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Pre-deposit autologous blood donation in Rh(D) negative pregnant women: a single-center study

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Abstract:

Objective The primary purpose of this study was to assess the practicability of pre-deposit autologous blood donation (PAD) in the practice of Rh(D) negative pregnant women.

Materials and methods: A cohort of 405 Rh(D) negative pregnant women who had a delivery in the comprehensive tertiary hospital in Nanjing was analyzed retrospectively.

Results: After PAD, 203 women experienced a slight drop in mean hemoglobin of 5.32±0.5g/L (PAD-associated anemia was not featured in our study). 13 women who received allogeneic blood might benefit from PAD practically.

Conclusion: PAD is applicable for Rh(D) negative pregnant women, as it ensures the availability of the patient's own blood in the event of perinatal hemorrhage, thus minimizing the need for transfusion from external sources. Also, more attention is needed to raise awareness of patient blood management (PBM). Recommended strategies include early screening and treatment of anemia, hemostasis promotion and blood loss reduction. Replacement of allogeneic transfusion with autotransfusion could be referred where feasible. We believe that PAD still has a promising potential for application in Rh(D) negative pregnant women.

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Pre-deposit autologous blood donation in Rh(D) negative pregnant women: a single-center study

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Objective：The primary purpose of this study was to assess the practicability of pre-deposit autologous blood donation (PAD) in the practice of Rh(D) negative pregnant women.

Materials and methods: A cohort of 405 Rh(D) negative pregnant women who had a delivery in the comprehensive tertiary hospital in Nanjing was analyzed retrospectively, over a 10-year period.

Results: After PAD, 203 women experienced a slight drop in mean hemoglobin of 5.32±0.5g/L (PAD-associated anemia was not featured in our study). 13 women who received allogeneic blood might benefit from PAD practically.

Conclusion: PAD is applicable for Rh(D) negative pregnant women, as it ensures the availability of the patient's own blood in the event of perinatal hemorrhage, thus minimizing the need for transfusion from external sources. Despite the autologous blood reinfusion of low proportion, PAD could still serve as an alternative when allogeneic blood resources are scarce. However, one challenge in future is to identify candidates who may benefit most from PAD. Also, more attention is needed to raise awareness of patient blood management (PBM). Recommended strategies include early screening and treatment of anemia, hemostasis promotion and blood loss reduction. Replacement of allogeneic transfusion with autotransfusion could be referred where feasible. We believe that PAD still has a promising potential for application in Rh(D) negative pregnant women.

Introduction

The Rh blood group is the most intricate and polymorphic in human blood group systems, arguably second only to ABO system in clinical significance and it exhibits high immunogenicity, especially the D antigen. Among transfusion medicine, D antigen deletion is typically termed as Rh (D) negative. Earlier studies uncovered that

D antigen distribution differs considerably from ethnicities. Approximately 15% in Caucasians express D negative phenotype, 8% in Africans. Comparatively, there is a lower prevalence of only 0.4% in Asians[1, 2]. Sparse Rh (D) negative population poses difficulty to obtain adequate blood resources from donors. In real life, blood transfusion services are often confronted with the challenge to provide Rh (D) negative blood products promptly.

On the other side, all over the world, maternal death is primarily caused by severe obstetric hemorrhage and blood transfusion is an irreplaceable rescue measure. Consistently, obstetricians and transfusionists face the vexing issue of how to ensure safe delivery in such groups. The lives of puerpera and fetus could be threatened when severe postpartum hemorrhage happens during blood resources shortage. Therefore, appropriate blood products should be prepared beforehand in anticipation of such emergency.

As concerns for transfusion safety and blood shortage become increasingly prominent, autotransfusion has garnered widespread attention. Autotransfusion is an alternative of allogeneic transfusion, which consists of three modalities: pre-deposit autologous blood donation (PAD), acute normovolemic hemodilution (ANH), and intraoperative cell salvage (ICS). ANH and ICS have been limited in some areas with underdeveloped medical conditions owing to higher technically demanding. In comparison, PAD is praised for its low cost and simplicity. It could not only stimuli erythrocyte regeneration but also avoid immune responses associated with allogenic transfusion and prevent blood-transmissible diseases. Since 1980, PAD has been

extensively applied in some high-bleeding-risk surgeries, including cardiac surgery, liver surgery and orthopedic surgery. It is considered as a good alternative to the allogeneic transfusion. Nevertheless, controversy regarding its safety and availability are retained in obstetric[3]. The study was conducted to evaluate its application in Rh (D) negative pregnant women, aiming to provide reference for perinatal blood management in this special group.

