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## RED BLOOD CELL TRANSFUSION IN PATIENTS WITH PLACENTA ACCRETA SPECTRUM : A SYSTEMATIC REVIEW

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### ABSTRACT

**Background:** *Placenta accreta spectrum, formerly known as morbidly adherent placenta, refers to the range of pathologic adherence of the placenta, including placenta increta, placenta percreta, and placenta accreta. Maternal morbidity and mortality can occur because of severe and sometimes life-threatening hemorrhage, which often requires blood transfusion.*

**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 32 articles, whereas the results of our search on SagePub brought up 25 articles. The results of the search conducted for the last year of 2013 yielded a total 32 articles for PubMed and 3 articles for SagePub. In the end, we compiled a total of 3 papers, 2 of which came from PubMed and 1 of which came from SagePub. We included five research that met the criteria.*

**Conclusion:** *Based on the studies included in this review, we are unable to recommend the minimum of units of red blood cells that should be available before delivery for patients with placenta accreta spectrum. Future studies in the form of large clinical trials is required to study the minimum of RBCs units for PAS patients before delivery, to better inform future guidelines for predelivery blood ordering and transfusion support.*

**Keyword:** *Placenta accreta, red blood transfusion*

## INTRODUCTION

Placenta accreta is defined as abnormal trophoblast invasion of part or all of the placenta into the myometrium of the uterine wall. Placenta accreta spectrum, formerly known as morbidly adherent placenta, refers to the range of pathologic adherence of the placenta, including placenta increta, placenta percreta, and placenta accreta. Maternal morbidity and mortality can occur because of severe and sometimes life-threatening hemorrhage, which often requires blood transfusion. Rates of maternal death are increased for women with placenta accreta spectrum. Additionally, patients with placenta accreta spectrum are more likely to require hysterectomy at the time of delivery or during the postpartum period and have longer hospital stays.<sup>1</sup>

Placenta accreta is characterised by abnormal infiltration of trophoblast cells, which results in the invasion of a portion or the entirety of the placenta into the myometrium of the uterine wall. The term "placenta accreta spectrum (PAS)," previously referred to as "morbidly adherent placenta," encompasses a variety of pathological conditions involving the abnormal attachment of the placenta. These conditions include placenta increta, placenta percreta, and placenta accreta. PAS is diagnosed based on clinical symptoms, pathological observations, or ultrasound imaging.<sup>2-4</sup>

In recent decades, the incidence of PAS disorders has increased substantially, and this trend appears to correspond with the rising rate of caesarean delivery. The incidence of PAS has increased from 0.12% to 0.31% over the past 30 years, according to a recent estimate of 9 per 1000 patients (0.91%).<sup>5</sup>

Maternal morbidity and mortality of PAS may arise due to significant and occasionally life-threatening haemorrhage, mostly due to postpartum haemorrhage caused by aberrant placental-myometrial separation. Spontaneous uterine rupture with subsequent hemoperitoneum, particularly when coupled with placenta percreta, is a less common cause of maternal morbidity and mortality. Overall, the mortality rate is 7%.<sup>6</sup>

Cesarean hysterectomy can be challenging and should be performed by the most experienced surgeons. Because of intrapartum and postpartum bleeding risk for women with placenta accreta spectrum, centers caring for these patients should have the ability to rapidly mobilize blood products for transfusion. When placenta accreta spectrum is encountered at the time of delivery without a prior suspicion or diagnosis and there are no extenuating circumstances mandating immediate delivery, anesthesia staff should be alerted, and the case should be temporarily paused until optimal surgical expertise can be garnered. If the delivering center lacks the expertise to perform a hysterectomy and the patient is stable after delivery of the fetus, the patient should be transferred to a facility that can perform the necessary level of care. Taking these limited published data together, and the accepted approach of hysterectomy to treat placenta accreta spectrum, conservative management or expectant management should be considered only for carefully selected cases of placenta accreta spectrum after detailed counseling about the risks, uncertain benefits, and efficacy and should be considered investigational.<sup>7</sup>

