

Research Paper

Risk Factors of Neonatal Anemia in Placenta Previa

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Abstract

Objectives: Placenta previa is a major cause of neonatal anemia. The purpose of this study was to elucidate the risk factors of neonatal anemia in placenta previa.

Methods: The study was conducted on 158 placenta previa patients at 3 hospitals in affiliation with the Catholic Medical Center, Seoul, Korea from May 1999 through December 2009. The subjects were divided into 2 groups: 47 placenta previa patients with neonatal anemia, and 113 placenta previa patients without neonatal anemia. The subjects' characteristics were compared. Logistic regression was used to control for confounding factors.

Results: Anterior placental location (OR 2.48; 95% CI: 1.20–5.11) was an independent risk factor of neonatal anemia after controlling for potential confounders.

Conclusion: To manage neonatal anemia in placenta previa patients, obstetricians should do their best to detect placental location. Pediatricians should consider the high possibility of neonatal anemia in cases involving anterior placental location.

Key words: neonatal anemia, preterm, placenta previa

Introduction

The overall incidence rate of placenta previa is approximately 4 out of 1000 births [1]. Moreover, it is reported that 10% of all infants born following placenta previa present with severe anemia. In addition, placenta previa is the most common placental anomaly causing neonatal anemia [2]. Together with preterm birth, neonatal anemia is a major factor of the 4–8% risk of perinatal mortality in placenta previa patients [2]. However, to our knowledge, there has been no study about the risk factors for neonatal anemia in placenta previa patients. In this study, we evaluated the risk factors of neonatal anemia in placenta previa by comparing a neonatal anemia group with a control group.

Patients and methods

Subjects

We conducted a retrospective case-control study on singleton births after 26 gestational weeks com-

plicated with placenta previa in 3 hospitals affiliated with the Catholic University of Korea (Seoul: St. Mary's Hospital, St. Vincent's Hospital, and Yeouido: St. Mary's Hospital) from May 1, 1999 to December 31, 2009. Cases were excluded if they met any of the following criteria: cases in which neonates were not checked for hemoglobin levels within 24 hours after birth, multiple births, successful vaginal deliveries among low-lying placentas, and other placental anomalies such as accessory placenta and circumvalated placenta. Other information, including maternal and neonatal outcomes, was collected from medical records. This study was approved by the Clinical Study Medical Ethics Committee (XC10RIMI0126V).

Methods

We divided subjects into 2 groups according to the presence of neonatal anemia: an anemia group and a control group. The following variables of the

pregnancies were studied: maternal age, previous cesarean sections, admission due to vaginal bleeding after 20 weeks of gestation, placental location by ultrasonography and operation findings, placenta accreta, maternal hemoglobin level prior to and 1 day after surgery, and estimated blood loss during surgery. Excessive blood loss was defined as blood loss >1000 mL. Cesarean sections were classified as elective or emergency. The following variables of the neonates were studied: gestational age at birth, birth weight, Apgar scores at 1 and 5 min, and neonatal hemoglobin level. Neonatal anemia was defined as hemoglobin <14.5 g/dL as examined by venous sampling within the first 24 hours after birth [3]. Placenta previa was classified as total, partial, marginal, low-lying, or vasa previa [4]; furthermore, it was classified as anterior placenta (defined as placenta located at the uterine incision site) or not [5]. The placenta was classified and located according to the results of the last transabdominal and transvaginal sonographic exams prior to delivery and confirmed at surgery.

Statistical analysis

All data were analyzed using SAS version 8 (SAS Institute, Berkley, CA, USA). Continuous variables were compared using independent *t*-tests or the Mann-Whitney *U*-test. Categorical variables were compared using the χ^2 or Fisher's exact test. Multivariate logistic regression analysis was used to identify the independent risk factors of neonatal anemia. The level of statistical significance was set at $p < 0.05$.