Keywords: Pre-deposit autologous blood donation; Postpartum hemorrhage; Gestational anemia; Patient blood management

Materials and method

The medical records of all Rh (D) negative pregnant women who had delivered in the comprehensive tertiary hospital in Nanjing, China from January 1, 2012 to January 31, 2022 were reviewed retrospectively. Only pregnancies with complete clinical data and transfusion records were included in this study. The indicated population for PAD were Rh (D) negative pregnant women in our institution. All eligible women were encouraged to carry out PAD. The participants corresponded with the following conditions: 1.The patient had a hemoglobin(Hb) value ≥110g/L or hematocrit ≥33%. 2.The patient who experienced cardiovascular and cerebrovascular diseases, liver and kidney dysfunction, blood system disease and other serious complications were excluded. 3.Every patient was advised of associated risks and then signed an informed consent. PAD was scheduled to initiate beyond 37 weeks' gestation with blood collection volume 200 ml each time and no more than twice throughout the program. All procedures were performed by experienced

transfusionists, and blood collection was completed within 5 minutes. The whole blood was collected into blood bag with CPDA1 preservation solution and stored in the dedicated refrigerator at 4 °C in blood transfusion branch for up to 35 days.

Vital signs, including oxygen saturation, respiratory rate, blood pressure, heart rate and body temperature, were monitored consistently throughout blood sampling, the fetal heart monitoring was performed to assess fetal wellbeing by obstetricians simultaneously. Hb value at separate stages (before PAD, before delivery and 24h after delivery) were recorded. Blood loss within postpartum 24h and the amount of transfused blood, autologous or allogeneic, or both were documented. Triggers are of the same for allogeneic and autogenous transfusion. Transfusion measures were taken for patient with postpartum hemorrhage(defined as blood loss exceeding 500 ml within 24 h following vaginal delivery or exceeding 1000 ml following caesarean delivery) or postpartum anemia (defined as Hb < 10 g/dL). Unused autologous blood were scrapped in accordance with medical waste by the blood transfusion branch.

Statistical analysis for obtained data were done with IBM SPSS Statistics version 23.0. Continuous variables were analyzed by independent two-sample t test, while categorical variables were analyzed by chi-square test. *P*-value < 0.05 was accepted as statistical significance. Figures were drawn using GraphPad Prism 8.0 software.

Result

Data on 405 Rh□D□negative women were enrolled in this study, after exclusion of 34 women who had either suffered a miscarriage at less than 28 weeks' gestation (n=2) or were found to have missing data in one or more laboratory records (n=32).

Among all (n=344) women who fulfilled PAD criterion, 141 women declined to participate because of various reasons, either for not supported by individual religiosity or having psychological fear when confronted with blood donation. (Figure 1) 203 women underwent PAD, vital signs were maintained well and no adverse blood donation reactions were observed, such as lightheadedness, shortness of breath, fatigue, palpitations or syncope caused by vagal nerve. Fetal heart monitoring indicated no appreciable abnormality.

The mean Hb before blood collection and pre-delivery of 203 women who underwent PAD were 123.59±8.81 g/L and 118.27±9.31 g/L respectively, with declining by only 5.32±0.5 g/L. (Figure 2) The pre-delivery mean Hb of 141 women who met criteria for PAD but did not undergo was 122.04±9.59 g/L. Comparison of the pre-delivery Hb was statistically difference in two groups.(118.27±9.31 g/L vs 122.04±9.59 g/L, *P*=0.001). Among these 203 individuals, 146 women had 1 unit and 57 women had 2 units of autologous blood respectively, 25 women reinfused 1 unit and 16 women reinfused 2 units of autologous blood, another 2 women reinfused 1 unit autologous blood and required additional allogeneic blood due to excessive postpartum bleeding. (Figure 3) 41 women received autologous of 273.17±96.33 ml, with pre-delivery Hb of 115.49±11.87 g/L and blood loss of 447.46±237.07 ml. Of the remaining 160 women, the collected autologous blood units were not used, with pre-delivery Hb of 119.13±8.30 g/L and blood loss of 380.97±118.61 ml. Among these 141 women who met criteria for PAD but failed to engage in, 128 women who required no transfusion had pre-delivery Hb of 122.38±9.85 g/L and blood loss of

418.77±140.01 ml. 13 women received allogeneic blood of 376.92±147.56 ml, with pre-delivery Hb of 118.77±5.34 g/L and blood loss of 569.62±282.17 ml. In the population of 61 women who were ineligible for PAD, 35 women had no need for transfusion, with pre-delivery Hb of 103.43±4.64 g/L and blood loss of 488.67±153.47 ml, 26 women received allogeneic blood transfusion of 892.31±989.14 ml, with pre-delivery Hb of 89.81±15.57 g/L and blood loss of 814.81±1085.45 ml. Table 1 (Figure 4 and Figure 5)

The primary indication for transfusion cases were assayed below. 41 women received only autologous blood and 2 women who required extra allogeneic blood were incorporated in the same autologous transfusion group. Of these 43 women, 16 women also experienced hypertension, diabetes, macrosomia, or twin pregnancies, which were indicated as postpartum hemorrhage induced by uterine atony. 7 women with indication of postpartum Hb<100g/L and 9 women with scarred uterus received autologous blood. There were no apparent transfusion indications for remaining 10 patients. Among 39 women who received allogeneic blood, gestational anemia accounted for 19, uterine atony accounted for 6, scarred uterus accounted for 5 and placenta previa accounted for 4. (Table 2)

