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Can postpartum blood loss be predicted via uterine artery Doppler analysis?**Uterin arter doppler analizi ile doğum sonrası kan kaybı tahmin edilebilir mi?**Halis ÖZDEMİR¹Ezgi TURGUT¹Deniz KARÇAALTINCABA¹Merih BAYRAM¹ Orcid ID:0000-0002-9194-8504 Orcid ID:0000-0002-5509-7888 Orcid ID:0000-0001-5276-9303 Orcid ID:0000-0003-1299-2433¹ MD, Department of Obstetrics, Gynecology & Reproductive Sciences, Gazi University, School of Medicine, Ankara, Turkey¹ Professor Dr., Department of Obstetrics, Gynecology & Reproductive Sciences, Gazi University, School of Medicine, Ankara, Turkey**ÖZ**

Amaç: Postpartum kanama anne ölümlerinin en önemli nedenlerinden biridir. Burada erken postpartum dönemde uterin arter doppler indekslerini gözlemleyerek hemoglobin (Hb) düşüşünü tahmin etmeye çalıştık.

Gereç ve yöntemler: Çalışma prospektif bir kohort çalışması olarak tasarlanmıştır. 09/01/2018-09/01/2019 tarihleri arasında Gazi Üniversitesi Hastanesi'ne normal vajinal doğum için başvuran gebeler dahil edilmiş olup, herhangi bir risk faktörüne yer verilmemiştir.

Bulgular: Aşağıdaki parametrelere sahip toplam 85 hasta dahil edildi: ortalama doğum yaşı, 28.4 ± 4.6 yıl; doğumda ortalama gebelik yaşı, 38.83 ± 1.21 hafta. Hb, hematokrit (Htc), WBC ve PLT'deki diğer değişiklikler ve ortalama uterin arter sistol/diyastol (S/D), direnç indeksi (RI) ve PI değerleri arasında anlamlı bir korelasyon gözlenmedi. Ayrıca uterus hacmi, ortalama uterin arter S/D, PI ve RI arasında istatistiksel olarak anlamlı bir ilişki gözlenmedi. Benzer şekilde uterus hacmi, Hb, Htc, WBC ve PLT farklılıkları arasında da anlamlı bir ilişki gözlenmedi. Primigravida ve multigravida ayrımında ortalama uterin arter PI medyan değerleri gruplara göre farklılık göstermedi.

Sonuç: Uterin arterdeki olası Hb düşüşü ile direnç arasında bir ilişki gözlenmedi. Aynı zamanda etkileyebilecek diğer faktörler (uterus boyutları, gravida, parite, membran rüptürü olup olmadığı, doğum süreleri, doğum sırasındaki yırtıklar, epizyotomi ve doğum ağırlığı) değerlendirildi ve bu faktörler arasında korelasyon saptanmadı.

Anahtar kelimeler: postpartum kanama, ultrasonografi, uterin arter

ABSTRACT

Objective: Postpartum bleeding is one of the most important causes of maternal mortality. Herein, we attempted to predict hemoglobin (Hb) decrease by observing uterine artery doppler indices during the early postpartum period.

Materials and Methods: The study was designed as a prospective cohort study. Pregnant women who visited Gazi University Hospital for normal vaginal delivery between 09/01/2018–09/01/2019 were included, and no risk factors were included.

Results: A total of 85 patients were included with the following parameters: average age at birth, 28.4 ± 4.6 years; average gestational age at birth, 38.83 ± 1.21 weeks. No significant correlation was observed among Hb, hematocrit (Htc), white blood cells (WBC), and other changes in platelets (PLT) and mean uterine artery systole/diastole (S/D), resistance index (RI), and pulsatility index (PI) values. Furthermore, no statistically significant relationship was observed among uterus volume, mean uterine artery S/D, PI, and RI. Similarly, no significant relationship was observed among uterus volume, Hb, Htc, WBC, and PLT differences. Upon dividing primigravida and multigravida, the mean uterine artery PI median values did not differ according to the groups.

Conclusion: No correlation was observed between possible Hb decrease and resistance in the uterine artery. At the same time, other factors that may affect were evaluated (uterus dimensions, gravida, parity, whether there was membrane rupture, delivery times, lacerations during delivery, episiotomy, and birth weight) and no correlation was noted among these factors.