Results

The records from the 11-year study period revealed that there had been 35,030 deliveries—560 (1.6%) of which were complicated with placenta previa. After excluding 353 cases in which neonatal hemoglobin levels were not checked within 24 hours after birth, there were 5 cases of births before 26 gestational weeks, 30 vaginal births, 10 multiple births, and 4 births with other placental anomalies; 45 cases were classified into the neonatal anemia group, and 113 cases into the control group. The maternal characteristics of the anemia and control groups are listed in Table 1. Neonatal anemia was significantly associated with emergency cesarean section (OR 2.53; 95% CI: 1.08–5.97) and anterior placental location (OR 2.53; 95% CI: 1.24–5.16). However, maternal age, previous cesarean section, admission for vaginal bleeding, placenta accreta, and complete previa were not significantly different between the 2 groups.

The results of the univariate analysis regarding maternal and neonatal outcomes are presented in Table 2. The gestational age of the anemia group was slightly lower than that of the control group (34.23 ± 3.00 vs. 35.28 ± 2.99 weeks, respectively). In addition, the incidence of preterm birth before week 37 was significantly greater in the anemia group (OR 2.44; 95% CI: 1.04–5.74). However, there were no significant differences between groups with respect to maternal pre- or post-operative hemoglobin levels, neonatal birth weight, or Apgar score <4 at 1 or 5 min. The estimated blood loss during operation was significantly greater in the anemia group than in the control group; however, there was no significant difference in excessive blood loss between groups.

Table 1. Maternal characteristics of placenta previa according to the presence of neonatal anemia

	Anemia (45)	Control (113)	OR (95% CI)	P-value	
Age (years)	32.38 (4.66)	32.82 (3.76)		0.570	
Previous C/S	0	29 (64.4%)	74 (65.5%)	1	0.411
	1	9 (20.0%)	29 (25.7%)	0.79 (0.33–1.88)	
	≥2	7 (15.6%)	10 (8.8%)	1.79 (0.62–5.14)	
Admission owing to vaginal bleeding	34 (75.6%)	81 (71.7%)	1.22 (0.55–2.70)	0.621	
Placenta accreta	7 (15.6%)	15 (13.5%)	1.18 (0.45–3.12)	0.740	
Emergency C/S	37 (82.2%)	73 (64.6%)	2.53 (1.08–5.97)	0.030	
Previa	Complete	20 (44.4%)	57 (50.4%)	1	0.346
	Partial	4 (8.9%)	15 (13.3%)	0.76 (0.23–2.56)	
	Marginal	4 (8.9%)	13 (11.5%)	0.88 (0.26–3.00)	
	Low-lying	16 (35.6%)	28 (24.8%)	1.63 (0.73–3.62)	
	Vasa previa	1 (2.2%)	0 (0%)	1.05 (0.95–1.16)	
Placenta	Anterior position	23 (51.1%)	33 (29.2%)	2.53 (1.24–5.16)	0.009

Values are expressed as mean (SD) or number (%).

C/S: Cesarean section.

Table 2. Univariate analysis of maternal and neonatal pregnancy outcomes according to the presence of neonatal anemia in placenta previa

	Anemia (45)	Control (113)	OR (95% CI)	P-value
Preop Hb (g/dL)	10.50 (1.56)	10.88 (1.48)		0.169
POD #1 Hb (g/dL)	10.20 (1.87)	10.11 (1.58)		0.759
Estimated blood loss (mL)	1135.56	801.77		0.029
Excessive blood loss (mL)	14 (31.1%)	24 (21.2%)	1.68 (0.77-3.64)	0.190
Neonatal Hb (g/dL)	12.98 (1.18)	16.39 (1.35)		<0.001
Gestational age (weeks)	34.23 (3.00)	35.28 (2.99)		0.044
Preterm birth	37 (82.2%)	74 (65.5%)	2.44 (1.04-5.74)	0.038
Birth weight (kg)	2.29 (0.67)	2.49 (0.64)		0.076
Apgar score <4 at 1 min	11 (24.4%)	14 (12.4%)	2.29 (0.95-5.52)	0.061
Apgar score <4 at 5 min	3 (6.7%)	2 (1.8%)	3.96 (0.64-24.57)	0.113

Values are expressed as mean (SD) or number (%).

Preop: preoperational.

POD #1: 1 day after operation.

Hb: hemoglobin.