Discussion

Pre-deposit autologous blood donation (PAD) is a technique that involves collecting and storing the patient's own blood prior to surgery or other medical procedures, with the intention of using this blood if a transfusion is needed. PAD is proved to be safe both theoretically and empirically. In theory, during the pregnancy

process, total blood volume normally increases by approximately 1450ml, not only offers the essential nutrients for fetal growth but also acts as a native protection mechanism to cope with delivery bleeding. Typically, blood loss within the range of 1000-1500ml would have no undesirable theoretically consequence for the pregnant women with normal Hb value[4]. Hence, PAD is possible to be performed safely. Empirically, PAD has been confirmed to be a safe and feasible therapy measure in our study, which is consistent with conclusions from various previous research projects[5-7]. Vital signs of 203 women during PAD presented well and no unfavorable blood donation reaction was observed. The fetal heart monitoring recordings revealed normal. PAD-associated anemia almost did not occur, with merely a slight decline in mean Hb of 5.32±0.5g/L. Additionally, no adverse transfusion reactions, such as fever, skin rash palpitations and chest tightness, were observed during autologous blood reinfusion. Our findings demonstrated that PAD could be added as a viable transfusion practice.

In the autotransfusion cohort, uterine factors take up a proportion 58.1% (25/43). Uterine atony after parturition causes uterine spiral artery dilation and then ultimately ends up with excessive bleeding, which is the main contributor to postpartum hemorrhage (PPH)[8]. Precipitating factors for uterine atony emerged in the present study included fetal macrosomia, twin pregnancy, gestational diabetes and scarred uterus. In addition, placenta factors and birth canal laceration are also high-risk factors of inducing PPH. All pregnant women practically could have potential probability of PPH. The latest guideline proposed that 60% women with PPH had no

preexisting known risk factors[9]. Rh (D) negative blood products are not routinely available due to extreme blood resources shortage in our country, especially where accesses to proper medical services are limited. Thus, blood preparation in advance is imperative in this specific population. PAD could serve as a proper alternative in the context of allogeneic blood resources shortage.

Among 344 patients who met the criteria for PAD, pre-PAD Hb and postpartum blood loss were similar between the autotransfusion group (n=41) and the un-transfused group(n=128). After checking medical records, we noted that 10 patients of autotransfusion group indeed lacked justifiable transfusion indications. We concluded that they might not truly need transfusion. Admittedly, transfusion triggers vary widely from medical institutions and are affected by the experience and subjective judgments from physicians. Some patients insisted upon being reinfused with their own blood, although lacked the indication for transfusion. One explanation is that pre-deposit autologous blood may inspire liberal transfusion policy, consistent with a prior study[10].

Among allogeneic transfusion group, we contemplated that 13 patients were virtually beneficiary population of PAD since they met criteria for PAD but failed to attend, such patients were accompanied by comorbidities including scarred uterine, twin pregnancies or macrosomia, which represented good indication of PAD. It was noteworthy that pregnancies solely with anemia accounted for 48.7% (19/39) of allogeneic transfusion group. Compared with non-anemic patients, anemia patients could be more prone to developing postpartum hemorrhage and peripartum

transfusion, because of poorer tolerance for blood loss[11, 12]. According to WHO data, approximately 40% pregnancies were accompanied by anemia all over the world[13]. About 15.1% patients (61/405) in this study had anemia of mild to moderate severity, and even severe anemia. Gestational anemia can trigger a series of adverse perinatal outcomes, including premature rupture of membranes, preterm delivery, and increased maternal and fetal mortality[14]. Furthermore, in the absence of PPH, blood transfusion can chiefly be attributed to pre-delivery anemia. Iron deficiency anemia(IDA) is the commonest type of anemia during pregnancy, which is characterized by depleted iron stores and impaired iron supply to tissues[15]. Guidelines set forth by ACOG(2021a) recommend to screen for anemia in all pregnant women and iron supplementation should be promptly administered once IDA is diagnosed[16]. Anemia is a modifiable risk factor since sufficient time are available to optimize Hb value before delivery. Early identification and management of anemia may be favorable to improve maternal and neonatal outcomes.

PAD has a prominent advantage that it minimizes exposure to allogeneic blood. PAD reduces the risk of infectious diseases that can be transmitted through blood transfusions, such as hepatitis B and C and HIV. The mother is assured that the blood she receives will be safe and compatible, as it is her own blood. Autologous blood protects pregnant women from being sensitized by exogenous erythrocyte antigen that will be conducive to another pregnancy[17]. In addition to its potential use in Rh(D) negative pregnant women, PAD may also be used in other clinical scenarios where blood transfusions are anticipated. For example, it may be used in patients undergoing

elective surgeries, such as joint replacement, where blood transfusions are common. PAD may also be used in patients with rare blood types or who have developed alloantibodies to common blood antigens.

