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Can requirement for blood transfusion be predicted before delivery? Analysis of risk factors for blood transfusion in patients with postpartum hemorrhage

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Background: The most frequent cause of maternal deaths in developing countries is severe postpartum hemorrhage. We aimed to determine the risk factors affecting blood and/or blood product transfusion in patients with postpartum hemorrhage who were admitted to intensive care unit and to reveal clinical outcomes. *Methods*: After local ethics committee approval, this retrospective study included patients monitored due to postpartum hemorrhage in the 2nd stage intensive care between 1 January 2019–1 January 2020. Patients were divided into two groups as those requiring transfusion (n = 156) and those not requiring transfusion (n = 162). Patients data such as age, blood group, pregnancy week, gravida, parity, previous cesarean history, maternal comorbidity were recorded. The form of delivery, trial of labor, cesarean type, indications, anesthesia type, multiple pregnancy, placental anomalies and predelivery hemoglobin were noteded. The amount of blood products used were identified. *Results*: High parity (P = 0.002), normal vaginal delivery rate ($P < 0.001$), primary cesarian delivery ($P < 0.001$), pre-delivery maternal comorbidity rate ($P < 0.001$) and low prepartum blood hemoglobin levels ($P < 0.001$) were statistically significant factors for transfusion. The rates of those with trial of labor, instrumental delivery, intrauterine fetal death, emergency cesarean and general anesthesia were high in blood transfusion group (P values 0.018, 0.024, 0.015, 0.001 and <0.001 respectively). In multivariate logistic regression analysis, positive correlations were identified between parity (aOR: 0.258), gravida (aOR: 1.452) and general anesthesia (aOR: 3.113) with postpartum blood transfusion. Antenatal hemoglobin level (aOR: 0.506) had negative correlation with blood transfusion. *Conclusions*: Among patients with postpartum hemorrhage, we were able to identify risk factors which predispose peripartum blood transfusion and developed a prediction model with good discrimination.

Keywords

Postpartum hemorrhage; Blood transfusion; Intensive care unit

1. Introduction

The most frequent cause of maternal deaths in developing countries is severe postpartum hemorrhage (PPH) which may cause blood transfusion requirements in 1.6% of obstetric cases [1, 2]. PPH, which may develop after normal vaginal delivery (ND) or cesarean delivery (CD), is reported to have incidence of 5–12% for all deliveries [3]. The most common cause of PPH is uterine atony, with other causes being uterus rupture, coagulopathies, genital injuries, placenta retention and placental anomalies [4–6]. Transfusion requirements may increase as a result of severe blood loss with the effect of placental abruption especially [7]. If PPH is not diagnosed early and necessary precautions are not taken, complications such as hemorrhagic shock, organ failures, disseminated intravascular coagulation and acute respiratory distress syndrome due to severe hemorrhage and blood product transfusions may increase maternal morbidity and mortality.

PPH treatment involves pharmacological methods such as intravenous fluid replacement, uterotonic agents, tranexamic acid and fibrinogen extracts, in addition possible emergency surgical interventions like uterine balloon tamponade, arterial ligation, b-lynch stitch, selective uterin artery embolization and hysterectomy to control bleeding [5, 6, 8–11]. At the same time, blood and blood product replacement comprise an essential part of PPH treatment in every stage. Factors that mostly increase the blood transfusion requirement in PPH are maternal anemia, preeclampsia/HELLP, coagulopathy and placental anomalies [12]. Determining these risk factors may assist in predicting and preventing transfusions, thus may help decreasing maternal morbidity and mortality due to PPH.

Due to inadequacies in the definition and prediction of postpartum hemorrhage, the most objective parameter to assess seems to be the requirement of blood transfusion. In this study, we aimed to determine the risk factors affecting blood and/or blood product transfusion in patients with PPH who were admitted to intensive care unit and to reveal clinical outcomes.

