

# The influence of antepartum hemorrhage on placenta previa: a multi-center, retrospective cohort study

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**Background:** Placenta previa (PP) can cause repeated and catastrophic bleeding that may lead to increased maternal and neonatal mortality and morbidity. The purposes of this study were to determine the relationship between antepartum hemorrhage (APH) and gestational week, the frequency of APH, the risk factors for APH, and whether patients with APH developed more severe adverse perinatal outcomes. **Methods:** This was a multi-center, retrospective study in which we enrolled all placenta previa patients between October 2015 and September 2018 within the Partners Healthcare System. **Results:** The mean APH frequency was  $2.2 \pm 1.3$  in women with PP, with the majority having experienced a one-time bleeding episode (36.4%, 44/121). The incidence of APH varied from 2.6% to 14.6% in every gestational week, with the highest incidence at 32 gestational weeks. Complete placenta was an independent risk factor for APH (odds ratios, 4.17; 95% confidence intervals, 1.805–9.634). Pregnant women with APH underwent more emergent cesarean deliveries (54.5%,  $p < 0.05$ ), and more newborns manifested respiratory distress syndrome (34.7%,  $p < 0.05$ ). **Conclusions:** The APH morbidity varied by gestational week, with the 32nd gestational week appearing to have the highest incidence of PP. Complete PP can cause more frequent APH, and PP plus APH may increase maternal and neonatal adverse outcomes.

## Keywords

Cesarean delivery; Placenta previa; Antepartum hemorrhage; Preterm; Perinatal outcome

## 1. Background

Placenta previa is a serious obstetric complication that may lead to increased maternal and neonatal mortality and morbidity [1], with an incidence that varies between 0.15% and 0.91% [2–6]. Clinically, placenta previa presents as recurrent painless vaginal bleeding in the antenatal period and massive hemorrhage during cesarean delivery (CD) and post-operatively. However, not all patients with placenta previa encounter antepartum hemorrhage (APH), and some may not experience any bleeding during the entire prenatal pe-

riod. It is thus currently unclear as to which risk factors contribute to APH or at which gestational week bleeding occurs. To our knowledge, there are no extant studies in the literature that describe the relationship between APH and gestational week.

Given the importance of this condition as well as the paucity of the existing literature on this topic, the aims of the current study were to identify the following in placenta previa patients: (1) the relationship between APH and gestational week, (2) the frequency of APH, (3) the risk factors for APH, and (4) whether patients with APH developed more severe adverse perinatal outcomes. This knowledge will assist in improving the antenatal management of placenta previa and optimize prophylactic measures to ameliorate outcomes.

## 2. Methods

The present investigation was a multi-center, retrospective study approved by the Institutional Review Board at Partners Healthcare System (PHS) (Protocol#2019P000028). We collected all patient delivery data between October 2015 and September 2018 within the PHS, which includes 7 different hospitals, 2 of which are large, tertiary, academic medical centers.

The total number of deliveries during this period was 39945, including 12884 cesarean deliveries (32.3%) and 27061 vaginal deliveries (67.7%). We sought patients in the PHS using the indication of placenta previa for “cesarean section” or “cesarean delivery”, and found 268 cases diagnosed with placenta previa by ultrasonography; 9 cases were excluded as inconsistent at intraoperative diagnosis. To avoid data bias in maternal and newborn outcomes, we excluded patients with multiple pregnancies ( $n = 8$ ), stillbirths ( $n = 1$ ), or delivery at less than 24 weeks of gestational age ( $n = 3$ ). A total of 247 patients were ultimately included in our study.