However, the use of PAD is not without controversy. There are drawbacks to conduct PAD, including the potential for inadequate blood volume or hemoglobin concentration at the time of delivery. If the mother experiences significant bleeding during delivery, she may require a transfusion of additional blood products, which may not be available if the PAD was insufficient or if the mother does not meet the donation criteria. In addition, PAD can be a time-consuming process that requires multiple visits to the blood donation center. This can be a burden to the mother, who may already be busy dealing with the stresses of pregnancy and preparing for childbirth. It is important to note that the procedure itself carries certain risks, such as anemia, infection, and venous thrombosis. Patients who undergo PAD should be closely monitored for potential complications, and appropriate interventions should be taken if needed. There are also concerns that PAD may promote unnecessary blood transfusions and contribute to overuse of healthcare resources. Additionally, the costs associated with PAD, including the cost of the blood tests and the cost of storage and processing, can be a barrier for some women. Thus, some critics argue that the costs and risks associated with PAD may outweigh the benefits.

Ultimately, the decision to undergo PAD should be based on individual risk factors and medical history. Women with a history of HDN, multiple pregnancies, or previous blood transfusions may be considered risky in allogeneic transfusion and

could benefit from PAD. PAD may also be recommended in cases where a planned caesarean section is scheduled, as these procedures can result in significant blood loss. Certain medical conditions such as placenta previa, placental abruption, or fetal distress may increase the risk of postpartum hemorrhage and the need for blood transfusions during or after delivery[11, 18]. In some geographic areas or healthcare systems, Rh(D) negative blood products are limited and PAD may be considered as a way to ensure that the patient has access to Rh(D) negative blood if needed.

It is important for healthcare providers to provide adequate education and counseling to women who are considering PAD. This includes explaining the benefits and risks of PAD, discussing the donation process, and addressing any concerns or questions patients may have. Women who choose to undergo PAD should also be given clear instructions on how to prepare for the donation, such as maintaining a healthy diet and hydration, and avoiding medications that may affect the blood donation process. Finally, it is important for healthcare providers to ensure that the PAD process is well-coordinated with the hospital or birthing center. This includes assuring that the donated blood is properly labeled and stored, and that hospital staffs are aware of the mother's PAD status and prepare to use the donated blood if necessary. In conclusion, adequate education, counseling, and coordination with the hospital or birthing center can help to ensure a safe and successful PAD process.

Furthermore, the use of PAD requires adequate resources and infrastructure, including trained personnel, appropriate storage and processing facilities, and access to blood testing and transfusion services. In some healthcare settings, these resources

may be limited, which may impact the feasibility of using PAD. To address potential shortages of PAD, healthcare providers may consider alternative strategies, such as intraoperative blood salvage, where blood lost during surgery is collected, processed, and reinfused back into the patient. This technique may be particularly useful in surgeries with high blood loss, such as cardiac or orthopedic surgeries[19, 20]. The overall use of blood transfusions has been declining in recent years due to efforts to reduce unnecessary transfusions and improve patient outcomes. For example, the use of restrictive transfusion strategies, which aim to maintain lower hemoglobin levels before transfusing blood, has been shown to reduce the need for transfusions and improve outcomes in certain patient populations[21, 22]. Healthcare providers may also consider other strategies to optimize patient outcomes, such as reducing surgical blood loss through the use of hemostatic agents, optimizing preoperative hemoglobin levels through iron supplementation or erythropoietin therapy, and improving patient blood management practices[23]. Furthermore, healthcare providers may also consider the use of non-blood alternatives to transfusions, such as intravenous fluids, medications, and oxygen therapies, which may be effective in certain clinical scenarios.

In summary, PAD is applicable for Rh(D) negative pregnant women, as it minimizes the risk of transfusion from external sources by utilizing the availability of the patient's own blood in the event of perinatal hemorrhage. Although it is not without defects, healthcare providers can work to address these challenges by exploring alternative strategies, collaborating with blood banks to improve the

availability of Rh(D) negative blood products, and implementing patient blood management practices to optimize patient outcomes and reduce the need for transfusions.

Conflict of Interest

The authors declare that they have no conflicts of interest in this article

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Table 1 Hb value and received transfusion and blood loss according to PABD

All included Rh□D□negative women 405 (100%)		
Met	YES 344 (84.9%)	NO 61 (15.1%)

criteria for PAD							
PAD	YES 203 (59.0%)			NO 141 (41.0%)			
Transfusion	Autologous 41 (20.2%)	Autologous and Heterologous 2 (1%)	No 160 (78.8%)	Heterologous 13 (9.2%)	No 128 (90.8%)	Heterologous 26 (42.6%)	No 35 (57.4%)
Mean Hb before delivery	115.49±11.87	108±7	119.13±8.30	118.77±5.34	122.38±9.85	89.81±15.57	103.43±4.64
Average blood loss (ml)	447.46±237.07	935±265	380.97±118.61	569.62±282.17	418.77±140.01	814.81±1085.45	488.67±153.47
Transfusion volume(ml)	273.17±96.33	450±50	0	376.92±147.56	0	892.31±989.14	0