Keywords: Postpartum hemorrhage; Ultrasonography; Uterine artery

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INTRODUCTION

During the postpartum period, blood loss within certain limits is normal. However, extensive bleeding may sometimes be observed during this period. Postpartum hemorrhage is one of the most common causes of maternal mortality, and early diagnosis and treatment is usually life-saving. Maternal mortality is one of the human development indices for each country. Therefore, each country strictly conducts various programs for its prevention and effective treatment.

Although there is a wide range of incidence of postpartum hemorrhage due to the differences in diagnostic criteria, its acceptable incidence is in 1%–5% of births [1,2]. Postpartum hemorrhage occurs due to various reasons; however, the main reason for this hemorrhage to become a life-threatening condition within seconds is the high-volume flow of blood to the uterus through the uterine arteries. Approximately 500–700 ml of blood flows to the uterus per minute, which is about 15% of the cardiac output. Although there are sufficient studies on the use of uterine artery doppler during the antenatal period, there are limited studies on the doppler analysis during the early postpartum period. During the first 8-week postpartum period, uterine artery notching is 22% at week 1 and reaches 95% at week 8. The uterine artery pulsatility index (PI) is 1.2 during the first week and >2 during the 8th week [3]. However, there is no study linking this with hemorrhage. Herein, we aim to determine the amount of possible blood loss during the early postpartum period using bilateral uterine artery flow doppler parameters.

MATERIALS AND METHODS

This prospective cohort study was approved by the Gazi University Faculty of Medicine, Clinical Research Ethics Committee with ethics committee's decision no 190 (24074710-17; March 12, 2018). Informed consent form was obtained from each patient.

Patient Selection

We included patients who were admitted to the Gazi University Faculty of Medicine, Department of Obstetrics and Gynecology and underwent spontaneous vaginal delivery between September 01, 2018 and September 01, 2019. Those not matching the exclusion criteria and eligible to take part in the study were included upon granting their informed consent. Postpartum bilateral uterine artery doppler recordings were obtained using pelvic doppler sonography, while the patient was still in the

delivery room after episiotomy repair. This process was performed using GE Voluson I Ultrasound Machine (GE Healthcare, Milwaukee, Wisconsin USA), Convex 4C-RS [2–5 MHz] probe. The hemoglobin (Hb), hematocrit (Htc) and other blood counts parameters were measured before delivery (when she was hospitalized) at 4 and 24 h after delivery were measured. The delivery data and durations were recorded.

Exclusion criteria were as follows: 1. <37 weeks of gestation and >41 weeks of gestation; 2. Pregnant women aged <18 and >45 years; 3. BMI of >35; 4. Instrumental delivery (vacuum, forceps etc.); 5. Pregnant women with any disease that might have an impact on the vascular bed such as hypertension, diabetes, vasculopathy, and autoimmune diseases; 6. Pregnant women with coagulopathy and receiving anticoagulant therapy; 7. Deep, 3rd and 4th degree perineal tears; 8. Puerperium patients with heavy bleeding from vaginal tissues after delivery; 9. Patients whose placenta have not spontaneously separated and have been taken by hand or those undergoing revision curettage; and 10. Patients who have undergone regional/epidural anesthesia

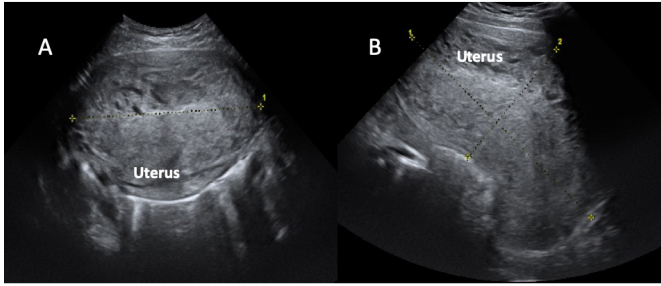
Delivery Method

Patients who were admitted to our hospital due to spontaneous labor or induction of labor were followed-up in their own rooms until the commencement of active labor and then in the delivery room to ensure intermittent fetal monitoring. Furthermore, uterine contraction was counted. When required, oxytocin augmentation was performed. If it was not spontaneous, amniotomy was performed. During the follow-up, partogram was used and the follow-ups were recorded. Upon the birth of the fetus, 2% oxytocin-RL solution (i.v.) was commenced at 250 cc/h. Upon the birth of the placenta, necessary checks were performed for bleeding and lacerations. If available, episiotomy was repaired.