Demographic data were collected from electronic medical records (EMR) and included maternal age, gravidity, par-

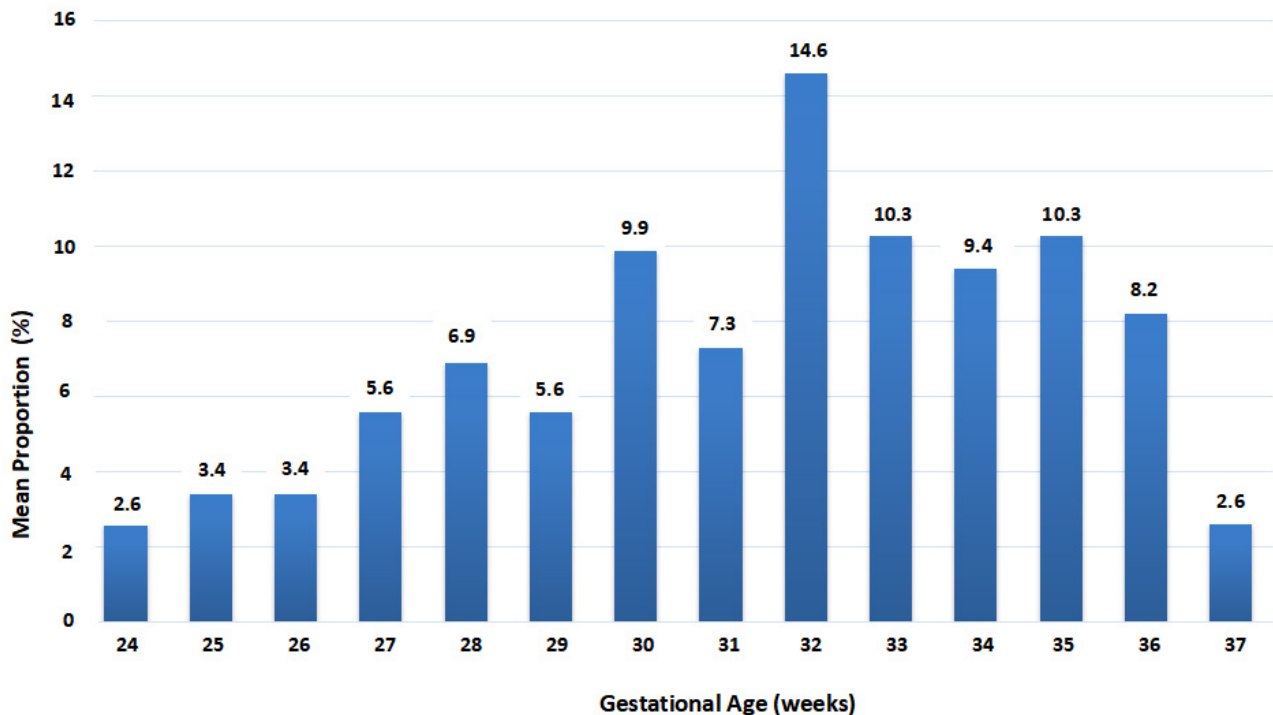


Fig. 1. The mean proportion of patients with APH at each gestational age.

ity, body mass index (BMI), smoking history, *in vitro* fertilization (IVF) history, prior number of CDs, history of CDs, and duration of the CD interval. The interval duration depicted the interval between the most recent CD and the current delivery. Gestational week was either calculated using the date of the last menstrual period or estimated from the first-trimester ultrasonographic measurements. Antepartum hemorrhage was defined as bleeding from or into the genital tract that occurred from 24<sup>+0</sup> weeks of pregnancy and prior to the birth of the baby [7]. We obtained placental location and classification from the last ultrasonographic report prior to delivery, and this was validated during CD. The placenta was classified as either complete (the lower edge of the placenta completely covering the cervical orifice), incomplete (marginal or partial, the lower margin of the placenta partially covering the cervical orifice), or low lying (the lower margin of the placenta was close to the cervical orifice and less than 20 mm) according to the ultrasonographic diagnostic criteria [8]. Placenta accreta was recorded from patient surgical records and confirmed by pathologic diagnosis. We also located maternal and neonatal outcomes in the surgical records as well as in anesthesia and neonatal records. The intraoperative variable of “total blood product” represented the sum total (units) of any blood product administered during the operative period, including packed red blood cells (PRBC), cell salvage, fresh frozen plasma (FFP), platelets, cryoprecipitate, and albumin. We defined postpartum hemorrhage (PPH) as an estimated blood loss (EBL) over 1000 mL. Hemoglobin (HGB) concentration and hematocrit (HCT) percentage during the first trimester, pre-operation,

and postoperatively were procured from laboratory results found in the EMR.