2. Materials and methods

This retrospective and cohort designed study included patients monitored due to PPH in the 2nd stage intensive care in our hospital between 1 January 2019–1 January 2020. After receiving local ethics committee approval, patients were enrolled from the hospital database. The inclusion criteria were women aged 16–55 years, ≥20 weeks of gestation, sin-

gleton or multiple pregnancies, cesarean or normal delivery, and who were followed up and treated in the intensive care unit for PPH (n = 347).

The files and observation forms for 347 patients were retrospectively investigated. Due to missing data in files and the hospital system, 29 patients were excluded from the study. 318 patients were analyzed. Patients with transfusion of red blood cell suspension (RBC), fresh frozen plasma (FFP) and platelet apheresis after delivery were identified. Patients were divided into two groups as those requiring blood or/and blood products transfusion (n = 156) and those not requiring transfusion (n = 162).

Indications for blood transfusion in our intensive care were; measured Hb value <8 g/dL, symptomatic anemia independent of Hb value or intrapartum or postpartum acute blood loss according to our clinic criteria. In accordance with literature definitions, in our clinic PPH is defined as blood loss more than 500 mL after vaginal delivery or more than 1000 mL after cesarean delivery [9, 13].

We recorded patients data such as age, blood group, pregnancy week, gravida, parity, previous cesarean history, maternal comorbid diseases and presence of risk factors. The form of delivery, trial of labor, cesarean indications, anesthesia type, whether cesarean was emergency or elective and presence of multiple pregnancy were noted. The presence of major placental anomalies such as ablation placenta and placental invasion anomaly also was recorded. The amount of blood products used, use of fibrinogen extract and tranexamic acid and surgical interventions were identified. The hemoglobin, hematocrit and platelet values on admission and discharge from intensive care were noted. The sex, height, weight, 1st min and 5th min APGAR scores of neonates and presence of stillbirth were recorded. The duration of admission to intensive care of patients, complications, need for transfer to an advanced center and mortality rates were assessed.

Statistical analyses used the SPSS 22.0 for Windows program. Numerical data are expressed as mean and standard deviation, while categoric data are given as frequency and percentage. The Kolmogorov-Smirnov test was used to assess whether non-categorical data abided by normal distribution or not. Comparison of data abiding by normal distribution used the student t test. Comparison of data not abiding by normal distribution used the Mann-Whitney U test, with results given as mean $\pm$ SD. Comparison of categoric data in the groups used the chi-square test with results given as % n. With the aim of analyzing independent risk factors related to blood transfusion, a multivariate logistic regression model was created presenting the Odds ratio (OR) and 95% confidence intervals (CI). Prepartum hemoglobin values were analyzed and a cut-off value for blood transfusion was created with receiver operating characteristic (ROC) curves and the area under the curve (AUC) was determined. All comparisons accepted $P < 0.05$ as significant.

3. Results

From 01.01.2019 to 01.01.2020, a total of 22,502 deliveries occurred at our hospital. Of these, 64.75% (14,569/22,502) were ND and 35.25% (7933/22,502) were CD. Among all cesarean delivery, primary CD rate was 3.8% (303/7933) and repeat CD rate was 96.2% (7630/7933). Among all deliveries, PPH rate was 1.54% (347/22,502). The PPH rate was 0.39% for those who with ND (57/14569) and 3.6% for those who with CD (290/7933), whereas PPH rate was 2.6% (8/303) in primary CD and 3.7% (282/7630) in repeat CD.

The demographic and obstetric datas of patients are shown in Table 1. Among patients taken to intensive care, 60.7% (193) had uterus atony-ablatio placenta, 16.4% (52) had placenta anomaly-retained placenta, 13.5% (43) had genital injury, 8.2% (26) had preeclampsia/HELLP and 1.3% (4) had thrombocytopenia indications.

