Does placental abruption cause neonatal anemia?

Marieke A. W. Bruinsma1,2 | Marjon A. de Boer1,2 | Sandra Prins3,4 | Carolien N. H. Abheiden1,2

1Obstetrics and Gynecology, Amsterdam UMC Location Vrije Universiteit Amsterdam, Amsterdam, The Netherlands
2Pregnancy and Birth, Amsterdam Reproduction and Development Research Institute, Amsterdam, The Netherlands
3Neonatology Amsterdam, Amsterdam UMC Location Vrije Universiteit Amsterdam, Amsterdam, The Netherlands
4Child Development, Amsterdam Reproduction and Development Research Institute, Amsterdam, The Netherlands

Abstract

Introduction: Placental abruption can result in serious perinatal morbidity and mortality. However, it is not clear whether placental abruption could lead to neonatal anemia, as a direct relation has not been described yet. The objective of this study is to investigate whether there is a relation between occurrence of placental abruption and neonatal anemia.

Material and Methods: All women with a clinical diagnoses of placental abruption between January 2016 and April 2021 in Amsterdam UMC, from both the VU University Medical Center and Amsterdam Medical Center, were included. Demographic data and delivery outcomes were collected retrospectively using the medical files. The primary outcome was neonatal anemia, defined as hemoglobin levels less than the fifth percentile for gestational age.

Results: A total of 65 mothers and 65 neonates were included in our study. Average gestational age was 30 + 5 weeks. Mean hemoglobin level of the neonates at birth was 16.5 g/dl (10.2 mmol/L) with hemoglobin levels comparable to the reference curve. Two neonates (3.6%) were diagnosed with anemia based on their hemoglobin level at birth, and six (9.2%) neonates received a blood transfusion within 24 h after birth.

Conclusions: With this study, we found that the hemoglobin levels of the neonates born after placental abruption are comparable to the reference curve and do not show more neonates than expected below the fifth percentile for gestational age. It remains unclear whether there is fetal blood loss during a placental abruption but our results suggest that at least a big amount of fetal blood is not lost, since we did not found a large number of anemic neonates. Severe neonatal anemia in the case of placental abruption does not need to be expected.

KEYWORDS
hemoglobin, neonatal anemia, placenta, placental abruption
Placental abruption, defined as the separation of the placenta from the uterus prior to delivery, is considered to be the cause of serious neonatal and maternal morbidity and mortality.\(^1\)\(^-\)\(^8\) It is assumed that it is the result of maternal blood coming between the decidua and placenta and consequently separating the placenta from the uterus.\(^5\) Placental abruption complicates about 0.4%-1% of pregnancies, with incidences lower in Nordic countries and higher in a few Asian countries.\(^1\)\(^,\)\(^2\)\(^,\)\(^4\)\(^-\)\(^8\)\(^,\)\(^9\) Clinical presentation of a placental abruption includes vaginal bleeding, abdominal pain, contractions of the uterus and abnormalities of the fetal heart rate pattern.\(^7\)\(^,\)\(^8\) There are two types of placental abruption: partial, in which only a part of the placenta is separated from the uterus, and total, in which the complete placenta is separated from the uterus.\(^3\) The placenta transports oxygen to the fetus, which means that a partial or total separation of the placenta could result in asphyxia or neonatal death. Consequently, placental abruption is undeniably a cause of mortality.\(^3\)\(^,\)\(^4\)\(^-\)\(^9\)

Risk factors for a placental abruption have been identified in previous studies. Smoking, alcohol and cocaine use, preeclampsia, chronic hypertension, uterine anomaly and adverse obstetric history such as a cesarean section or a previous placental abruption increase the risk for (recurrent) placental abruption.\(^1\)\(^,\)\(^2\)\(^,\)\(^4\)\(^-\)\(^9\) Also, several short- and long-term adverse outcomes for both mother and child are associated with placental abruption. Maternal adverse outcomes include postpartum hemorrhage, need for blood transfusion, hysterectomy because of severe blood loss, venous thromboembolism, sepsis, acute kidney injury, diffuse intravascular coagulation and hypertensive disorders of pregnancy.\(^2\)\(^,\)\(^8\)\(^,\)\(^10\)\(^,\)\(^11\)