All vaginal bleeding was recorded in our data, including the number of bleeding episodes and specific gestational week when bleeding occurred. Persistent bleeding was recorded once at the beginning of bleeding; however, if the patient experienced an interval without bleeding for more than 1 week, then the next bleeding was considered a second bleeding incident. Repeated bleeding was recorded several times according to the number of bleeding episodes. All hemorrhages were recorded, including those that occurred during inpatient and outpatient visits; however, bleeding caused by labor was not included. We observed no bleeding caused by neoplasm, infection, trauma, or iatrogenesis in any of our cases. There was also no bleeding due to vasa previa or placental abruption. The amount of bleeding was not included in our data because the amount was not quantified; here, some cases describe the amount of bleeding as spotting, or baseball- or golf-ball sized. As such, to avoid any data bias, we did not analyze the specific amount of vaginal bleeding.

All included cases met the recommendations and guidelines for data collection and analysis for APH in placenta previa [9].

We conducted our statistical analysis using the Statistical Package for Social Sciences (SPSS) software, version 23.0 (International Business Machines Corporation, Armonk, NY, USA). Continuous variables were presented as means  $\pm$  standard deviation (SD) or medians with an inter-quartile range, and we made comparisons between placenta previa with or without APH using the independent-sample *t* test or non-

parametric Mann-Whitney U test depending upon normality of the data distribution. Categorical variables are depicted as counts and percentages, and the differences were assessed using Chi-squared analysis; Fisher's exact-probability test was used when appropriate. A value of  $p < 0.05$  was considered statistically significant. We used logistic regression to study the independent risk factors for APH: the dependent variable was APH, and age, gravidity, parity, BMI, history of CD, number of prior CDs, duration of CD interval, placental location, and placental classification all served as covariates, with  $p < 0.01$  representing a significant difference. Results were reported using odds ratios (OR) and 95% confidence intervals (CI). We used a Kaplan-Meier survival curve to show placenta previa patients with or without APH who remained undelivered at each gestational week.

### 3. Results

The prevalence of placenta previa in our study was 0.65% (259/39945). We identified 247 patients who underwent CD for placenta previa: 17 of these underwent a hysterectomy (6.9%, 17/247), 7 were treated with a uterine balloon (2.8%, 7/247), 3 underwent bilateral uterine artery embolization (1.2%, 3/247), and 7 patients received ureteral stents (2.8%, 7/247).

The incidence of APH in placenta previa was 49.0% (121/247). The mean number of bleeding episodes was  $2.2 \pm 1.3$ . While most experienced a one-time bleeding episode (36.4%, 44/121), 26.4% had 2 (32/121), 23.1% had 3 (28/121), 9.1% had 4 (11/121), 1.7% had 5 (2/121), 2.5% had 6 (3/121), and 0.8% had 7 hemorrhagic episodes (1/121). With respect to all APH patients, the week in which bleeding occurred was gestation week  $31.4 \pm 3.3$ , with the highest incidence of bleeding occurring at 32 weeks of gestation—at a rate of 14.6% (Fig. 1). No bleeding occurred after the 38th gestational week, as most placenta previa patients underwent elective CD at 36–37 weeks. If there was a history of bleeding, CD was performed before 37 weeks. The difference between APH in the second trimester (21.9%, 51/233) and APH in the third trimester (78.1%, 182/233) was statistically significant  $\chi^2 = 73.625$ ,  $p = 0.000$ .

Although we did not observe any statistical differences in the demographic characteristics between patients with or without APH (Table 1) ( $p > 0.05$ ), there was a significant difference in placental classification ( $p < 0.05$ ), particularly with respect to the complete-placenta category, where the APH group exhibited a higher prevalence than the non-APH group (72.9% vs 47.4%). Having complete-placental coverage was thus an independent risk factor for APH in placenta previa patients (OR, 4.17; 95% CI, 1.805–9.634).