Table 2 Transfusion cases by primary indication for study enrollment

Indication	n	Incidence (%)	Blood loss (ml)	Autologous blood Transfusion (N=43)	Allogeneic blood Transfusion(N=39)	Hysterectomy （n）
Uterine atony (Fetal macrosomia，Twin pregnancies，Gestational hypertension， Gestational diabetes)	22	25.6	541.43±270.17	16	6	1

Scarred uterus	14	17.1	584.29±201.69	9	5	01
Placenta previa	5	6.1	1913±2056.18	1	4	00
Anemia	19	24.3	6a08.75±348.69	0	19	00
Cervical laceration	1	1.2	925	0	1	
Postpartum Hb <100g/L	8	9.8	370.63±82.78	7	1	
Others	13	15.9	278.92±90.97	10	3	

Figure 1. Flowchart for the patient inclusion and exclusion in this study

Figure 2. Changes in Mean Hb values before PAD and before delivery in 203 patients.

Hb : hemoglobin; ns: not significant

Figure 3. Details of patients who received transfusion among PABD group (n=203) and non-PABD group (n=141).

PABD: pre-deposit autologous blood donation; PBL: postpartum blood loss

Figure 4. Distribution of hemoglobin value before delivery among four groups.

Figure 5. Distribution of postpartum blood loss among four groups.

Group 1autologous blood transfusion group (n=43).

Group 2: patients who met criteria for PAD but did not undergo and required no transfusion (n=128).

Group 3: patients who met criteria for PAD but did not undergo and need transfusion (n=13).

Group 4: patients who were ineligible for PAD and received allogeneic blood transfusion (n=26).

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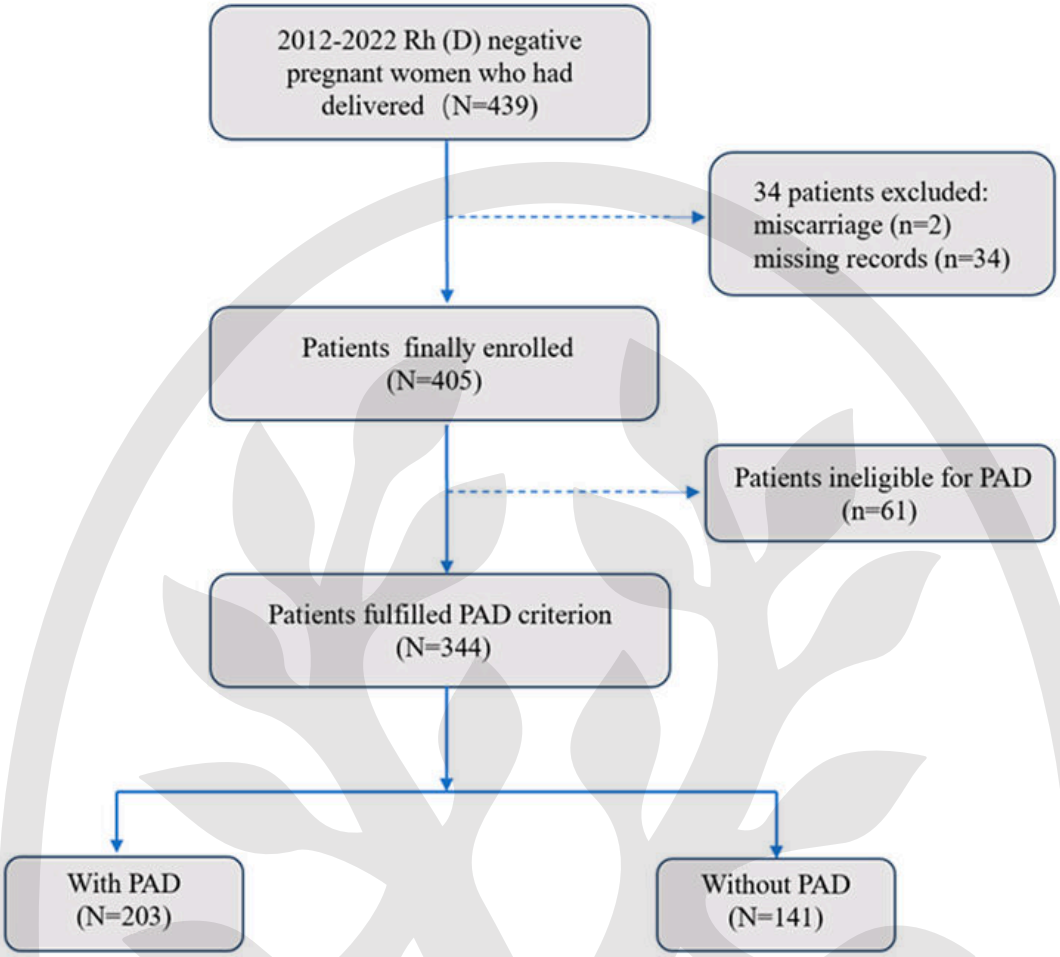