Eight patients had uterine balloon tamponade, three patients had hysterectomy and one patient had hypogastric arterial ligation. Four patients (1.25%) had hemorrhagic shock, transfusion-related acute lung injury, disseminated intravascular coagulation, acut renal failure and pleural effusion and required 3rd stage intensive care monitoring so they were transferred to an advanced center. Mortality was not seen in any patient.

Among patients with blood and/or blood transfusion performed, the RBC unit was 2.12 $\pm$ 1.15. Mean 1.13 $\pm$ 1.34 units of FFP and 0.14 $\pm$ 0.63 units platelet apheresis replacement was administered. It was identified that 14 patients were given tranexamic acid and 8 patients were given fibrinogen concentrate.

When factors that may affect transfusion are investigated, high parity ($P = 0.002$) and normal vaginal delivery rate ($P < 0.001$) were identified to be statistically significant factors. Among those with blood transfusion, primary CD ($P < 0.001$) and pre-delivery maternal comorbidity rate ($P < 0.001$) were statistically significantly higher. There were no statistically significant differences identified in the groups for maternal age, gravida, pregnancy week, nulliparity, gestational hypertensive disease presence, presence of gestational diabetes mellitus, multiple pregnancy, blood group and Rh factor. When assessments by gynecologists are investigated, there were no differences between the groups for placental anomalies and ablatio placenta rates ($P > 0.05$).

Of patients, 267 had CD and 51 had ND. The ND rate was identified to be statistically higher among those with blood and/or blood product transfusion administered ($P < 0.001$).

The duration of intensive care admission was higher by a statistically significant degree for those with blood and/or blood product transfusion performed ($P < 0.001$).

Among patients, 21.3% (68) had comorbidities. The most common comorbidity was prepartum anemia at 15.7% (50). The comorbidity rate for those requiring transfusion was identified to be high by a statistically significant level ($P = 0.001$).

Table 1. Demographic and obstetric datas of the patients.

Characteristics	Blood transfusion (n = 156)	No blood transfusion (n = 162)	*P* value
Maternal age (years)	30.06 ± 7.23	30.75 ± 6.25	0.400
Gravidity	2.93 ± 1.80	2.60 ± 1.49	0.214
Parity	2.4 ± 2.0	2.0 ± 1.5	0.002*
0	50 (32.1)	43 (26.5)	
1	2 (1.3)	14 (8.6)	
2	27 (17.3)	43 (26.5)	
≥3	77 (49.4)	62 (38.3)*	
Gestational week	35.23 ± 4.88	35.89 ± 3.73	0.177
Preterm delivery (<37 weeks) (%)	59 (37.8)	55 (34.0)	0.472
Nulliparous (%)	49 (31.4)	44 (27.1)	0.406
Mode of delivery (%)			
Spontaneous vaginal	40 (25.6)	11 (6.8)	<0.001*
In-labor cesarean	61 (52.6)	49 (32.5)	<0.001*
Elective cesarean	55 (47.4)	102 (67.5)	
Number of previous cesarean deliveries			0.001*
0	42 (26.9)	12 (7.4)*	
1	54 (34.6)	67 (41.4)	
2	29 (18.6)	46 (28.4)	
≥3	31 (19.9)	37 (22.8)	
Previous cesarean (No)	42 (26.9)	12 (7.4)	0.001*
Comorbidity (%)	45 (28.8)	23 (14.2)	0.001*
Gestational hypertensive disorders (%)	14 (9.0)	12 (7.4)	0.610
Gestational diabetes mellitus (%)	3 (1.9)	5 (3.1)	0.508
Multifetal gestation (%)	2 (0.6)	8 (4.9)	0.062
Days in intensive care unit	1.88 ± 0.75	1.52 ± 0.59	<0.001*

All continuous variables are expressed as medians [interquartile range] (mean), *Statisticaly significant.

The peripartum features of patients are shown in Table 2. It was identified that those requiring transfusion had low prepartum blood hemoglobin levels ($P < 0.001$). The rates of those with trial of labor, instrumental delivery and intrauterine fetal death were identified to be high by a statistically significant degree among those with blood transfusion (*P* values 0.018, 0.024 and 0.015, respectively).