The gestational week in which delivery occurred for patients without APH was much later than for patients with APH ( $37.1 \pm 1.6$  vs  $35.6 \pm 1.9$ ,  $p = 0.000$ ). Fig. 2 depicts a Kaplan-Meier curve of the proportion of placenta previa patients with or without APH who remained undelivered at each gestational week, showing that without APH 89% were

**Table 1. Demographic and obstetric characteristics of the study.**

	Without APH (n = 126)	With APH (n = 121)	p value
Age (years), mean $\pm$ SD	34.7 $\pm$ 4.6	34.9 $\pm$ 4.2	0.893
Gravidity, median (range)	2 (2–4)	3 (2–4)	0.172
Parity, median (range)	1 (0–2)	1 (1–2)	0.116
BMI (kg/m <sup>2</sup> ), mean $\pm$ SD	29.7 $\pm$ 5.2	29.1 $\pm$ 5.7	0.182
Smoking, n (%)	24 (19.0)	19 (15.7)	0.488
IVF, n (%)	31 (24.8)	33 (27.3)	0.659
Prior CD number, median (range)	0 (0–1)	0 (0–0)	0.217
CD history, n (%)	34 (27.0)	25 (20.7)	0.244
CD interval (year), median (range)	2.7 $\pm$ 4.3	2.9 $\pm$ 3.9	0.239
Fetal presentation, n (%)			0.590
Vertex	110 (87.3)	100 (82.6)	
Breech	9 (7.1)	12 (9.9)	
Transverse	7 (5.6)	9 (7.4)	
GBS infection, n (%)	99 (88.4)	102 (87.9)	0.914

APH, antepartum hemorrhage; BMI, body mass index; IVF, *in vitro* fertilization; CD, cesarean delivery; GBS, group B streptococcus.

undelivered beyond 34 weeks of gestation, and that 53% were undelivered beyond 37 weeks of gestation.

In addition to gestational week, we observed significant differences between the 2 groups regarding maternal outcomes including length of hospital stay, first trimester and pre-operative levels of HGB and HCT, emergent CD, blood transfusion rate, total blood product, general anesthesia (GA), and American Society of Anesthesiologists (ASA) physical status classification ( $p < 0.05$ ). There were no differences in placenta accreta (11.1% vs 13.2%,  $p = 0.611$ ) or other parameters, including anesthesia time, procedural duration, total fluid infusion, EBL, PPH, hysterectomy, or intensive care unit (ICU) admission ( $p > 0.05$ ) (Table 2).

Neonatal outcomes were also significantly different between the 2 groups. The APH group manifested a higher rate of preterm delivery and a lower birth weight ( $p < 0.001$ ) relative to the non-APH group. Infants with an Apgar score less than 7 at 1 minute had a higher prevalence of APH compared to those without APH ( $p = 0.003$ ), but there was no difference in infants with an Apgar score of less than 7 at 5 minutes ( $p = 0.09$ ). The number of newborns admitted to the neonatal intensive care unit (NICU) was also statistically different between the 2 groups, while the women with APH exhibited a higher admission rate than those without APH ( $p = 0.002$ ). The APH group required a higher rate of antenatal corticosteroid treatment to prevent respiratory distress syndrome (RDS) ( $p < 0.001$ ) relative to the non-APH group (Table 3).