Uterus and Uterine Artery Doppler Measurement

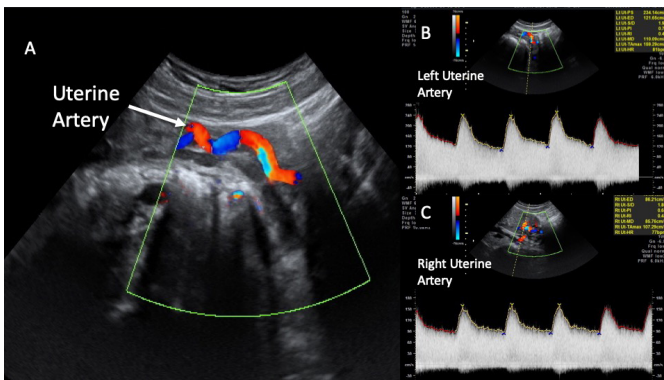
While the patient was in the delivery room and hemodynamically stable, necessary bleeding checks were performed, and if available, episiotomy and laceration repair was performed, and then when the patient was in the supine position, three-dimensional measurements of the uterus were obtained first by transabdominal sonography [Figure 1]

Figure 1. Postpartum uterine sonography: (A) measurement of transverse diameter and (B) measurement of longitudinal and anterior–posterior diameter



followed by the midsagittal view of the uterus. Then, the cervical canal was detected, the ultrasound probe was gently shifted laterally, and paracervical vascular structures and uterine arteries were detected using color doppler ultrasonography [Figure 2].

Figure 2. Uterine artery doppler: (A) Color doppler image, (B) Left uterine artery doppler measurement, and (C) Right uterine artery doppler measurement



The measurements were obtained using PW doppler. At least three consecutive waves were measured, and systole/diastole (S/D) ratio, pulsatility index (PI), and resistance index (RI) values were recorded bilaterally [Figure 2]. All patients' sonographic examinations were made by two expert physicians (HO and ET).

Postpartum Management

The hemodynamically stable patients were followed in their rooms during the postpartum period. The vital signs and bleeding were followed first every 15 min and then every 30 min. Thereafter, 2% oxytocin-RL solution was administered for 4 h. Necessary analgesia and IV hydration support were provided. In case of no bleeding during the follow-up and normal uterus tone, uterotonic infusion was discontinued. Breastfeeding and

uterine massage were encouraged. Complete blood counts were obtained from the patients at postpartum hours 4 and 24 and the results were recorded.

Statistical Analysis

The data were analyzed using IBM SPSS Statistics 17.0 (IBM Corporation, Armonk, NY, USA). The distribution of continuous numerical variables was examined using Kolmogorov–Smirnov and Shapiro–Wilk tests. Descriptive statistics: For continuous numerical variables, mean \pm standard deviation values were used for numerical data with normal distribution and median and minimum–maximum values were used for numerical data with abnormal distribution.

The significance of the difference in terms of continuous numerical variables between the groups was examined using Mann–Whitney U-test when the number of independent groups was two and using Kruskal–Wallis test when the number of independent groups was higher than two. Pearson's correlation test was used for categorical variables and chi-Square test was used for comparisons. The continuity was evaluated using corrected chi-Square or Fisher's exact tests of probability. Unless otherwise specified, p value of <0.05 was considered statistically significant. However, in all possible multiple comparisons, a Bonferroni correction was performed to control type I errors.

RESULTS

We included 85 patients with the following parameters: average age at birth, 28.4 ± 4.6 years; mean gestational age at birth, 38.83 ± 1.21 weeks; postpartum average uterus length, 150.18 ± 107.85 mm; anterior–posterior diameter, 90.88 ± 8.34 mm; transverse diameter, 102.64 ± 12.73 mm; uterine volume, $1,381 \pm 685$ cm³; right uterine artery PI, 1.09 ± 0.45 ; left uterine artery PI, 1.03 ± 0.39 ; mean uterine artery PI, 1.06 ± 0.35 ; first stage of birth, 279.66 ± 179.16 min; second stage of birth, 33.48 ± 26.78 min; third stage of birth, 5.74 ± 3.02 min; mean birth weight, $3,212.14 \pm 409.8$ g; prenatal Hb, 11.95 ± 1.22 g/dL; 11.28 ± 1.39 g/dL at postpartum 4 h; and 10.53 ± 1.62 g/dL at postpartum 24 h [Table 1].