Additional analysis was performed to assess patients with CD. For patients with CD, emergency cesarean and general anesthesia were statistically significant factors for blood transfusions ($P = 0.001$ and $P < 0.001$). Patients with cesarean performed due to repeated cesareans, ablatio placenta, placenta previa, intrauterine fetal death and hypertensive diseases in pregnancy were identified to have statistically similar results. There was no difference between the groups for premature birth rate and cesarean indications.

The weight, height and sex of neonates were similar between the groups. The 1st and 5th minute APGAR scores for neonates in the group with blood transfusion were statistically lower ($P = 0.011$ and 0.015).

Multivariate logistic regression analysis was performed to assess factors related to postpartum transfusion (Table 3). Positive correlations were identified between parity (aOR [95% CI]: 0.258 (0.119–0.562)), gravida (aOR [95% CI]: 1.452 (1.150–1.833)) and general anesthesia (aOR [95% CI]: 3.113 (1.593–6.086)) with postpartum blood transfusion. Antenatal hemoglobin level (aOR [95% CI]: 0.506 (0.422–0.607)) had negative correlation with blood transfusion. The area under the ROC curve was 0.813 and this shows acceptable differentiation ability. If the cut-off value of 9.45 g/dL is taken for antenatal hemoglobin level, sensitivity was 0.603, specificity was 90.1 (1-0.099) and successful prediction rate was 81.3% (AUC) ($P < 0.001$).

4. Discussion

In this study, blood transfusion requirements were greater for cases with high parity, vaginal delivery, instrumental delivery, emergency cesarean, general anesthesia, maternal comorbidity, intrauterine fetal death, low prepartum hemoglobin level and prepartum anemia. Cases with fewer previous cesareans had greater transfusion requirements. Additionally, in multivariate logistic regression analysis gravida, parity, general anesthesia and low prepartum maternal hemoglobin levels were identified as risk factors for requiring blood transfusion.

While uterine atony is the most frequent cause of PPH, other causes include placenta retention, placental anomalies, genital injury and coagulopathy [14, 15]. A comprehensive study by Kramer *et al.* [16] reported 75% of PPH were due to uterine atony, while Evensen *et al.* [5] stated 70% of PPH was due to atony, 20% to genital trauma, 10% to the placenta and 1% to coagulopathy. In our study, 60.7% of pa-

Table 2. Peripartum data of the patients.

Characteristics	Blood transfusion (n = 156)	No blood transfusion (n = 162)	*P* value
Predelivery hemoglobin (g/dL)	8.96 ± 2.28	11.51 ± 1.83	<0.001*
Trial of labor (%)	44 (37.9)	37 (24.5)	0.018*
Attempted instrumental delivery (%)	11 (7.1)	3 (1.9)	0.024*
Intrauterine ex fetus (%)	8 (5.1)	1 (0.6)	0.015*
Type of cesarean delivery			0.001*
Elective	55 (47.4)	102 (67.5)	
Nonelective	61 (52.6)	49 (32.5)	
Type of anesthesia			<0.001*
General	41 (35.3)	20 (13.2)	
Neuraxial	75 (64.7)	131 (86.8)	
Use of tranexamic acid/fibrinogen extract (%)	9 (5.8)	8 (4.9)	0.742
Use of surgical procedure (%)	8 (5.1)	4 (2.5)	0.214

All continuous variables are expressed as medians [interquartile range] (mean), *Statisticaly significant.

Table 3. Multivariate logistic regression analysis of factors associated with postpartum hemorrhage blood transfusion.