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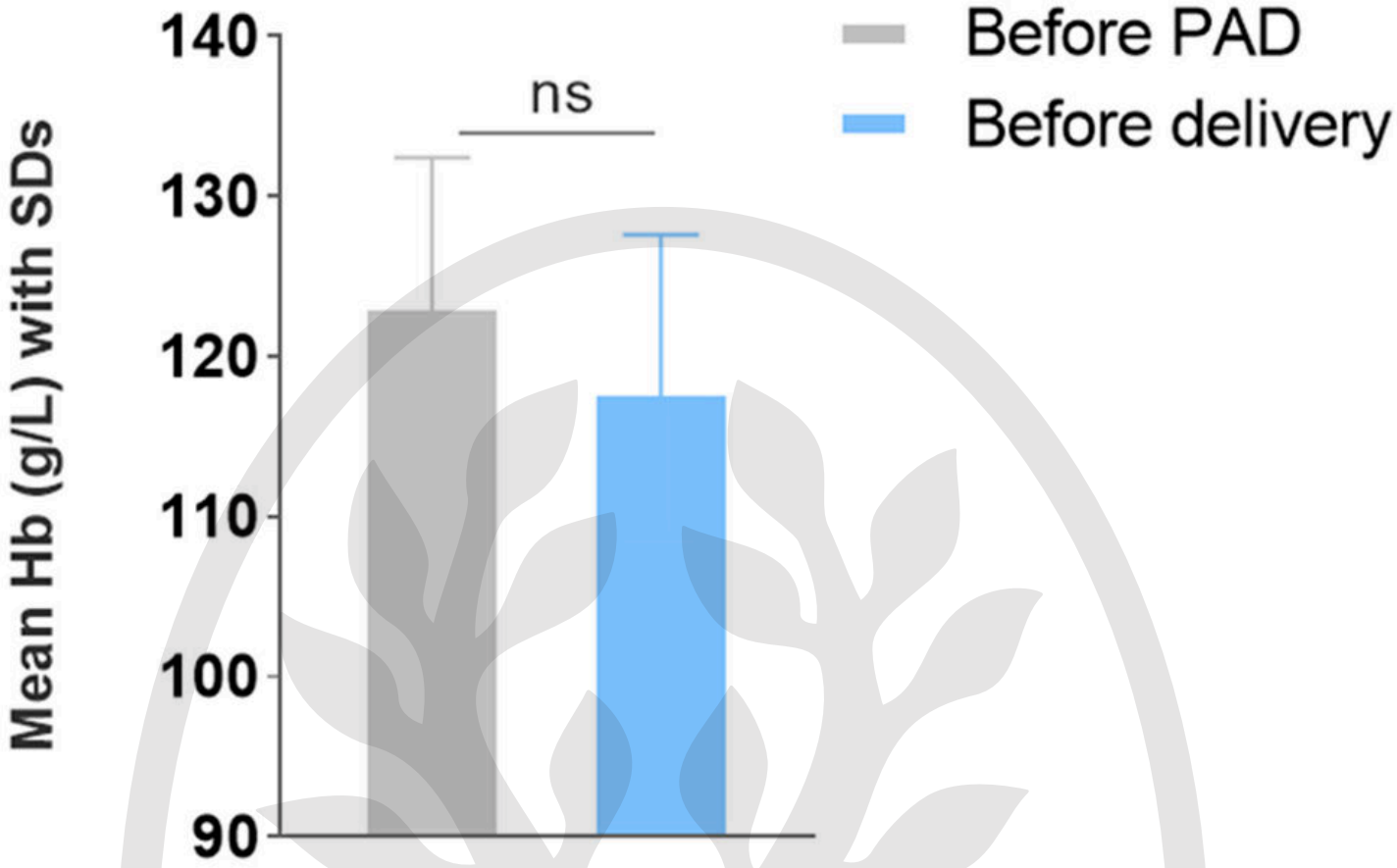