### 4. Discussion

We found that the incidence of APH was different for each gestational week, and the number of APH events varied between 1 and 7 episodes, with nearly half of the patients experiencing 2 to 3 incidents throughout their preg-

**Table 2. Placental characteristics and maternal outcomes of cesarean delivery among parturients with placenta previa.**

	Without APH (n = 126)	With APH (n = 121)	p value
ASA status, n (%)			0.049
1	13 (10.3)	6 (5.0)	
2	95 (75.4)	85 (70.2)	
3–4	18 (14.3)	30 (24.8)	
Placental location, n (%)			1.000
Anterior	31 (26.7)	30 (25.9)	
Posterior	66 (56.9)	67 (57.8)	
Lateral	5 (4.3)	5 (4.3)	
Anterior + posterior	14 (12.1)	14 (12.1)	
Placental classification, n (%)			0.000
Complete	55 (47.4)	86 (72.9)	
Incomplete	37 (31.9)	23 (19.0)	
Low lying	24 (20.7)	9 (7.6)	
Placenta accreta, n (%)	14 (11.1)	16 (13.2)	0.611
Emergent CD, n (%)	15 (11.9)	66 (54.5)	0.000
Duration of procedure (min), mean $\pm$ SD	63.6 $\pm$ 48.0	66.8 $\pm$ 45.9	0.801
Anesthetic type, n (%)			0.024
General anesthesia (GA)	1 (0.8)	9 (7.4)	
Neuraxial anesthesia (NA)	121 (96.0)	108 (89.3)	
NA converted to GA	4 (3.2)	4 (3.3)	
Anesthesia time (min), mean $\pm$ SD	123.8 $\pm$ 78.1	136.9 $\pm$ 116.0	0.114
EBL (mL), median (range)	800 (775–1000)	900 (800–1215)	0.109
PRBC product (mL), mean $\pm$ SD	1112.7 $\pm$ 812.4	863.0 $\pm$ 898.7	0.269
All blood products (mL), mean $\pm$ SD	238.3 $\pm$ 1046.4	297.5 $\pm$ 1170.4	0.045
Blood transfusion, n (%)	12 (9.5)	23 (19.0)	0.033
Total fluid infusion (mL), median (range)	1600 (1000–2000)	1500 (1100–2225)	0.395
HGB (g/dL), mean $\pm$ SD			
First trimester	12.4 $\pm$ 1.1	12.0 $\pm$ 1.2	0.022
Pre-operation	11.8 $\pm$ 1.3	11.2 $\pm$ 1.3	0.000
Post-operation	9.9 $\pm$ 2.5	9.5 $\pm$ 1.4	0.207
HCT (%), mean $\pm$ SD			
First trimester	36.8 $\pm$ 3.0	35.6 $\pm$ 3.6	0.012
Pre-operation	35.0 $\pm$ 3.1	33.3 $\pm$ 3.8	0.001
Post-operation	28.9 $\pm$ 3.7	28.4 $\pm$ 4.2	0.245
PPH, n (%)	46 (36.5)	56 (46.3)	0.119
Hysterectomy, n (%)	9 (7.1)	8 (6.6)	0.869
ICU admission, n (%)	3 (2.4)	1 (0.8)	0.643
Inpatient days (day), mean $\pm$ SD	4.6 $\pm$ 3.7	7.2 $\pm$ 7.2	0.000

APH, antepartum hemorrhage; ASA, the American Sociological Association; CD, cesarean delivery; EBL, estimated blood loss; PRBC, packed red blood cells; HGB, hemoglobin; HCT, hematocrit; PPH, postpartum hemorrhage; ICU, intensive care unit.

nancies. The 32nd gestational week appearing to be the most precarious and possessing the highest incidence of APH. We evaluated the incidence of APH in placenta previa patients as it was first described and during the gestational week in which it occurred, and to the best of our knowledge, there are no other extant reports on this specific topic. In general, the 32nd week marked a turning point in that prior to

32 weeks, bleeding gradually increased commensurate with increasing gestational week. However, after 32 weeks, the bleeding began to diminish. This pattern appears to be consistent with data demonstrating that as the numbers of CDs gradually increase commensurately with the increase in gestational weeks, the resulting incidence of vaginal bleeding is markedly reduced [10]. It is possible that augmented uter-