Table 1. Demographic statistics

Parameters	Mean ± Standard Deviation	Median (Minimum–Maximum)
Age	28.44 ± 4.66	28 (19–41)
Gravida	1.86 ± 1.06	2 (1–5)
Parity	0.66 ± 0.8	0 (0–3)
Abortus	0.21 ± 0.54	0 (0–3)
Living	0.66 ± 0.8	0 (0–3)
Ectopic pregnancy	0.01 ± 0.11	0 (0–1)
Gestational age at delivery	38.83 ± 1.21	38.6 (36–42)
Uterus longitudinal axis (mm)	150.18 ± 107.85	134 (97–1113)
Uterus anterior–posterior diameter (mm)	90.88 ± 8.34	91 (75–114)
Uterus transverse diameter (mm)	102.64 ± 12.73	102 (79–135)
Uterus volume longitudinal axis X anterior–posterior diameter X transverse diameter (cm ³)	1381 ± 685	1273 (624–6682)
Right uterine artery S/D	2.9 ± 1.27	2.45 (1.43–7.47)
Right uterine artery PI	1.09 ± 0.45	0.97 (0.43–2.29)
Right uterine artery RI	0.6 ± 0.13	0.59 (0.3–0.87)
Left uterine artery S/D	2.65 ± 0.89	2.56 (1.11–5.5)
Left uterine artery PI	1.03 ± 0.39	1 (0.13–2.4)
Left uterine artery RI	0.58 ± 0.15	0.6 (0.1–0.97)
Mean uterine artery S/D	2.77 ± 0.89	2.52 (1.37–5.12)
Mean uterine artery PI	1.06 ± 0.35	1.02 (0.33–2.04)
Mean uterine artery RI	0.59 ± 0.12	0.6 (0.24–0.85)
First stage of birth (min)	279.66 ± 179.16	240 (30–1020)
Second stage of birth (min)	33.48 ± 26.78	25 (5–135)
Third stage of birth (min)	5.74 ± 3.02	5 (2–15)
Intrapartum perineal laceration	0.05 ± 0.21	0 (0–1)
Intrapartum vaginal laceration	0.02 ± 0.15	0 (0–1)
Median episiotomy	0.02 ± 0.15	0 (0–1)
Mediolateral episiotomy	0.93 ± 0.26	1 (0–1)
Birth weight	3212.14 ± 409.8	3240 (2290–4010)
Prenatal Hb	11.95 ± 1.22	12.1 (9–15)
Prenatal Htc	36.03 ± 3.15	35.7 (29–43)
Prenatal WBC	10336.35 ± 2286.99	10040 (6350–18020)
Prenatal platelet	215258.82 ± 58697.8	213000 (83000–416000)
Hb at 4 h	11.28 ± 1.39	11.4 (8–15)
Htc at 4 h	517.17 ± 4454.23	34 (25–41100)
WBC at 4 h	16223.65 ± 4116.02	15780 (7890–26010)
Platelet at 4 h	228305.88 ± 176986.08	212000 (105000–1780000)
Hb at 24 h	10.53 ± 1.62	10.8 (2–14)
Htc at 24 h	32.26 ± 3.34	32.1 (25–42)
WBC at 24 h	13720.68 ± 3433.01	13950 (9–26930)
Platelet at 24 h	206847.06 ± 50100.5	205000 (100000–370000)

S/D, systole/diastole; PI, pulsative index; RI, resistance index; Hb, hemoglobin; Htc, hematocrit

The difference between the values of mean uterine artery S/D and WBC measured prior to delivery and at 4 h positively correlated at a minor level ($r = 0.332$; $p = 0.002$). Similarly, this minor correlation was observed among the changes in WBC before delivery and at 4 h and the mean uterine artery PI and RI values. A significant negative minor correlation was observed among the changes in PLT before delivery and at 4 h and the mean uterine artery S/D and PI values, whereas a positive minor correlation was observed among the mean uterine artery RI and PI values and changes in PLT at 4 and 24 h. No significant correlation was observed among the changes in Hb, Htc, WBC, PLT, mean uterine artery S/D, RI, and PI values [Table 2].