The risk of life-threatening bleeding is present throughout pregnancy but is particularly high at the time of delivery. Although the exact cause is unknown, the result is clear: Severe PAS distorts the uterus and surrounding anatomy and transforms the pelvis into an extremely high-flow vascular state. Screening for risk factors and assessing placental location by antenatal ultrasonography are essential for timely diagnosis. Further evaluation and confirmation of PAS are best performed in referral centers with expertise in antenatal imaging and surgical management of PAS. In the United States, cesarean hysterectomy with the placenta left in situ after delivery of the fetus is the most common treatment for PAS, but even in experienced referral centers, this treatment is often morbid, resulting in prolonged surgery, intraoperative injury to the urinary tract, blood transfusion, and admission to the intensive care unit. Postsurgical complications include high rates of posttraumatic stress disorder, pelvic pain, decreased quality of life, and depression. Team-based, patient-centered, evidence-based care from diagnosis to full recovery is needed to optimally manage this potentially deadly disorder. In a field that has relied mainly on expert opinion, more research is needed to explore alternative treatments and adjunctive surgical approaches to reduce blood loss and postoperative complications.<sup>8</sup>

In many instances of PAS, haemorrhage necessitates blood transfusion. The median of visually estimated, measured, and/or weighted blood loss in a recently published international multicenter study of 338 women with PAS was 2 L. When compared to scheduled hysterectomy, focused resection, or conservative therapy when delayed hysterectomy was not required, unplanned hysterectomy or delivery by surgeons with no experience in PAS was linked with an increased risk of blood loss > 3.5 L. Furthermore, it has been shown that individuals diagnosed with placenta accreta spectrum have a higher likelihood of necessitating hysterectomy either at the moment of childbirth or in the postpartum phase, as well as experiencing prolonged durations of hospitalisation. In this study, the author aim to assess the utilisation of red blood cells in patients diagnosed with placenta accreta spectrum during the process of childbirth.<sup>9-11</sup>

## 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

For the purpose of this literature review, we review the red blood cell transfusion for patients with placenta accreta spectrum. This is done to provide an explanation and improve the handling of treatment at the patient. As the main purpose of this paper, to show the relevance of the difficulties that have been identified as a whole.

In order for researchers to take part in the study, it was necessary for them to fulfil the following requirements: 1) The paper needs to be written in English. In order for the manuscript to be considered for publication, it needs to meet both of these requirements. 2) The studied papers include several that were published after 2013, but before the time period that this systematic review deems to be relevant. Examples of studies that are not permitted include editorials, submissions that do not have a DOI, review articles that have already been published, and entries that are essentially identical to journal papers that have already been published.

### Search Strategy

We used "red blood cell transfusion" and "placenta accreta spectrum" as keywords. The search for studies to be included in the systematic review was carried out using the PubMed and SagePub databases by inputting the words: (("erythrocyte transfusion"[MeSH Terms] OR ("erythrocyte"[All Fields] AND "transfusion"[All Fields]) OR "erythrocyte transfusion"[All Fields] OR ("red"[All Fields] AND "blood"[All Fields] AND "cell"[All Fields] AND "transfusion"[All Fields]) OR "red blood cell transfusion"[All Fields]) AND (("placenta accreta"[MeSH Terms] OR ("placenta"[All Fields] AND "accreta"[All Fields]) OR "placenta accreta"[All Fields]) AND ("spectrum"[All Fields] OR "spectrum s"[All Fields] OR "spectrums"[All Fields])) AND ((clinicaltrial[Filter]) AND (2013:2023[pdat])) used in searching the literature.