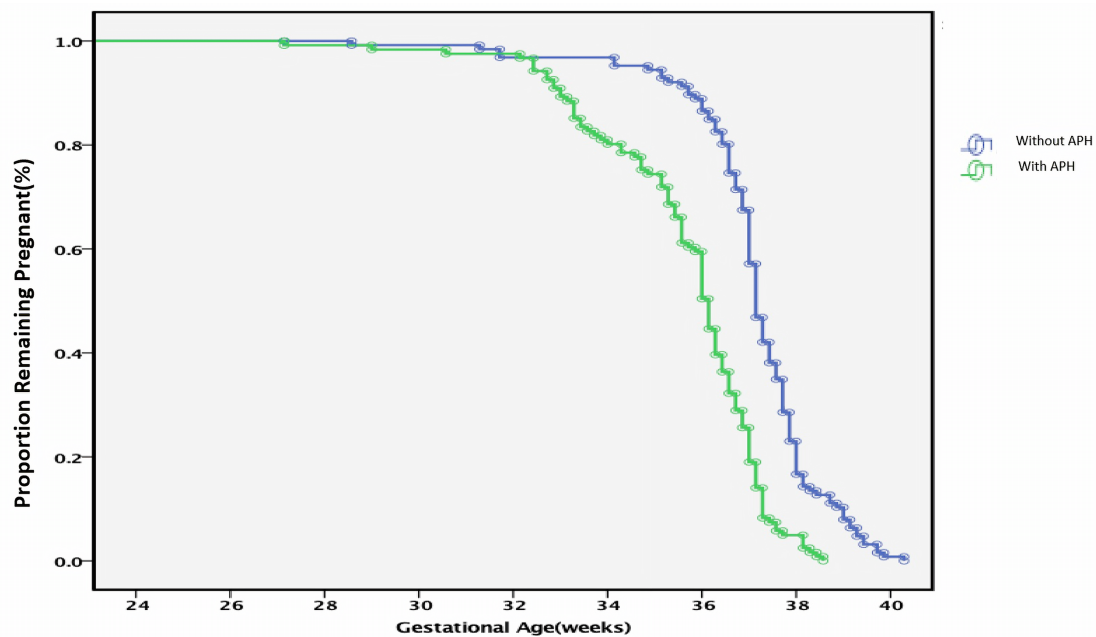


Fig. 2. Time to delivery for women with placenta previa with or without APH.

ine contractions (particularly after 32 weeks) may lead to a shortened cervical length and further separation of the placenta from the uterine wall, thus allowing hemorrhaging to occur more readily. Previous investigators have postulated that the etiology of APH in placenta previa comprises a poor blood supply that induces atrophy of thin portions of the placenta implanted over the cervix; this subsequently leads to placental migration as gestation continues, ensuring an improved blood supply from a more richly vascularized area (a process known as trophotropism) [11]. Oppenheimer *et al.* [12] reported that the placenta did not overlap the cervical orifice consistently; rather, placental migration occurred at an average rate of +5.4 mm/week, while the rate was only +0.3 mm/week in placenta previa. Uterine contractions, cervical effacement, and dilatation during the third trimester can also cause separation of the placenta, which leads to small amounts of bleeding; this bleeding may subsequently stimulate further placental separation and unavoidable hemorrhage [13].

Our finding of complete placenta previa as a risk factor for APH is consistent with prior studies. Bahar *et al.* [3] for example, reported that women with major (complete or partial) placenta previa manifested a significantly higher incidence of APH (OR, 3.18; 95% CI, 1.58–6.4;  $p = 0.001$ ). Similarly, Atsuko *et al.* [14] reported that APH was more prevalent in women with complete placenta previa compared to those with incomplete previa (59.1% vs. 17.6%; OR, 6.79; 95% CI, 3.31–13.92). Yang *et al.* [15] also reported a higher frequency of APH in complete previa compared to marginal previa. From these studies, it appears that complete previa is likely to be an independent risk factor in predicting APH in these patients. Some authors have also used ultrasonog-