Table 2. Mean uterine artery systole/diastole (S/D), pulsative index (PI), and resistance index (RI) values and hemoglobin (Hb), hematocrit (Htc), WBC, and PLT correlation analysis results

Parameter	Difference		Mean uterine artery S/D	Mean uterine artery PI	Mean uterine artery RI
Hb	Prenatal-4 h	r	-0.108	-0.062	-0.127
		p	0.324	0.572	0.247
	Prenatal-24 h	r	0.044	0.090	0.027
		p	0.687	0.412	0.803
		r	0.164	0.178	0.185
		p	0.135	0.103	0.090
Htc	Prenatal-4 h	r	-0.031	0.009	-0.042
		p	0.776	0.932	0.700
	Prenatal-24 h	r	0.035	0.080	0.046
		p	0.750	0.466	0.678
		r	0.102	0.112	0.137
		p	0.353	0.307	0.210
WBC	Prenatal-4 h	r	0.332	0.328	0.324
		p	0.002	0.002	0.003
	Prenatal-24 h	r	0.210	0.194	0.221
		p	0.053	0.076	0.042
		r	-0.131	-0.125	-0.105
		p	0.232	0.254	0.338
PLT	Prenatal-4 h	r	-0.231	-0.211	-0.213
		p	0.033	0.052	0.050
	Prenatal-24 h	r	-0.086	-0.071	-0.071
		p	0.434	0.518	0.519
		r	0.212	0.226	0.215
		p	0.052	0.038	0.048

r, Spearman's Rho

$p < 0.05$ was statistically significant

Furthermore, no statistically significant correlation was observed among the uterus volume, mean uterine artery S/D, RI, and PI values. Similarly, no significant correlation was observed among the uterus volume, Hb, Htc, WBC, and PLT differences [Table 3].

Table 3. Correlation between uterus volume and mean uterine artery systole/diastole (S/D), pulsative index (PI), resistance index (RI), hemoglobin (Hb), hematocrit (Htc), WBC, and PLT

	Uterus Volume	
	r	p
Mean uterine artery S/D	-0.021	0.852
Mean uterine artery PI	-0.054	0.626
Mean uterine artery RI	-0.028	0.800
Hb prenatal-4 h	-0.092	0.402
Hb prenatal-24 h	-0.148	0.178
Hb 4–24 h	-0.097	0.376
Htc prenatal-4 h	-0.110	0.318
Htc prenatal-24 h	-0.129	0.238
Htc hour 4–24 h	-0.009	0.938
WBC prenatal-4 h	0.083	0.449
WBC prenatal-24 h	0.020	0.852
WBC 4–24 h	-0.092	0.403
PLT prenatal-4 h	-0.131	0.231
PLT prenatal-24 h	-0.179	0.100
PLT 4–24 h	0.012	0.910

r, Spearman's Rho

$p < 0.05$ was statistically significant

Figure 1. Postpartum uterine sonography: (A) measurement of transverse diameter and (B) measurement of longitudinal and anterior–posterior diameter

When the patients were classified into groups as primigravida and multigravida, the mean UtA S/D, PI, and RI median values did not differ between the groups ($p = 0.60$, $p = 0.61$, $p = 0.63$, respectively). The median WBC values before delivery and at 4 h did not differ between the groups; this difference was higher in primigravida patients (7,280/mm³ vs 4,940/mm³; $p = 0.02$). No statistically significant difference was observed between the primigravida and multigravida patients in terms of other parameters. When the patients were classified into groups as primipara and multipara, no statistically significant difference was observed between the groups.

When the patients were classified into groups based on the method of commencing labor, no statistically significant difference was observed between the groups. Moreover, when the patients were classified into groups based on whether they had premature membrane rupture (PMR), a difference was observed between the median WBC values at 0 and 24 h in the presence or non-presence of PMR ($p = 0.003$). The initial WBC value was higher in the group with PMR (1560/mm³ vs 3355/mm³). No statistically significant difference was observed in terms of other parameters.