### 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.

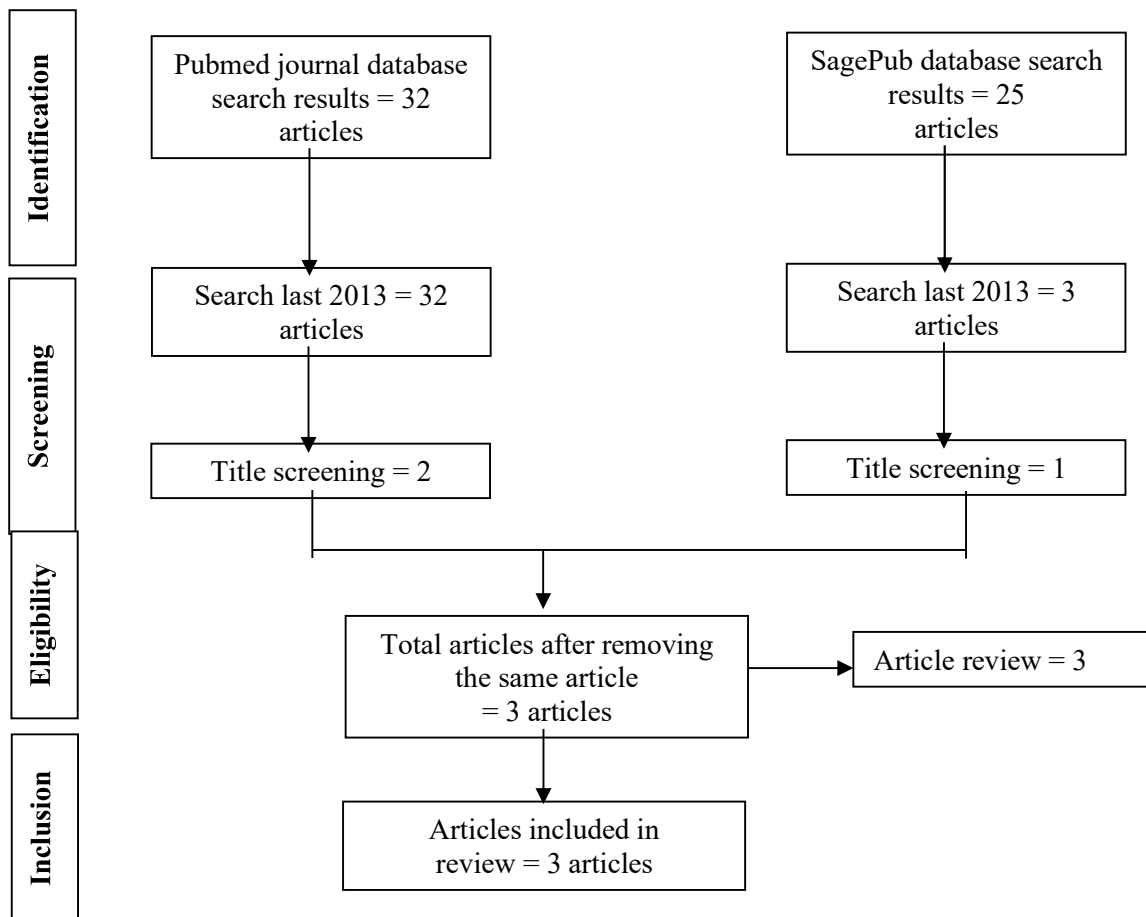


Figure 1. Article search flowchart

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 32 articles, whereas the results of our search on SagePub brought up 25 articles. The results of the search conducted for the last year of 2013 yielded a total 32 articles for PubMed and 3 articles for SagePub. In the end, we compiled a total of 3 papers, 2 of which came from PubMed and 1 of which came from SagePub. We included five research that met the criteria.

Seoud, et al<sup>12</sup> (2017) showed that elective cesarean hysterectomy for this indication using a clearly outlined surgical approach is associated with significantly lower blood loss and hence less need for transfusion, compared to its emergent counterpart.

Setyawan, et al<sup>13</sup> (2021) showed that retrospective case series review of patients diagnosed with placenta accreta undergoing cesarean section with massive bleeding and massive transfusion was conducted between April 2018 and March 2019 in Dr. Moewardi General Hospital using the medical record data. A total of five patients with placenta accreta underwent cesarean section, and massive bleeding as well as massive transfusion was identified. Hysterectomy was

performed at the time of cesarean section in all cases. All patients underwent general anesthesia, had central venous catheter, and required massive transfusion. Patients were transferred to the intensive care unit postoperatively. There were no transfusion reactions and maternal death.