Fetal and neonatal adverse outcomes include fetal death, asphyxia, preterm birth, severe respiratory disorder, acidosis, encephalopathy and cerebral palsy;\(^1\)\(^,\)\(^2\)\(^,\)\(^4\)\(^,\)\(^7\)\(^,\)\(^8\)\(^,\)\(^10\) neonatal anemia was not described as an adverse neonatal outcome in those studies. In a small study from 1987, three cases of fetomaternal hemorrhage were described after placental abruption with no urgency for immediate delivery.\(^12\) Moreover, some clinical doctors assume there is fetal blood loss during a placental abruption, which could cause neonatal anemia.\(^13\)\(^,\)\(^14\) On the other hand, since the maternal and fetal circulation are separated, one could argue that it is unlikely that fetal blood is lost during placental abruption.

Based on discussion in clinical practice and absence of clear evidence in the literature, the question has risen whether neonatal anemia could be the result of a placental abruption. A direct relation between the two has not been described yet. If there is a relation between placental abruption and neonatal anemia, this could have consequences for the treatment of the neonate, for example anticipating making packed cells more easily accessible.

Therefore, the aim of this study is to investigate whether there is a relation between placental abruption and neonatal anemia.

### 2 | MATERIAL AND METHODS

We conducted a historical, observational cohort study. A search for patients with a placental abruption between January 2016 and April 2021 was performed in the electronic medical files (EPIC) of Amsterdam UMC, both in the VU University Medical Center and Amsterdam Medical Center. All women with a clinical diagnosis of placental abruption were included. The clinical diagnosis of placental abruption was made based on clinical signs, abrupt onset of vaginal bleeding antepartum, acute abdominal or back pain, contractions and/or fetal distress, in combination with evidence of retroplacental blood clots or the sonographic visualization of abruption.\(^15\) Cases were excluded in cases of fetal death, since neonatal hemoglobin (Hb) levels were not available.

Descriptive data of both mother and child were collected from their medical files. This included (among others) information about maternal characteristics, obstetric history, clinical presentation of the placental abruption and risk factors for placental abruption. Details about the birth, neonate and adverse outcomes were also extracted from the medical files. The primary outcome of this study was neonatal anemia, based on the first Hb level measurement within 24h after birth.

Neonatal anemia is defined as Hb levels less than the fifth percentile.\(^16\) Because the Hb levels are gestational age-dependent, we compared our results with gestational age-based norms. We chose the reference ranges of Henry and Christensen, since this conforms to the erythrocyte transfusion protocol of the neonatal intensive care unit of the Amsterdam UMC.\(^14\)\(^,\)\(^17\) Because g/dl is used internationally and mmol/L is used in the Netherlands, the Hb levels are presented in both units.

Pregnancy-induced hypertension was defined as a systolic blood pressure $>$140mmHg and/or a diastolic blood pressure $>$90mmHg. Hypertensive disorders of pregnancy consisted of three disorders: preeclampsia, eclampsia and HELLP syndrome. For these disorders we used the definitions of the International Society for the Study of Hypertension in Pregnancy.\(^18\) We did not include pregnancy-induced hypertension in the definition of hypertensive disorders of pregnancy because it is a milder diagnosis. Blood loss $>$1000ml during labor or cesarean section was defined as postpartum hemorrhage in line with Dutch guidelines.\(^19\) Preterm birth was defined as birth before 37 weeks of gestation.

Neonatal death is divided into four groups conforming to the definition of the World Health Organization: death during delivery, early neonatal death ($<$7days), late neonatal death (7–28days) and death $>$28days. Small-for-gestational age is defined as a birthweight under the 10th percentile for gestational age.\(^20\) Apgar scores were registered within 1 and 5min after birth. Scores below 7, at 5min were considered low.
2.1 | Statistical analyses

IBM SPSS version 27 was used for statistical analysis. Descriptive statistics as well as statistical tests, including an independent samples t-tests and Chi-square tests, were performed. An additional sub-analysis was done; the group of neonates was divided into two groups based on their Apgar scores 5 min after birth: Apgar <7 and ≥7 and a relation with Hb was investigated. p-values <0.05 were considered to be statistically significant.