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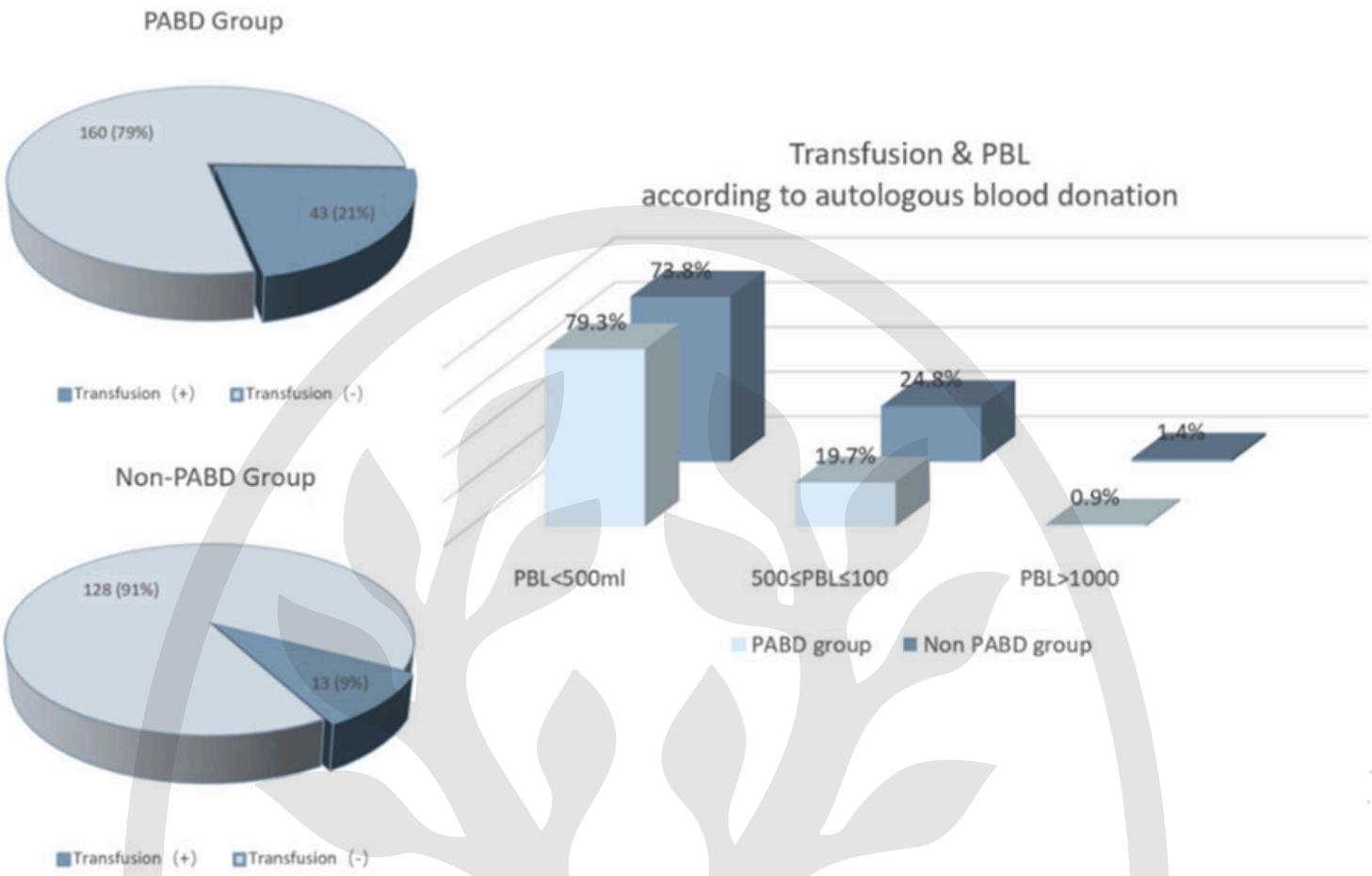

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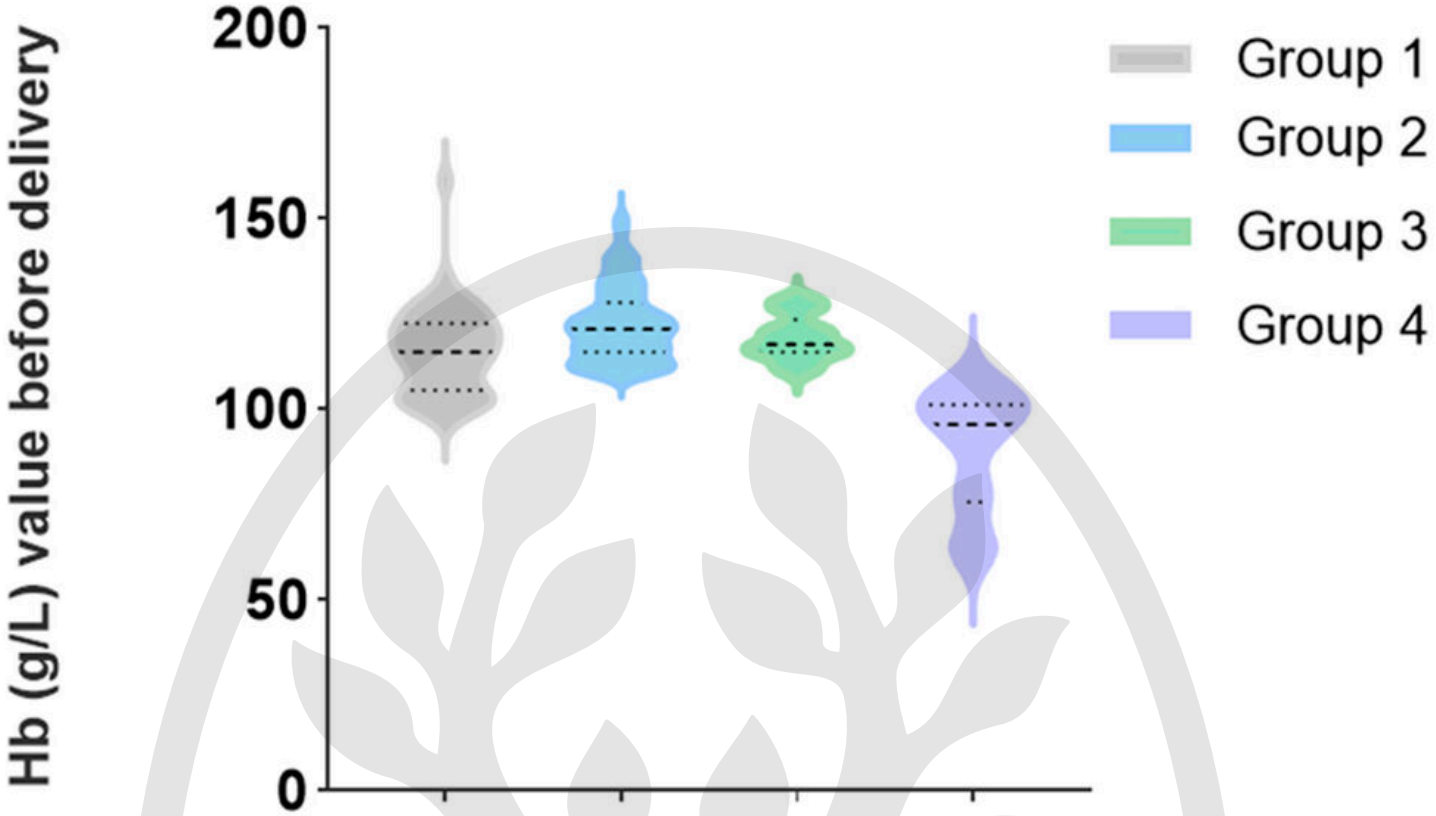