**Table 1. The literature include in this study**

Author	Origin	Method	Sample	Result
Seoud et al, 2017 <sup>12</sup>	USA	Prospective cohort	28 patients	A total of 28 cases of confirmed placenta accreta underwent peripartum hysterectomy, including 22 as elective and 6 as emergent. Eleven out of 22 (50%) subjects in the elective group received blood transfusion, while all subjects in the emergency group required transfusion (p = 0.03). More importantly, the number of units of packed red blood cells transfused was only 1.90 (±2.20) units in the elective cases compared to 7.83 (±4.90) units in cases performed emergently (p = 0.03).
Setyawan et al, 2021 <sup>13</sup>	Indonesia	Case series	5 patients	From the 5 samples of the research, with the mean age of 31-40 years old patients. Five patients with placenta accreta were indicated to do transfusion of red blood cells. The number of red blood cells were 4-10 units. The researchers reported a case series of patients with placenta accreta requiring massive transfusions.
Munoz et al, 2022 <sup>14</sup>	USA	Prospective cohort	34 patients	We observed comparable results in post-operative outcomes with fewer overall transfusions and subsequently, lower volumes of resuscitation (p=.03) with whole blood initial resuscitation.

Munoz, et al<sup>14</sup> (2022) showed that whole blood transfusion may represent a viable option for initial resuscitation with lower resuscitation volumes and transfusion-associated complications without directly effecting post-operative outcomes in cases of PAS.

## DISCUSSION

Placenta accreta is a major cause of maternal morbidity. In this study the incidence of transfusion requirements ranges from 95% to 100%. All studies included in this systematic review reported a varied number of RBCs transfusion units. According to Seoud et al.<sup>12</sup>, a significant proportion of both the elective and emergency groups necessitated transfusion with 10 or more units of packed RBCs. Specifically, this requirement was observed in 50.0% and 54.2% of the elective and emergency groups, respectively. Furthermore, Setyawan & Permana<sup>13</sup> reported a case series of patients with placenta accreta requiring massive transfusions. In the event of severe haemorrhage, massive transfusion protocols are established to provide a prompt blood replacement. It is defined when (1) total blood volume is replaced within 24 hours, (2) 50 percent of total blood volume is replaced within three hours, or (3) rapid haemorrhage rate is documented or observed.<sup>13</sup>

Fortunately, the identification of placenta accreta typically occurs within the prenatal period through the utilisation of ultrasonography or placental magnetic resonance imaging. While the early identification of a medical condition during pregnancy allows for effective management and planning of the birth process, it does not offer guidance in terms of anticipating the amount of blood loss or arranging for potential transfusions. Furthermore, despite the anticipation of a higher demand for transfusion in patients with placenta accreta, there was no significant variation in the utilisation of blood components among the different subtypes of disease across study population.<sup>12-14</sup>

Regarding the transfusion ratio of blood components in obstetric patients, there is no consensus. Transfusions utilising a 1:1 ratio of red blood cells to plasma have been shown to enhance the prognosis in trauma patient studies. Uncertainty remains as to whether this practice should be applied to the obstetric population. The California Maternal Quality Care Collaborative has published transfusion guidelines for enormous obstetric haemorrhage that recommend an RBC:plasma:SDP ratio of 6:4:1.<sup>15</sup>

If the patient's fibrinogen level drops below 100 mg/dL, cryoprecipitate is also recommended. This is comparable to the MTP followed by Stanford University Medical Centre, which includes cryoprecipitate when the fibrinogen level declines below 100 mg/dL and a 6:4:1 initial ratio.<sup>15</sup>

Due to the scarcity of risk categorisation techniques, healthcare professionals are compelled to consider all deliveries involving placenta accreta as high-risk procedures that can necessitate substantial transfusion support. Planned delivery is firmly associated with lower blood transfusion requirements and improved neonatal outcomes compared to unplanned delivery. In patients with PAS disorders, antenatal vaginal haemorrhage and preterm labour are risk factors for emergency delivery. On the basis of the findings of this study, we recommend that the management strategies for patients with PAS disorders be individualised in order to determine the optimal timing of delivery and reduce the rate of emergency caesarean section.<sup>15</sup>

