in twenty-six different cases. Fourteen people were excluded because they underwent caesarean hysterectomy. Seven of the other 12 individuals had their uteri maintained without issues, 58%. Even if they didn't want children, all treated ladies resumed normal menstrual cycles. Three patients had severe post-partum haemorrhage, two had intestinal adhesion/peritonitis, and one had subsequent hemorrhage/sepsis, requiring primary or delayed hysterectomy. This represents 42% of patients.

Kilicci, et al (2018)[17] study conducted study with 51 pregnant women satisfied the criteria for participation in the study. In 29 patients, caesarean hysterectomy was conducted, and in 22 patients, segmental resection was performed. Both the main complications that occurred during and after the operation were comparable between the two groups. There were statistically significant differences ($p < 0.05$) between the groups regarding gestational age, pre- and post-operative haemoglobin concentrations, the number of packed red blood cell transfusions, and operating time.

Chung, et al (2013)[18] conducted a study with six women were treated by postoperative uterine artery embolisation and having the placentas left where they were throughout the delivery process. Ten women were treated with an extirpative method, while nine women underwent a hysterectomy performed through direct caesarean section. The non-removal of the placenta via uterine artery embolisation was successful four out of six times (or 67% of the time). The group that did not remove the placenta had the least amount of intraoperative blood loss, the fewest required for blood transfusions, and the shortest operation times. However, this group also had a greater risk of secondary complications and stayed in the hospital for longer.

Hwang, et al (2013)[19] showed initial clinical success was 82.5 % (33/40). After 24 hours of embolisation, three PA patients had hysterectomy. The other three patients had re-embolisation (two on the next day and one 6 h after the initial) and stopped bleeding. Clinical success was 92.5%. Pelvic discomfort, nausea, and urticaria occurred four times. Three mild problems, temporary menopause, and no severe difficulties occurred late. 35 individuals resumed menstruation, including two straightforward pregnancies, after the treatment. Disseminated intravascular coagulopathy and intracerebral haemorrhage killed one patient after embolisation.

DISCUSSION

When the placenta is improperly situated above the internal cervical opening (ICO), this condition is known as placenta praevia. The spectrum of conditions known as abnormal placental attachment includes the extremely invasive placenta accreta, increta, and percreta.[4] Because there is no consensus on the most effective method, individualization is the most effective treatment for placenta adhesion issues. In cases like these, gynaecologists, interventional radiologists, and general surgeons need to collaborate on a treatment plan using a multidisciplinary approach. The deleterious effects of pharmaceuticals can also be mitigated by highly trained clinical chemists and other specialists.

Individualization continues to be the most effective method of therapy regardless of the fact that the most effective method for the management of placenta sticky problems is a contentious topic. In addition, in order to effectively handle these situations, a multidisciplinary strategy is required. This approach must include the participation of the gynaecologist, the interventional radiologist, and the general surgeon. Additionally, the presence of a knowledgeable clinical chemist, in addition to the participation of other specialists, will be of great assistance in reducing the adverse effects caused by the pharmaceuticals.

Clinicians opt to conduct caesarean hysterectomy in the majority of instances with aberrant placentation because it is the technique of choice, despite the fact that there is a possibility of significant bleeding during the procedure as well as additional complications caused by the morbidly adherent placenta to the neighbouring tissues. This is in spite of the fact that the surgery is not without its challenges, as well as the fact that there is a chance of serious bleeding. In addition, it is probable that it is not a good choice for younger women who want to maintain their fertility and keep their uterus intact. This is a concern for women who wish to have children in the future.[20]

The analysis suggests various conservative solutions. These include leaving the placenta in situ with or without selective vascular embolisation, cervical inversion, stepwise caesarean section, and Triple P.[21,22] Arterial embolisation helps postpartum haemorrhage. Arterial embolisation may be appropriate for a stable patient with persistent bleeding, especially if the loss rate is low. In this analysis, 89.8% succeeded. Due to the need for specialised equipment and the urgency of postpartum haemorrhage, the surgery can protect fertility but is limited to skilled facilities. Preventive embolisation with an AIP caesarean section may be useful.[23]

Occlusion balloons have been implanted from the aorta to the anterior division of the internal iliac arteries. This technique often involves arterial embolisation. Small sample sizes limit most research. Occlusion balloons to control AIP haemorrhage are rarely studied. Occlusion balloon implantation in the aorta, common iliac, internal iliac, and uterine arteries has shown promise for intraoperative management.[24] Traditional procedures included letting the placenta alone after birth. This approach preserved 84% of uterines in one case series. Complications lessened. However, this procedure was not compared to caesarean hysterectomy.[25–27]

Babaei et al. (2019)[16] carried out one of the most extensive case series in order to evaluate the efficacy and safety of combining UAE and MTX in the treatment of placental sticky diseases. The current study found that 58% of women were able to have their uteruses successfully preserved, but 42% of women had some kind of maternal morbidity. Many case reports and case series evaluated the effectiveness and safety of the combination of UAE and MTX in the treatment of clinicalepathological or radiologically aberrant placenta implantation.[28]

The action of MTX against rapidly dividing cells is the key mechanism that leads to its efficacy against proliferating trophoblast. MTX's ability to inhibit trophoblast proliferation has been shown to have a positive impact on pregnancy outcomes. Not only is the administration of MTX regarded to be one of the major therapy choices for the treatment of ectopic pregnancy, but it is also considered to be one of the primary therapy options for the treatment of prenatal trophoblastic sickness. This is because of the reason stated above. There have been a number of studies that raise doubt on the benefits of utilising MTX as part of a more conservative treatment approach for atypical sticky placenta. These publications have been cited in a number of different scientific papers.[16,29]

It is recommended that medicinal and surgical procedures be used to attempt to maintain the uterine cavity prior to PPH; nevertheless, in the event that this is not successful, a hysterectomy is the final life-saving option. PPH may be necessary in individuals who have anemia and increased gravidity since the risk of bleeding is likely to be considerable in the first twenty-four hours after delivery in such patients, and it is important to remember this fact. Because there is a risk of complications, the need for greater blood transfusions, and the demand for intensive care, patients who have placentation defects should preferably have their surgeries performed in centers that have prior expertise.[15]

CONCLUSION

Due to the intricacy of surgery, conservative management should be reserved for individuals who are interested in preserving their fertility as well as those who have major disease.

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