2.2 | Ethical approval

The Institutional Review Board of the VU University Medical Center decided that permission from a medical ethical committee was not necessary because of the observational character of this study (medical ethical committee-number; 2021.0127). No informed consent was requested from the participants, since only routinely collected observed data from medical files were used. Moreover, since most of the women in this study have a severe obstetric history, requesting informed consent is thought be too confrontational.

3 | RESULTS

During the study period, a total of 14208 clinical deliveries were registered in EPIC. Placental abruption complicated 0.46% of all deliveries. Overall, 65 pregnancies were eligible for this study: 63 singleton pregnancies and two twin pregnancies. The twin pregnancies were both dichorial diamniotic. Therefore, we excluded the two neonates of the dichorial diamniotic twin pregnancies where placental abruption did not occur. In total, 65 mothers and 65 neonates were included in our study. Baseline characteristics of the women are presented in Table 1. Four women used drugs in their pregnancy: all smoked marihuana and one used cocaine at the same time.

Clinical manifestations of the placental abruption are shown in Table 2. In 49 (75.4%) women the placental abruption occurred before delivery and in 16 (24.6%) women the placental abruption occurred during delivery. The abruption was classified as a partial abruption in 44 (67.7%) women and as a total abruption in six (9.2%) women. In 15 (23.1%) women it was unknown whether the abruption was partial or total. In total, 58 (89.2%) women underwent a cesarean section and 54 (83.1%) placentas were examined by the pathologist. In 27 (50.0%) cases, the pathologist described signs of placental abruption in the pathology report. Table 2 gives a detailed description of how the diagnosis placental abruption was given for every woman included in the study. Only women with a partial abruption had a time interval of more than 90 min between the first symptoms of the abruption and the birth of their child.

Table 3 shows the maternal and neonatal outcomes. A total of 61 (93.8%) women delivered preterm. One woman developed hemorrhagic shock after postpartum hemorrhage. No maternal death was registered. Of the nine neonatal deaths, 88.9% were defined as early neonatal deaths and 11.1% as late neonatal deaths. Among 55 of the 65 neonates, the Hb level was measured within 24 h after birth. When comparing the Hb levels of the individual neonates with the reference ranges, two (3.6%) neonates were diagnosed with anemia. The pediatricians suspected 14 (25.5%) neonates of anemia after birth, based on symptoms such as tachypnea, paleness and hypotension. Six (9.2%) neonates received a blood transfusion within the first 24 h after birth. The mean Hb level of these neonates at birth was 14.4 g/dl (8.9 mmol/L). This included one of the two neonates who was diagnosed with anemia based on their Hb level at birth. Her Hb level at birth was 10.3 g/dl (6.4 mmol/L).

The other five neonates were given a blood transfusion for other reasons than a low Hb level at birth: two because they showed clinical signs of anemia, one because of circular insufficiency and asphyxia caused by persistent pulmonary hypertension and a perinatal infection, one because of circular insufficiency caused by persistent pulmonary hypertension and bleeding in a lung, and one during resuscitation to boost the heart action.

| TABLE 1 | Baseline characteristics and risk factors of placental abruption |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Characteristic  | n (%)           | Characteristic  | n (%)           | Characteristic  | n (%)           | Characteristic  | n (%)           | Characteristic  | n (%)           | Characteristic  | n (%)           | Characteristic  | n (%)           | Characteristic  | n (%)           | Characteristic  | n (%)           | Characteristic  | n (%)           | Characteristic  | n (%)           | Characteristic  | n (%)           |
| Mean maternal age (years) | 31.85 ± 4.89 | Parity  | 0 | 25 (38.5) | 1 | 24 (36.9) | ≥2 | 16 (24.6) | Ethnicity  | Caucasian | 35 (53.7) | Asian | 3 (4.6) | African | 17 (26.2) | Turkish | 2 (3.1) | Other | 4 (6.2) | Unknown | 4 (6.2) |
| Smoking during pregnancy | 12 (18.5) | Drug use during pregnancy | 4 (6.2) | Chronic hypertension | 1 (1.5) | Pregnancy diabetes | 5 (7.7) | Hypothyroidism | 3 (4.6) | Anemia | 12 (18.5) | Risk factors in obstetric history |
| Cesarean section | 17 (26.2) | Miscarriage | 23 (35.4) | Preeclampsia | 6 (9.2) | Still birth | 4 (6.2) | Placental abruption | 5 (7.7) |