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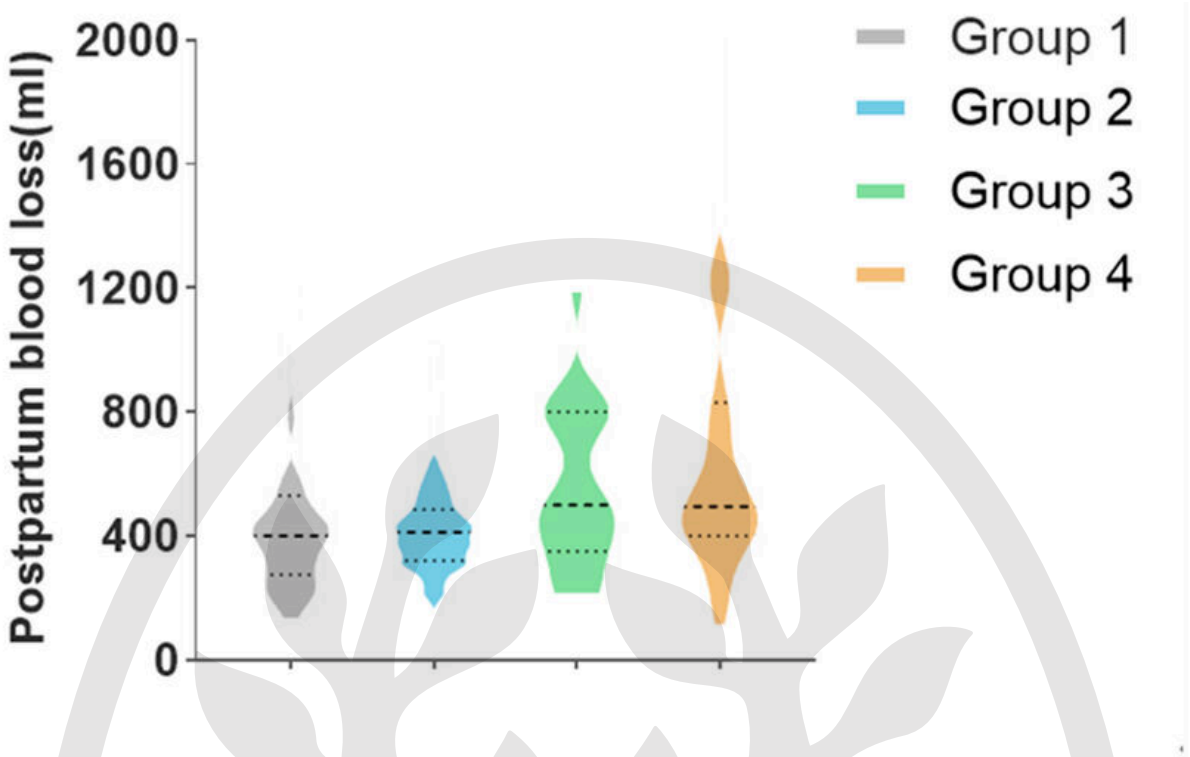

Figure 5. Distribution of postpartum blood loss among four groups.