raphy to identify short uterine cervical length (observed in the third trimester) and the sinus venosus at the margin of the placenta as risk factors for APH in placenta previa [16]. Regarding complete placenta previa, there may exist other risk factors for APH caused by placenta previa. Stafford *et al.* [17] demonstrated that in the third trimester, a cervical length of 30 mm or less was associated with an increased risk for hemorrhage (79% vs 28%) in placenta previa patients, whereas Saitoh *et al.* [18] reported that the risk of massive antenatal hemorrhage was higher (83.3%) in placenta previa patients with an echo-free space in the placental edge overlying the cervical orifice compared to other locations (7.7–10%). We must, however, admit that the evidence remains controversial, with other investigators showing contrasting results. Hasegawa *et al.* [19] maintained that the use of ultrasonography could not predict bleeding episodes, and according to the 2011 RCOG Green-top guidelines No.63, APH possesses a heterogeneous pathophysiology and thereby cannot be predicted reliably. Intriguingly, the location of the placenta was not reported to influence APH [14], and the anterior placenta may only increase hemorrhage during and after CD [20]. Contradicting our original hypothesis, placenta accreta did not serve as a protective factor in ameliorating APH.

With regard to maternal outcomes, we also demonstrated that recurrent or major APH enhanced hospitalizations, led to maternal anemia, and increased emergent CDs, blood transfusion rate, and total blood-product infusion; these findings were also confirmed by Takayama [21] and Crane *et al.* [22]. Although these authors also reported that APH elevated rates of hysterectomy [21] and PPH [22, 23], we did not find an increase in bleeding with hysterectomy or PPH in our study. In placenta previa, abundant blood flow enters



**Table 3. Neonatal outcomes in parturients with placenta previa.**

	Without APH (n = 126)	With APH (n = 121)	p value
Gestational age (weeks), mean $\pm$ SD	37.1 $\pm$ 1.6	35.6 $\pm$ 1.9	0.000
Newborn birth weight (grams), mean $\pm$ SD	2920 $\pm$ 524	2686 $\pm$ 544	0.000
Apgar score at 1 min, n (%)			0.003
$\leq 7$	23 (18.3)	42 (34.7)	
$> 7$	103 (81.7)	79 (65.3)	
Apgar score at 5 min, n (%)			0.090
$\leq 7$	7 (5.6)	14 (11.6)	
$> 7$	119 (94.4)	107 (88.4)	
Preterm delivery, n (%)	41 (32.5)	90 (74.4)	0.000
Endotracheal intubation of newborns, n (%)	40 (31.7)	52 (43.3)	0.060
NICU admission, n (%)	47 (37.3)	68 (56.7)	0.002
Antenatal corticosteroids, n (%)	12 (9.5)	67 (55.3)	0.000

APH, antepartum hemorrhage; NICU, neonatal intensive care unit.

the uterus not only from the internal iliac artery but also via anastomoses of the external iliac artery, inferior mesenteric artery, lumbar artery, and median sacral artery. Therefore, it is difficult to control bleeding [24].

We additionally treated our hysterectomy or PPH patients with various hemostatic methods including uterine balloons, B-Lynch sutures, arterial ligation, or bilateral uterine artery embolization. To avoid repeated or massive bleeding, scheduled CDs for placenta previa are performed at 36–37 weeks of gestation, and preterm CD is performed only when massive, uncontrollable hemorrhage or fetal distress occurs. The American Society for Maternal-Fetal Medicine (SMFM) and the RCOG guidelines both recommend delivery dates for placenta previa to be between 36<sup>+0</sup> and 37<sup>+0</sup> weeks of gestation for women who are stable and show no bleeding [1, 25]. In placenta previa patients with a history of vaginal bleeding or other associated risk factors, delivery should be considered between 34<sup>+0</sup> and 36<sup>+6</sup> weeks of gestation [1]. SMFM also recommends that for women with active hemorrhaging in the late preterm period, delivery should not be delayed for the purpose of administering antenatal corticosteroids [25].