hemorrhagic shock after ppostpartum hemorrhage. No maternal death was registered. Of the nine neonatal deaths, 88.9% were defined as early neonatal deaths and 11.1% as late neonatal deaths. Among 55 of the 65 neonates, the Hb level was measured within 24 h after birth. When comparing the Hb levels of the individual neonates with the reference ranges, two (3.6%) neonates were diagnosed with anemia. The pediatricians suspected 14 (25.5%) neonates of anemia after birth, based on symptoms such as tachypnea, paleness and hypotension. Six (9.2%) neonates received a blood transfusion within the first 24 h after birth. The mean Hb level of these neonates at birth was 14.4 g/dl (8.9 mmol/L). This included one of the two neonates who was diagnosed with anemia based on their Hb level at birth. Her Hb level at birth was 10.3 g/dl (6.4 mmol/L). The other five neonates were given a blood transfusion for other reasons than a low Hb level at birth: two because they showed clinical signs of anemia, one because of circular insufficiency and asphyxia caused by persistent pulmonary hypertension and a perinatal infection, one because of circular insufficiency caused by persistent pulmonary hypertension and bleeding in a lung, and one during resuscitation to boost the heart action. In
6/63 (9.5%, two unknown) neonates a congenital abnormality was present: one ventricular septal defect, one esophageal atresia, one deformity of the vulva, one hypospadias, one with multiple congenital defects and one with a diaphragmatic hernia and a unilateral cheilognathopalatoschisis.

In a sub-analysis, we divided the group of neonates into two groups based on their Apgar score 5 min after birth: Apgar <7 and ≥7. The Apgar score of one neonate was missing, which makes a total of 64 neonates for inclusion in the sub-analysis. The mean Hb value, number of neonates who received blood transfusion during their stay at Amsterdam UMC, and mortality rate of both groups are shown in Table 4.

Figure 1 presents the reference ranges of Henry & Christensen (2015) and the individual Hb measurements of the neonates. Two dots (3.6%) lay below the fifth percentile.

### Discussion

In this study, we found 65 neonates after an abruption. Among 55 neonates, the Hb level was measured within 24 h after birth and two neonates (3.6%) were diagnosed with anemia, which is comparable to a normal reference population. This supports the hypothesis that only maternal blood, and no fetal blood, is lost during a placental abruption. Remarkably, in 14 neonates (25.5%) anemia was suspected by pediatricians on the basis of clinical signs such as paleness, tachypnea
and hypotension. However, this was not seen in their Hb level at birth. This discrepancy could have multiple reasons. Some neonates are pale due to acidosis, not to anemia. Tachypnea can be interpreted as a result of anemia but can also have other causes such as infant respiratory distress syndrome and infection. The same holds true for hypotension after birth. Clinical suspicion of a placental abruption can cause pediatricians to be cautious about neonatal anemia. In contrast, research has shown that when infants experience acute blood loss, the Hb levels can be completely normal immediately after delivery, because the first response of the body is vasoconstriction. Therefore Asher et al. (2008) states that the diagnosis of anemia based on blood loss is largely dependent on physical findings and evidence of blood loss. An incorrect hypothesis based on the symptoms may lead to a delay in correct management and the use of unnecessary blood products, and therefore could be a risk to the patient.