After the multivariate logistic regression analysis was adjusted for estimated blood loss, preterm birth (≤ 37 weeks), emergency cesarean section, and anterior placental location, we found that anterior placental location (OR 2.39; 95% CI: 1.15-4.96) was more common in the anemia group, suggesting that it is an independent risk factor of neonatal anemia (Table 3).

Table 3. Risk factors for developing neonatal anemia in placenta previa (multivariate analysis)

	OR	95% CI	Significance
Preterm birth*	1.56	0.46-5.26	0.475
Anterior position of placenta**	2.39	1.15-4.96	0.020
Emergency C/S***	1.76	0.52-5.91	0.363

C/S: Cesarean section.

* Adjusted for estimated blood loss, anterior position of placenta, and emergency cesarean section.

** Adjusted for estimated blood loss, preterm birth, and emergency cesarean section.

*** Adjusted for estimated blood loss, preterm birth, and anterior position of placenta.

Discussion

It is very difficult to define neonatal anemia because the timing and site of sampling, as well as gestational age, can influence blood measurements in neonatal blood [6].

In preterm infants, hemoglobin values increase up until 26 gestational weeks and subsequently plateau until term [2]. After birth, the increase in blood oxygen content and tissue oxygen delivery downreg-

ulate erythropoietin production, suppressing erythropoiesis [7]. Among full-term infants, hemoglobin values fall from 14.6-22.5 g/dL at birth to 10.0-12.0 g/dL by 8-10 weeks of age; this is known as physiologic anemia [3].

The expected decline is more severe among preterm infants than in full-term infants [3]. This is mainly due to suboptimal erythropoietin response; shorter red blood cell lifespan; dull response of the fetal liver, which produces the most erythropoietin due to hypoxia; a lack of folate and vitamins B₁₂ and E; and frequent blood sampling [7].

In this study, preterm babies before 26 gestational weeks were excluded because there were only 5 of them. Moreover, neonatal anemia was defined as venous hemoglobin concentration <14.5 g/dL within 24 hours after birth to exclude types of physiologic anemia and anemia due to phlebotomy loss [3] in order to identify risk factors influencing neonatal anemia only before and during birth.

As a result, preterm birth was not independently associated with neonatal anemia in this study.

The high incidence of emergency cesarean section is possibly related to the high incidence of preterm birth in the anemia group; however, poor neonatal outcomes such as low birth weight and low Apgar score [8,9] were not significant different between groups. This is may be due to the fact that the 353 healthy infants in whom hemoglobin levels were not examined were excluded from this study; therefore, the gestational weeks of the control group were lowered such that the effects of preterm birth were not distinctive.

This is the first study indicating that anterior placental location is an independent risk factor of neonatal anemia in placenta previa patients.

However, there are only a few reports regarding anterior placental location in placenta previa.

Molteni et al. [10] and Hasegawa et al. [5] reported that anterior placental location is associated with profound hemorrhage. However, its precise relationship with neonatal anemia, especially in placenta previa, has not been reported.

McShane [11] reports a correlation between neonatal anemia and the amount of intrapartum maternal blood loss. In this study, the risk factors of massive hemorrhage in placenta previa such as abortion, previous cesarean section, complete previa, and placenta accreta [12-15] were not significantly higher in the anemia group; the only factor that correlated with hemorrhage was anterior placental location. Consequently, massive hemorrhage (>1000 mL) was not significantly different between groups, although there was more estimated blood loss in the anemia group. When the placenta is in an anterior position, intrapartum hemorrhage can occur before birth through direct placental incision, quickly causing maternal and fetal hemorrhage. Although mothers can sometimes tolerate this hemorrhage, it might be sufficient to cause neonatal anemia; we believe this might be the mechanism underlying our findings.

Ogawa et al. [16] reported a case of successful transfundal approach, and Boehm et al. [17] reported 2 cases of paramedian incision when the placenta was located in the anterior position, refusing direct placental incision; however, they did not evaluate the effect of neonatal anemia. Furthermore, another well-known method for preventing neonatal anemia—delayed umbilical cord clamping—is reported to be dangerous enough to increase maternal hemorrhage [18]; therefore, more studies on the optimal surgical approach for lowering the incidence of neonatal anemia are needed.