In our study, 79 pregnant women received antenatal corticosteroids to prevent RDS because of irregular contractions or vaginal bleeding and were admitted 34 weeks ago. Antenatal corticosteroids are an essential component in the management of women at risk for preterm labor; they promote lung maturation and reduce the risk of other preterm neonatal complications [26].

Our research has shown that recurrent APH caused higher rates of NICU admission, preterm delivery, respiratory distress and other adverse neonatal outcomes, all of which are consistent with previous results [27–29]. Jing *et al.* [5] also reported that such adverse outcomes may be due to recurrent antenatal vaginal bleeding that affects the placental blood supply, which subsequently leads to insufficient fetal blood supply. The guidelines for the diagnosis and management of placenta previa also mention that recurrent hemorrhage, lo-

cal infection, and production of inflammatory factors in pregnant women with placenta previa stimulate uterine contractions, which can easily lead to premature birth [1]. In contrast, however, some investigators have not found that severe bleeding leads to increased adverse maternal or neonatal outcomes [30]. The discrepancies among these aforementioned studies may reflect differences in maternal background and patient management, and suggest that additional large, multicenter studies are needed to confirm the effects of APH on both maternal and neonatal outcomes.

To our knowledge, this is the first study to identify an association between APH in placenta previa patients and gestational week. Our work adds to the important literature regarding risk factors for APH and its significant implications for maternal and neonatal outcomes. Although it is difficult to reliably predict APH among women, we identified the third trimester—especially around 32 weeks—as a potential turning point with respect to bleeding risk. We also found complete placenta previa to be an independent risk factor for APH in this specific patient population.

Several limitations to this study should be noted. First, this was a relatively small study limited to one healthcare system, which may result in informational and regional biases that require increased case numbers and an expanded research area. Second, because of the retrospective nature of the study design, we were unable to collect and report on data regarding other important information, including the amount of APH, cervical length, neonatal arterial pH data, and long-term neonatal complications. In the future, large prospective studies are needed to assist clinicians and researchers in better understanding the risks and implications of APH in placenta previa patients.

## 5. Conclusions

The gestational week and frequency of APH varied by patient with placenta previa and might have resulted in an increase in adverse maternal and neonatal outcomes. Clinicians

should thus be cognizant of placenta previa as increasing the risk for prenatal bleeding, especially in the third trimester at approximately the 32nd gestational week. It is also important for clinicians to recognize that women who do experience APH may be at higher risk for requiring blood transfusions and undergoing emergent CD, and their newborns are at an increased likelihood for manifesting lower birth weight, asphyxia, and additional NICU admissions. Pediatric involvement in the delivery of these patients may therefore be warranted. Thus, healthcare providers should consider transferring patients with complete placenta previa to a tertiary medical center to tailor their personal antenatal management, identify potential risks and outcomes, and provide advanced, multidisciplinary care to prevent adverse consequences.

## Abbreviations

CD, Cesarean delivery; APH, Antepartum hemorrhage; PHS, Partners Healthcare System; EMR, Electronic medical records; BMI, Body mass index; IVF, *In vitro* fertilization; PRBC, Packed red blood cells; FFP, Fresh frozen plasma; PPH, Postpartum hemorrhage; EBL, Estimated blood loss; HGB, Hemoglobin; HCT, Hematocrit; SPSS, Statistical Package for the Social Sciences; SD, Standard deviation; OR, Odds ratio; CI, Confidence interval; SMFM, Society for Maternal-Fetal Medicine.

## Author contributions

WJQ and LW drafted the manuscript and participated in data collection and analysis; DL, LMW and XY reviewed the manuscript; LL analyzed data and prepared the manuscript; AV performed the statistical analysis and reviewed the manuscript; and JZ contributed to the development of the study, the study design, and manuscript preparation for publication. All authors read and approved the final manuscript.

## Ethics approval and consent to participate

The authors confirm that they obtained approval by the Ethics Committee of Brigham and Women's Hospital, Harvard Medical School (Protocol#2019P000028); and that written consent for use of the data in scientific research was also acquired from patients before operation.

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## Conflict of interest

The authors declare no conflict of interest.

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