When we examined the patients in terms of the duration of delivery, no significant correlation was observed between the duration of delivery and other parameters. When we examined the patients in terms of lacerations at delivery, a negative minor correlation was observed between the Hb values at 4 and 24 h and vaginal lacerations at delivery ($p = 0.031$). No significant correlation was observed between the intrapartum lacerations and other parameters. When we examined the patients in terms of the types of episiotomy, no significant correlation was observed between the parameters with median episiotomy and mediolateral episiotomy. Moreover, when we examined the patients in terms of birth weight, no significant correlation was observed between the birth weight and other parameters.

Discussion

The most common reason for heavy bleeding in postpartum hemorrhage is nearly 15% of the cardiac output is distributed to the uterine arteries. Even the slightest increase in resistance on this artery will reduce the amount of bleeding. The present study aimed to determine if there is a correlation between postpartum blood loss and doppler analysis. Therefore, the patients' postpartum and prenatal Hb and Htc values were compared. No correlation was observed between the possible Hb decrease and resistance in the uterine artery. Other factors that

might have an impact were also evaluated (uterine dimensions, gravida, parity, form of labor commencement, presence or non-presence of premature membrane rupture, duration of delivery, intrapartum lacerations, episiotomy, and birth weight) and no correlation was noted among these factors.

The mechanisms involved in the obliteration of the spiral artery lumen are thrombosis, endarteritis, and increased local vascular resistance due to intima-media thickness. Although these findings reflect the changes in systemic circulation, the most common reason for this mechanical pressure is the mechanical pressure imposed by the contracted postpartum myometrium, which develops due to local immunological reasons [3, 4].

To the best of our knowledge, there is no other study on this hypothesis. However, there are studies including postpartum uterine artery doppler analysis and examining the changes in the parameters at postpartum weeks 4 and 6. The study by Guedes-Martins et al. investigated the uterine arterial changes during the postpartum first 8-week period using transvaginal doppler ultrasonography. In this study, they determined the mean uterine artery PI value at week 1 to be 1.22 (50th percentile value) [3]. In the present study, this value during the first postpartum minutes was 1.06. In the subgroup analysis for primipara and multipara by Guedes-Martins et al., the mean PI values (50th percentile) for primipara and multipara patients were 1.29 and 1.12, respectively [3]. In the present study, the mean PI values for women who had never given birth (nullipara), those who had given birth once (primipara), and those who had multiple births (multipara) were 0.99, 1.02 and 1.16, respectively. However, no statistical significance was observed ($p=0.510$) [3]. The study by Diniz et al. evaluated uterine blood flows using two ultrasonography examinations (the first at 48 h and the second between days 31 and 50) [5]. In this study, the ultrasonography evaluation within the first 48 h showed that the mean bilateral uterine artery PI value was 1.29. In the same study, this value for primipara and multipara patients was 1.25 and 1.33, respectively [5].

In their conference report in 2019, Kajdy et al. compared the antenatal and postpartum uterine doppler values. In this retrospective cohort study, no correlation was observed between postpartum blood loss and uterine doppler flows [6].

Leukocytosis condition increases stably during pregnancy and postpartum period. The WBC values may reach 15–20 × 10⁹/L, whereas it was 5–12 × 10⁹/L during the pre-pregnancy period. The mean WBC values at delivery may be as high as 14–16 × 10⁹/L. There may be many causes for

increased leukocyte count in the blood, and its etiology and mechanism is unclear. Leukocytosis is actually a physiological response during delivery and afterwards [7]. Leukocytosis may also be observed in case of stress and dehydration. In the present study, a minor correlation was observed between uterine doppler indices and WBC differences ($p = 0.002$). Especially, intrapartum loss of blood and fluid causes hypovolemia, which may have resulted in changes in the doppler parameters in the vascular system. Accordingly, the reason for the correlation we found in the present study is the increase in uterine artery resistance secondary to hypovolemia and blood loss.

Our study has strengths and weaknesses. Primarily, our study was a prospective and single-centered with a standard follow-up protocol, which is a strength, but the limited number of patients and the lack of a cohort involving postpartum hemorrhage were the weaknesses.

CONCLUSION

No correlation was observed between postpartum uterine artery doppler indices and postpartum early blood loss. However, a minor correlation was observed between leukocytosis and uterine artery doppler parameters. In the present study, decreased Hb levels were within normal acceptable limits. However, this correlation may be more prominent in cases of higher Hb differences or postpartum hemorrhage conditions such as possible uterine atony. There is a need for further studies to determine this correlation.

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