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

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Abstract
Introduction: Placenta accreta spectrum (PAS) is associated with high maternal morbidity and mortality, mostly due to postpartum haemorrhage caused by aberrant placental-myometrial separation. In many instances of PAS, haemorrhage necessitates blood transfusion.

Objective: To assess the utilisation of red blood cells in patients diagnosed with placenta accreta spectrum during the process of childbirth.

Methods: A systematic review of literature published between 2003 and August 3, 2023 was performed across several databases including PubMed, Cochrane Library, and Google Scholar. Duplicate publications, review articles, and incomplete articles were excluded.

Results: The databases search identified a total of 13,613 articles (Table 1) and resulted in 13,500 articles after duplicates removed. Of these, 13,420 articles were excluded due to non-original study and titles and abstract not represented the focus of interest; and resulting in 80 articles for screening process. Articles not evaluating the focus of interest and articles in which full-text are not available are excluded, resulting in 25 articles for evaluation of eligibility criteria. Among them, 21 articles given were not specified for RBCs transfusion and did not give sufficient details. Hence, we found 4 appropriate studies included.

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.

Keywords: Red blood cells transfusion, Transfusion, Placenta accreta
Introduction
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.1,2 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.3 These conditions include placenta increta, placenta percreta, and placenta accreta.4 PAS is diagnosed based on clinical symptoms, pathological observations, or ultrasound imaging.4

In recent decades, the incidence of PAS disorders has increased substantially, and this trend appears to correspond with the rising rate of caesarean delivery.5 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%).5,7

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.5,9 Spontaneous uterine rupture with subsequent hemoperitoneum, particularly when coupled with placenta percreta, is a less common cause of maternal morbidity and mortality.9 Overall, the mortality rate is 7%.10

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.11 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.1,8 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

Method
Search Strategy
A systematic review of literature published between 2003 and July 2023 was performed across several databases including PubMed, Cochrane Library, and Google Scholar. The search strategy involved the following combinations of these keywords: “Red blood cells transfusion”, “Transfusion”, “Placenta accreta”.

Table 1. Literature search strategy

<table>
<thead>
<tr>
<th>Database</th>
<th>Keywords</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>PubMed</td>
<td>(Red blood cells transfusion) OR (Transfusion) AND (Placenta acrreta)</td>
<td>100</td>
</tr>
<tr>
<td>Cochrane Library</td>
<td>(Red blood cells transfusion) OR (Transfusion) AND (Placenta acrreta)</td>
<td>13</td>
</tr>
<tr>
<td>Google Scholar</td>
<td>(Red blood cells transfusion) OR (Transfusion) AND (Placenta acrreta)</td>
<td>13.500</td>
</tr>
</tbody>
</table>

Eligibility Criteria
The following inclusion criteria were adopted: original articles published or accepted for publication in English, published during 2003–2023, the subjects of the study were patients with placenta accreta spectrum (accreta, increta, percreta), and the subjects were given red blood cells transfusion. The exclusion criteria of the studies are articles that are not indexed by Scopus, editors, reviews, and articles that did not evaluate the focus of interest of this study. The research selection was carried out in three successive phases. The titles and abstracts of all search results were initially screened and evaluated for relevance. Second, complete access was gained to all potentially eligible studies. Finally, the systematic review included only those studies that met our inclusion criteria. The Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guideline is used for the selection.

Data Extraction and Parameter Measured
The authors extracted the data from the articles. The following data regarding the factors associated with voice disorders in elderly are collected: Author, year of publication, sample size, age of study subjects, incidence of transfusion, the number of RBCs transfusion needed (units).

Results
The databases search identified a total of 13,613 articles (Table 1) and resulted in 13,500 articles after duplicates removed. Of these, 13,420 articles were excluded due to non-original study and titles and abstract not represented the focus of interest; and resulting in 80 articles for screening process. Articles not evaluating the focus of interest and articles in which full-text are not available are excluded, resulting in 25 articles for evaluation of eligibility criteria. Among them, 21 articles given were not specified for RBCs transfusion and did not give sufficient details. Hence, we found 4 appropriate studies included (Figure 1). The summary of the main findings of the selected studies is presented in Table 2.
Figure 1. The search strategy based on PRISMA flow diagram

Table 2. Characteristics of studies included

<table>
<thead>
<tr>
<th>Author &amp; year of publication</th>
<th>Study design</th>
<th>Sample</th>
<th>Age (years)</th>
<th>Placenta accreta spectrum</th>
<th>Incidence of transfusion</th>
<th>No. of RBC Transfusion (units)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stotler et al. (2011)⁹</td>
<td>Cross-sectional</td>
<td>66</td>
<td>22–59</td>
<td>Accreta: 47 Increta: 6 Percreta: 13</td>
<td>95% (39% of patients requiring 10 or more RBC units and 11% requiring 20 or more RBC units)</td>
<td>Accreta: 0–36 Increta: 2–20 Percreta: 2–46 Mean RBC use: 10 ± 9 Median RBC use: 6.5</td>
</tr>
<tr>
<td>Setyawan &amp; Permana (2021)¹³</td>
<td>Case series</td>
<td>5</td>
<td>31–40</td>
<td>Accreta: 5</td>
<td>100%</td>
<td>4–10</td>
</tr>
<tr>
<td>Munoz et al. (2022)¹³</td>
<td>Prospective cohort</td>
<td>34</td>
<td>Mean age in group receiving whole blood: 32.4 ± 5.9 Mean age in group receiving components: 31.3 ± 5.28</td>
<td>Previa: 7 Accreta: 16 Increta: 1 Percreta: 10</td>
<td>NR</td>
<td>2–6.8</td>
</tr>
</tbody>
</table>

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 Stotler et al.⁹, 95% of patients required transfusions (mean RBC use: 10 9 units; median: 6.5 units), with 39% requiring 10 or more RBC units and 11% requiring 20 or more RBC units. According to Seoud et al.¹², 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 & Permana¹³ 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.¹³

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 percreta, there was no significant variation in the utilisation of blood components among the different subtypes of disease accros study population.⁹,¹²–¹⁶

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.¹⁷ Uncertainty
remains as to whether this practise 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.\(^\text{18}\)

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.\(^\text{13}\)

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.\(^\text{3}\)

**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.

**References**