Characteristics	OR	95% CI	*P* value
Maternal age	1.173	0.582–2.365	0.656
Parity	0.258	0.119–0.562	0.001*
Gravidity	1.452	1.150–1.833	0.002*
Vaginal delivery (%)	0.638	0.112–3.631	0.613
Previous cesarean	0.240	0.050–1.157	0.075
Multifetal gestation (%)	0.843	0.111–6.430	0.843
Other maternal diseases	0.696	0.299–1.622	0.401
Trial of labor (%)	1.605	0.863–2.984	0.135
Attempted instrumental delivery (%)	0.210	0.033–1.352	0.100
Intrauterine ex fetus (%)	6.680	0.548–81.45	0.137
Gestational hypertensive disorders	3.041	0.869–10.64	0.082
Major placental abnormalities	1.075	0.495–2.335	0.855
Predelivery hemoglobine	0.506	0.422–0.607	<0.001*
Nonelective cesarian delivery	1.300	0.694–2.436	0.413
General anesthesia	3.113	1.593–6.086	0.001*

*Statisticaly significant; CI, confidence interval; OR, Odds-ratio.

tients had tonus (atony, ablation placenta), 16.4% had tissue (retained placenta, placenta anomalies), 13.5% had genital injury, 8.2% had HELLP-preeclampsia and 1.3% had coagulopathy as causes of PPH.

PPH is still an important public health problem due to elevated blood transfusion rates of 1.3–3.2% that should not be underestimated [12, 13]. This rate is reported to be higher (4.7%) for cesarean deliveries [17]. Many studies have focused on resolving this problem as an important and preventable cause of maternal morbidity and mortality. However, most previous studies have researched risk factors related to PPH and etiological causes, while there are a few studies assessing blood and/or blood product requirements, as an objective findings of hemorrhage. In this study, 49% of cases monitored in intensive care for PPH were identified to be administered blood and/or blood product replacement. As the study only included patients with intensive care requirements, our blood transfusion rate is significantly higher than rates in the literature. This rate of 0.69% (156/22502 for all deliveries) may be compared with previous studies. Chawla *et al.* [12] identified that patients requiring blood products used 2.46 units RBC, 2.06 units FFP and 0.46 units platelet apheresis for replacement in a study assessing obstetric patients. In our study, patients with transfusions used mean 2.12 RBC, 1.13 units FFP and 0.14 units platelet apheresis. The low mean values for blood transfusions compared to previous studies is considered to be due to our study being a supplementary hospital serving pregnant cases specifically with more frequent prepartum pregnancy monitoring, routine tests to identify prepartum anemia and routine treatment of anemia, routine examination of prepartum risk factors and routine use of oxytocin by all patients in the postpartum period.

Many studies reported that instrumental delivery like cesarean increase PPH risk [14, 18, 19]. Balki *et al.* [20] identified that there were higher rates of blood transfusion requirements for those with emergency cesarean compared to elective CD and ND in 104 patients monitored in the intensive care unit. Rottenstreich *et al.* [17] stated that emergency cesarean increased blood transfusion requirements in a study of cesarean patients. It was identified that cesarean patients being administered general anesthesia led to more transfusion requirements compared to regional anesthesia as inhaled anesthetics reduce uterus contractility and platelet functions [13, 14, 17]. Compatible with previous studies, in our study patients with general anesthesia and emergency cesarean were identified to have more transfusion requirements.

It is a known reality that blood transfusion requirements increase with the increase in cesarean rates [21, 22]. Though many studies observed that there is a positive correlation between cesarean and blood transfusion requirements, in our patients more blood transfusions were administered to women with normal deliveries, contrary to previous studies. Although it may be considered that inadequacies in monitoring hemorrhage may be experienced as patients attending our

hospital from rural areas have high anemia rates and there is a high daily ND rate in our hospital, we believe there is a need to research this topic in larger studies.