Placenta accreta spectrum (PAS) is an abnormal condition in which the placenta invades the myometrium, other pelvic tissue and sometimes the organs. PAS includes placenta accreta, placenta increta, and placenta percreta. The incidence of PAS disorders has increased significantly in the last few decades and seems to correlate with the increasing rate of caesarean delivery. One recent estimate for the incidence of PAS is 9 in 1000 patients (0.91%), which has increased from 0.12% to 0.31% over the last 30 years. PAS disorders have become a life-threatening obstetric problem with a mortality rate of approximately 7%.<sup>3,6</sup>

The optimal management method for PAS disorders is still controversial. A planned, scheduled delivery with a multidisciplinary team is associated with shorter operative time, decreased maternal hemorrhagic morbidity, and fewer intensive care unit admissions when compared with an unscheduled, emergent delivery. The ideal timing of delivery in patients with PAS disorders has not been decided. The American College of Obstetricians and Gynecologists recommends a scheduled delivery at 34 weeks of gestational age, whereas others advise delaying delivery to 36 weeks as a balance between maternal risks and fetal immaturity. Thus, the purpose of this study was to compare the clinical outcomes and to identify possible risk factors for urgent caesarean delivery and scheduled caesarean delivery in Indonesia.<sup>3</sup>

It is important to set the strategy to minimize the risk of emergent caesarean delivery. First, we need to detect women with PAS early by combining obstetrics history, clinical findings and imaging techniques (ultrasound, MRI). After then, we should refer these women to specialized obstetrics referral centers whenever possible. A multidisciplinary team of obstetricians, gynecologist, vascular surgeons, interventional radiologists, urologists, and hematologists in referral centers increases accuracy of the diagnosis, and subsequent management by experts reduces maternal morbidity and mortality. In our hospital, the strategy of a planned caesarean section included blood typing, cross-matching of at least 2 units of packed red cells, and invitation of multiple team works. In planned cases of caesarean hysterectomy, we used a midline vertical incision to minimize dissection of tissue planes and provide good visualization of the abdomen and pelvis.<sup>16,17</sup>

## CONCLUSION

Based on the studies included in this review, we are unable to recommend the minimum of units of red blood cells that should be available before delivery for patients with placenta accreta spectrum. Future studies in the form of large clinical trials is required to study the minimum of RBCs units for PAS patients before delivery, to better inform future guidelines for predelivery blood ordering and transfusion support.