To see whether there is a relation between the Apgar score and Hb level at birth, we did a sub-analysis in which we divided the group of neonates into a group with a low Apgar score (<7) and a group with a high Apgar score (≥7) 5 min after birth. We found no significant difference in the mean Hb level at birth between two groups (p = 0.065), although there was a lower mean Hb level in the group with a lower Apgar score. The lower Apgar score can be explained by asphyxia as a result of less placental oxygen transport in the case of a placental abruption. A lower Hb level and a lower Apgar score can also be explained by early cord clamping during an emergency cesarean section. No additional blood from the placenta can flow into the infant when the cord is clamped early. Recent studies have shown that delayed cord clamping gives better outcomes, eg higher Hb levels, fewer transfusions and higher Apgar scores. Although after abruption the placenta receives less or no oxygen from the mother, placental transfusion still takes place after birth, so delayed cord clamping could be something to consider in clinical practice. In this study, the time interval of the cord clamping was not registered and so we cannot determine whether these results are caused by early cord clamping.

To our knowledge, this is the first study investigating the relation between placental abruption and neonatal anemia. This study can help in clinical practice, since pediatricians will not need to anticipate neonatal anemia with packed cells, if placental abruption is expected. A limitation in the present study is the absence of a control group. Since it is unethical to draw blood from healthy neonates to measure Hb levels, we used reference ranges. These reference ranges are based on neonates with little pathology; however, they could still differ from Hb levels of healthy neonates. Our findings should be confirmed in a larger study.

5 | CONCLUSION

In this study, we found that the hemoglobin levels of the neonates born after placental abruption are comparable to the reference curve

| Apgar score at 5 min after birth related to hemoglobin level, blood transfusion and mortality | <7 | ≥7 |
|---|---|---|
| No. (%) or mean ± SD | No. (%) or mean ± SD | p |
| Mean Hb (g/dl) | (n = 23) 15.8 ± 2.8 | (n = 31) 16.9 ± 2.6 | 0.065 |
| Mean Hb (mmol/L) | (n = 23) 9.8 ± 1.7 | (n = 31) 10.5 ± 1.6 | 0.065 |
| Blood transfusion during stay at Amsterdam UMC | 10 (38.5) | 12 (31.6) | 0.57 |
| Mortality | 8 (30.7) | 1 (2.6) | 0.001 |

Abbreviations: Hb, hemoglobin; SD, standard deviation.

FIGURE 1 Reference ranges (5th percentile, mean, 95th percentile) with individual hemoglobin measurements of the neonates. Figure from Ref. [14], is reproduced with permission of E. Henry and R.D. Christensen and the Copyright Clearance Center of Clinics in Perinatology
and did not have more neonates than expected with hemoglobin below the fifth percentile for gestational age. It remains unclear whether there is fetal blood loss during a placental abruption, but our results suggest that at least a large amount of fetal blood is not lost, since we did not find a large number of anemic neonates. Severe neonatal anemia does not need to be anticipated in the case of placental abruption. We show a discrepancy between anemia based on Hb levels and anemia based on clinical symptoms (3.6% vs 25.5%).

ACKNOWLEDGMENTS
Special thanks to Erick Henry and Robert D. Christensen for giving us their original data and permission to use the figure of the reference ranges of Hb levels.

AUTHOR CONTRIBUTIONS
CNHA and MAB: study design. MAWB: requested permission at IRB with supervision of CNHA, data collection, statistical analysis, manuscript drafting with supervision of CNHA. MAB, SP and CNHA read the final version of the manuscript and made comments.

CONFLICT OF INTEREST
The authors have stated explicitly that there are no conflicts of interest in connection with this article.

FUNDING INFORMATION
None.