One of the important factors affecting blood transfusion is the presence of prepartum maternal comorbidity and blood hemoglobin level linked to the most common comorbidity of anemia [8, 17, 20]. Rottenstreich *et al.* [17] reported that presence of prepartum anemia (hemoglobin level <11.0 g/dL) was very important in terms of blood transfusion and that women with hemorrhage risk should have hemoglobin levels regulated with pharmacological methods in the preoperative period. In this study, we identified the presence of maternal comorbidity was a risk factor increasing blood transfusion requirements and the most commonly seen comorbidity was anemia. The prepartum maternal blood hemoglobin levels of patients with blood transfusion administered were lower. However, there was no difference in platelet levels. Our ROC analysis found the prepartum maternal hemoglobin cut-off value was 9.45 g/dL and patients with hemoglobin values below this value were identified to have more blood replacement administered. This value predicted 81.3% of patients. Based on this value, prepartum hemoglobin values should be identified and necessary precautions may be taken against postpartum blood transfusion risk for patients with PPH risk factors. Elevating patients' prepartum hemoglobin levels with pharmacological agents may reduce blood transfusion requirements.

High maternal age (>35 years), parity, multiple pregnancy, trial of labor, previous cesarean history, vascular diseases, previous surgery, PPH history and hypertensive diseases in pregnancy are among common risk factors increasing transfusion [1, 5, 16, 18, 19, 23, 24]. In our study, parity, comorbidity presence, maternal anemic and instrumental delivery were identified as factors increasing blood replacement requirements. However, age was not a factor affecting transfusion, contrary to previous studies. It is considered that the mean age of pregnant cases (30.4 $\pm$ 6.7) served in our hospital and the low birth age may have caused this. Contrary to the literature, more blood transfusion requirements were observed for those with primary cesarean compared to those with previous cesarean history. This situation may be explained by those with previous cesarean history giving birth with planned cesareans in a more controlled operation, while cases with first cesarean were taken for emergency cesarean after trial of labor for ND and the reality that emergency cesarean increases hemorrhage.

This study has some strengths and limitations. Meticulous data collection and standardized blood transfusion protocol are among the strengths of this study. We have records of all blood products delivered. Another important strength is that we were able to evaluate potential risk factors for the required for postpartum blood transfusion. Limitations in this study include its retrospective design and lack of information on anticoagulant medication use history, previous PPH history and previous abdominal surgery history. We had no data about maternal obesity which is one of the risk factors for hemorrhage. Therefore, the effect of maternal obesity on blood transfusion could not be evaluated. Our study included a 1-year period, but the sample size is at a level that can be adapted to the general population. In the postpartum period, there were no records of the amount of bleeding could not be determined. In future studies on this subject, evaluating the amount of bleeding may also be a guide. Transfusion-related reactions and complications could not be obtained from the records.

5. Conclusions

The strongest antepartum and intrapartum independent risk factors affecting blood and/or blood product transfusion of patients monitored in the intensive care due to PPH were parity, normal delivery, presence of maternal comorbidity, trial of labor, manipulation during delivery, intrauterine fetal death, emergency cesarean and general anesthesia. Based on these risk factors, PPH development risk analysis may be performed in the prepartum period, hemorrhage risk may be classified and pregnant cases with high transfusion risk may be predicted and clinical precautions taken to reduce transfusion. We suggest that preoperative intervetions for correctable risk factors may reduce transfusion requirements, thus in-clinical management targets may be determined to avoid preventable maternal mortality and morbidity due to PPH.

Abbreviations

CD, cesarean delivery; FFP, fresh frozen plasma; ND, normal vaginal delivery; PPH, postpartum hemorrhage; RBC, red blood cell.

Author contributions

FS initiated and designed the study, and analyzed and interpreted the patient data, and was a major contributor in writing the manuscript. MB, designed the study database and performed statistical processing and drafting of the manuscript. All authors read and approved the manuscript in its final version.

Ethics approval and consent to participate

This study was approved by the Local Ethics Committee University of Health Sciences Gazi Yaşargil Training and Research Hospital (approval date and number: 13.03.2020-448). Our institution's Review Board does not require informed consent for retrospective study. Therefore, consent was not obtained in accordance with institutional guidelines.

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Conflict of interest

The authors declare no conflict of interest.

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