Further prospective randomized studies including early preterm births will help clarify these results.

The high incidence of placenta previa (1.6%) found in this study may reflect the fact that our hospitals are referral hospitals [1].

In conclusion, in this study, anterior placental location was an independent risk factor of neonatal anemia in placenta previa patients. Thus, to manage neonatal anemia, obstetricians should make every effort to detect anterior placental location rather than complete previa and develop better surgical methods to avoid direct placental incision. Pediatricians also need to provide management while considering the

high possibility of neonatal anemia in cases of anterior placental location.

Conflict of Interest

All authors have no conflicts of interest to disclose.

References

1. Faiz AS, Ananth CV. Etiology and risk factors for placenta previa: an overview and meta-analysis of observational studies. *J Matern Fetal Neonatal Med.* 2003; 13:175-90.
2. Bizzarro MJ, Colson E, Ehrenkranz RA. Differential diagnosis and management of anemia in the newborn. *Pediatr Clin North Am.* 2004; 51:1087-107.
3. Widness JA. Pathophysiology of anemia during the neonatal period, including anemia of prematurity. *Neoreviews.* 2008; 9:e520.
4. Dola CP, Garite TJ, Dowling DD, et al. Placenta previa: does its type affect pregnancy outcome? *Am J Perinatol.* 2003; 20:353-60.
5. Hasegawa J, Matsuoka R, Ichizuka K, et al. Predisposing factors for massive hemorrhage during Cesarean section in patients with placenta previa. *Ultrasound Obstet Gynecol.* 2009; 34:80-4.
6. Lokeshwar MR, Singhal T, Shah N. Anemia in the newborn. *Indian J Pediatr.* 2003; 70:893-902.
7. Aher S, Malwatkar K, Kadam S. Neonatal anemia. *Semin Fetal Neonatal Med.* 2008; 13:239-47.
8. Salihi HM, Li Q, Rouse DJ, et al. Placenta previa: neonatal death after live births in the United States. *Am J Obstet Gynecol.* 2003; 188:1305-9.
9. Ananth CV, Demissie K, Smulian JC, et al. Relationship among placenta previa, fetal growth restriction, and preterm delivery: a population-based study. *Obstet Gynecol.* 2001; 98:299-306.
10. Molteni RA. Perinatal blood loss. *Pediatr Rev.* 1990; 12:47-54.
11. McShane PM, Heyl PS, Epstein MF. Maternal and perinatal morbidity resulting from placenta previa. *Obstet Gynecol.* 1985; 65:176-82.
12. Oya A, Nakai A, Miyake H, et al. Risk factors for peripartum blood transfusion in women with placenta previa: a retrospective analysis. *J Nippon Med Sch.* 2008; 75:146-51.
13. Ohkuchi A, Onagawa T, Usui R, et al. Effect of maternal age on blood loss during parturition: a retrospective multivariate analysis of 10,053 cases. *J Perinat Med.* 2003; 31:209-15.
14. Bergholt T, Stenderup JK, Vedsted-Jakobsen A, et al. Intraoperative surgical complication during cesarean section: an observational study of the incidence and risk factors. *Acta Obstet Gynecol Scand.* 2003; 82:251-6.
15. Zaki ZM, Bahar AM, Ali ME, et al. Risk factors and morbidity in patients with placenta previa accreta compared to placenta previa non-accreta. *Acta Obstet Gynecol Scand.* 1998; 77:391-4.
16. Ogawa M, Sato A, Yasuda K, et al. Cesarean section by transfundal approach for placenta previa percreta attached to anterior uterine wall in a woman with a previous repeat cesarean section: case report. *Acta Obstet Gynecol Scand.* 2004; 83:115-6.
17. Boehm FH, Fleischer AC, Barrett JM. Sonographic placental localization in the determination of the site of uterine incision for placenta previa. *J Ultrasound Med.* 1982; 1:311-4.
18. Widness JA. Treatment and Prevention of Neonatal Anemia. *Neoreviews.* 2008; 9:526-33.