ORCID
Marieke A. W. Bruinsma https://orcid.org/0000-0003-4546-0759

REFERENCES
1. Ananth CV, Berkowitz GS, Savitz DA, Lapinski RH. Placental abruption and adverse perinatal outcomes. JAMA. 1999;282:1646-1651.
2. Downes KL, Grantz KL, Shenassa ED. Maternal, labor, delivery, and perinatal outcomes associated with placental abruption: a systematic review. Am J Perinatol. 2017;34:935-957.
3. Oyelese Y, Ananth CV. Placental abruption. Obstet Gynecol. 2006;108:1005-1016.
4. Tikkanen M. Placental abruption: epidemiology, risk factors and consequences. Acta Obstet Gynecol Scand. 2011;90:140-149.
5. Tikkanen M. Etiology, clinical manifestations, and prediction of placental abruption. Acta Obstet Gynecol Scand. 2010;89:732-740.
6. Tikkanen M, Luukkaala T, Gissler M, et al. Decreasing perinatal mortality in placental abruption. Acta Obstet Gynecol Scand. 2013;92:298-305.
7. Tikkanen M, Nuutila M, Hiilesmaa V, Paavonen J, Ylikorkala O. Clinical presentation and risk factors of placental abruption. Acta Obstet Gynecol Scand. 2006;85:700-705.
8. Boisrame T, Sananes N, Fritz G, et al. Placental abruption: risk factors, management and maternal-fetal prognosis. Cohort study over 10 years. Eur J Obstet Gynecol Reprod Biol. 2014;179:100-104.
9. Riihimaki O, Mesaranta M, Paavonen J, et al. Placental abruption and child mortality. Pediatrics. 2018;142:e20173915.
10. Li Y, Tian Y, Liu N, Chen Y, Wu F. Analysis of 62 placental abruption cases: risk factors and clinical outcomes. Taiwan J Obstet Gynecol. 2019;58:223-226.
11. Takeda J, Takeda S. Management of disseminated intravascular coagulation associated with placental abruption and measures to improve outcomes. Obstet Gynecol Sci. 2019;62:299-306.
12. Cardwell MS. Ultrasound diagnosis of abruptio placentae with fetomaternal hemorrhage. Am J Obstet Gynecol. 1987;157:358-359.
13. Lokehswar MR, Singhal T, Shah N. Anemia in the newborn. Indian J Pediatr. 2003;70:893-902.
14. Henry E, Christensen RD. Reference intervals in neonatal hematology. Clin Perinatol. 2015;42:483-497.
15. Elsesser DA, Ananth CV, Prasad V, Vintzileos AM. New Jersey-placental abruption study I. diagnosis of placental abruption: relationship between clinical and histopathological findings. Eur J Obstet Gynecol Reprod Biol. 2010;148:125-130.
16. Janus J, Moerschel SK. Evaluation of anemia in children. Am Fam Physician. 2010;81:1462-1471.
17. UMC Amsterdam bVAA. Erytrocyten transfusierichtlijn[ERYTHROCYTE transfusion guideline] (in Dutch). VKC-NICU; 2020.
18. Brown MA, Magee LA, Kenny LC, et al. Hypertensive disorders of pregnancy: ISSHP classification, diagnosis, and management recommendations for international practice. Hypertension. 2018;72:24-43.
19. Nederlandse Vereniging voor Obstetrie en Gynaecologie. NVOG-richtlijn Hemorragia postpartum (HPP). [NVOG guideline Hemorragia postpartum (HPP)] (in Dutch). Nederlandse Vereniging voor Obstetrie en Gynaecologie; 2013.
20. Hofteizer L, Hof MHP, Dijs-Elsinga J, Hogeveen M, Hukkelhoven C, van Lingen RA. From population reference to national standard: new and improved birthweight charts. Am J Obstet Gynecol. 2019;220(383):e1-e17.
21. Aher S, Malwatkar K, Kadam S. Neonatal anemia. Semin Fetal Neonatal Med. 2008;13:239-247.
22. Raju TN, Singhal N. Optimal timing for clamping the umbilical cord after birth. Clin Perinatol. 2012;39:889-900.
23. Rabe H, Gyte GM, Diaz-Rossello JL, Duley L. Effect of timing of umbilical cord clamping and other strategies to influence placental transfusion at preterm birth on maternal and infant outcomes. Cochrane Database Syst Rev. 2019;2019(9):CD003248.
24. Qian Y, Ying X, Wang P, Lu Z, Hua Y. Early versus delayed umbilical cord clamping on maternal and neonatal outcomes. Arch Gynecol Obstet. 2019;300:531-543.

How to cite this article: Bruinsma MA, de Boer MA, Prins S, Abheiden CN. Does placental abruption cause neonatal anemia? Acta Obstet Gynecol Scand. 2022;101:917-922. doi: 10.1111/aogs.14376