## REFERENCE

- [1] American College of Obstetricians and Gynecologists. Levels of Maternal Care. Obstetric Care Consensus No 2 [Internet]. 2015 [cited 2023 Nov 17];125:502–15. Available from: <https://www.acog.org/clinical/clinical-guidance/obstetric-care-consensus/articles/2019/08/levels-of-maternal-care>
- [2] American College of Obstetricians and Gynecologists; Society for Maternal-Fetal Medicine. Obstetric Care Consensus No. 7: Placenta Accreta Spectrum. *Obstet Gynecol* [Internet]. 2018 [cited 2023 Nov 19];132(6):259–75. Available from: <https://pubmed.ncbi.nlm.nih.gov/30461695/>
- [3] Jauniaux E, Chantraine F, Silver RM, Langhoff-Roos J. FIGO consensus guidelines on placenta accreta spectrum disorders: Epidemiology. *Inj J Gynaecol Obstet*. 2018;140(3):265–73.
- [4] Silver RM, Branch DW. Placenta Accreta Spectrum. *N Engl J Med*. 2018;378(16):1529–36.
- [5] Enste R, Cricchio P, Dewandre PY, Braun T, Leonards CO, Niggemann P, et al. Placenta Accreta Spectrum Part II: hemostatic considerations based on an extended review of the literature. *J Perinat Med* [Internet]. 2022 [cited 2023 Nov 19]; Available from: <https://www.degruyter.com/document/doi/10.1515/jpm-2022-0233/html>
- [6] Cui R, Li M, Lu J, Bai H, Zhang Z. Management strategies for patients with placenta accreta spectrum disorders who underwent pregnancy termination in the second trimester: a retrospective study. *BMC Pregnancy Childbirth* [Internet]. 2018 [cited 2023 Nov 19];298. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6042202/>
- [7] Berek JS, Hacker NF. *Berek & Hacker's gynecologic oncology*. 2018. 849 p.
- [8] Einerson B, Gilner J, Zuckerwise LC. Placenta Accreta Spectrum. *Obstetrics & Gynecology Journal* [Internet]. 2023 [cited 2023 Nov 17];142(1):31–50. Available from: [https://journals.lww.com/greenjournal/abstract/2023/07000/placenta\\_accreta\\_spectrum.6.aspx](https://journals.lww.com/greenjournal/abstract/2023/07000/placenta_accreta_spectrum.6.aspx)
- [9] Morlando M, Sarno L, Napolitano R, Capone A, Tessitore G, Maruotti GM, et al. Placenta accreta: incidence and risk factors in an area with a particularly high rate of cesarean section. *Acta Obstet Gynecol Scand* [Internet]. 2013 [cited 2023 Nov 19];92(4):457–60. Available from: <https://obgyn.onlinelibrary.wiley.com/doi/10.1111/aogs.12080>
- [10] Schwickert A, van Beekhuizen HJ, Bertholdt C, Fox KA, Kayem G, Morel O, et al. Association of peripartum management and high maternal blood loss at cesarean delivery for placenta accreta spectrum (PAS): A multinational database study. *Acta Obstet Gynecol Scand*. 2021 Mar 1;100(S1):29–40.
- [11] Nieto-Calvache AJ, Palacios-Jaraquemada JM, Osanan G, Cortes-Charry R, Aryananda RA, Bangal VB, et al. Lack of experience is a main cause of maternal death in placenta accreta spectrum patients. *Acta Obstet Gynecol Scand*. 2021 Aug 1;100(8):1445–53.
- [12] Seoud MA, Nasr R, Berjawi GA, Zaatari GS, Seoud TM, Shatila AS, et al. Placenta accreta: Elective versus emergent delivery as a major predictor of blood loss. *J Neonatal Perinatal Med* [Internet]. 2017 [cited 2023 Nov 19];10(1):9–15. Available from: <https://pubmed.ncbi.nlm.nih.gov/28304318/>
- [13] Setyawan N, Permana S. Massive transfusion in cesarean section patients with placenta accreta: A case series. *Bali Journal of Anesthesiology*. 2021;
- [14] Munoz JL, Kimura AM, Xenakis E, Jenkins DH, Braverman MA, Ramsey PS, et al. Whole blood transfusion reduces overall component transfusion in cases of placenta accreta spectrum: a pilot program. *J Matern Fetal Neonatal Med* [Internet]. 2022 [cited 2023 Nov 19];35(25):6455–60. Available from: <https://pubmed.ncbi.nlm.nih.gov/33902384/>
- [15] Thang NM, Anh NTH, Thanh PH, Linh PT, Cuong TD. Emergent versus planned delivery in patients with placenta accreta spectrum disorders. *Medicine (Baltimore)* [Internet]. 2021 [cited 2023 Nov 19];100(51). Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8702197/>
- [16] Bienstock JL, Eke AC, Hueppchen NA. Postpartum Hemorrhage. *N Engl J Med* [Internet]. 2021 [cited 2023 Nov 19];384(17):1635–45. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10181876/>
- [17] van Beekhuizen HJ, Stefanovic V, Schwickert A, Henrich W, Fox KA, Gziri MM, et al. A multicenter observational survey of management strategies in 442 pregnancies with suspected placenta accreta spectrum. *Acta Obstet Gynecol Scand* [Internet]. 2021 [cited 2023 Nov 19];100:12–20. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8048500/>