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MATERNAL-FETAL MEDICINE

Placenta previa: an outcome-based cohort study in a contemporary obstetric population

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Abstract
Objective The objective of the study is to characterize the maternal and neonatal morbidities of women with placenta previa.
Study design This retrospective group study used the Consortium on Safe Labor electronic database, including 12 clinical centers, and 19 hospitals. Patients with placenta previa noted at the time of delivery were included. Maternal and neonatal variables were compared to a control group of women undergoing cesarean delivery with no previa. Logistic regression and general linear regression were used for the analysis, with $p < 0.05$ significance.
Results There were 19,069 patients in the study: 452 in the placenta previa group and 18,617 in the control group. Neonates born to mothers with placenta previa had lower gestational ages and birth weights. In univariate analysis only, these neonates were at increased risk of lower 5 min Apgar scores, neonatal intensive care unit admission, anemia, respiratory distress syndrome, mechanical ventilation, and intraventricular hemorrhage. There was no association of placenta previa with small for gestational age infants, congenital anomalies or death. As previously shown, women with placenta previa have significantly more maternal morbidities.
Conclusion Increased maternal morbidity was noted; however, only those neonatal morbidities associated with preterm delivery occurred in the placenta previa group.

Keywords Placenta previa · Neonatal morbidity · Neonatal outcomes · Maternal outcomes

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Introduction

Placenta previa, defined as a placenta that is located over or within 2 cm of the internal cervical os, is an abnormality complicating 0.3–1 % of all deliveries, with variance in the number due to when placenta previa is defined in the pregnancy [1–3]. Clinically, these patients present with vaginal bleeding, classically in the third trimester and are at an increased risk of morbidity [3]. Investigations have documented adverse events such as peripartum hysterectomy, blood transfusion, vasa previa, postpartum hemorrhage and sepsis [3]. Additional reports have addressed similar findings, revealing that these patients had a significant chance of longer hospital stays, higher blood loss at the time of surgery and increased need for blood transfusion, especially if placenta accreta was present [4].

In addition to maternal complications, there are neonatal complications associated with placenta previa, often related to preterm delivery [5–8]. In women with a known placenta previa, prior studies report a 14-fold increase in the preterm birth rate [8]. Two reports have demonstrated increased mortality in neonates born to women with known placenta previa at term [1, 9]. Other investigators, however, have documented no change in perinatal mortality [3, 5].

An increase in congenital anomalies and neonatal anemia was further demonstrated by Cran et al. [5].

Due to the abnormal placentation associated with placenta previa and possible utero-placental insufficiency, it is plausible that neonates of patients with placenta previa could be at an increased risk for intrauterine growth restriction or decreased fetal growth as compared to gravidas without placenta previa. Studies report differing findings, with some showing that intrauterine growth restriction does occur in the neonates [3, 6]. Other investigations revealed no differences in growth between control populations without placenta previa and women with placenta previa [5, 10].

As the prevalence of cesarean delivery is rising, and thus, the possibility of increasing numbers of women with placenta previa, it is important to clearly define the complications, both maternal and neonatal, that are associated with this diagnosis. Previous investigators compared their previa cases to the general population, so it is not surprising that marked increases in complications were noted. The primary objective of our study was to report the neonatal outcomes associated with placenta previa known at the time of delivery compared to those undergoing cesarean delivery, without placenta previa in a large contemporary population. The secondary objective of the study was to report the maternal outcomes associated with placenta previa.

Study design

This retrospective study was performed using the Consortium on Safe Labor database. Data was obtained from the electronic medical records at each contributing institution from 2002 to 2008. The complete database contained 233,730 deliveries from 12 clinical centers from 19 distinct hospitals across nine American Congress of Obstetricians and Gynecologists districts. Detailed description of the study is provided elsewhere [11, 12]. Institutional Review Boards of all participating institutions approved the initial data collection.

All patients with placenta previa noted either at admission for delivery or as a reason for cesarean delivery were included in the study group. The control group was defined as women undergoing cesarean delivery, without placenta previa, for any indication. Inclusion criteria for both groups were first pregnancy in the database and singleton gestation. None of the women in the study underwent trial of labor, defined as more than two cervical exams in the database or a vaginal delivery. The definition of placenta previa in the Consortium on Safe Labor Database was a yes or no response to whether placenta previa was present. No further information regarding the definition of placenta previa was included in the database, i.e., marginal, complete or distance from the internal cervical os. Placenta accreta was defined as yes or no response as to whether placenta accreta was present. Admission reason and indication for cesarean delivery were analyzed for each group. Baseline maternal demographics were obtained, including maternal age, gravidity, parity, prepregnancy weight, prepregnancy body mass index (BMI), race, education, presence of pregestational diabetes, highest level of education and marital status. Neonatal outcomes studied included gestational age at delivery, Apgar score at 5 min, cord arterial pH, birth weight, neonatal intensive care unit (NICU) admission, respiratory distress syndrome, need for mechanical ventilation, intraventricular hemorrhage, anemia, congenital anomalies, small for gestational age, defined as <10 % for birthweight, and neonatal death. Maternal outcomes studied included the incidence of postpartum hemorrhage, need for blood transfusion, ICU admissions, cesarean hysterectomy and maternal death. The above stated outcomes were acquired for the women and their neonates in both groups, and then were compared between the placenta previa group and the cesarean delivery group.

Mean and standard deviations were used to present continuous variables with normal distribution while median and interquartile ranges were used in non-normally distributed data. Categorical variables were presented as count and percentages. Chi-square test/Fischer exact test, and two-sample t test/Wilcoxon rank-sum test were used for comparison of categorical and continuous variables, accordingly. Logistic regression and general linear regression were used for the univariate and multivariable analysis. A multivariable analysis was performed to control for confounding variables. Odds ratios (OR) and 95 % confidence intervals (CI) for categorical outcomes and difference in means for continuous outcomes were reported. A p value <0.05 was considered significant. SAS software (version 9.2; SAS Institute Inc, Cary, NC, USA) was used for all analyses.

Results

There were 19,069 total patients in our study: 452 in the placenta previa group and 18,617 in the cesarean delivery, without placenta previa, group. Of the total database, 0.2 % patients were diagnosed with placenta previa at the time of delivery. The mean age in the placenta previa group was older, 31.7 years compared to 30.4 years in the cesarean delivery group, $p < 0.01$ (Table 1). There was no difference in gravidity and parity between the two groups, $p = 0.36$ and 0.12, respectively. Prepregnancy weight and BMI were significantly lower in the placenta previa group.

Table 1 Maternal demographics of study group, women with placenta previa, and controls, women without placenta previa delivered via cesarean delivery

	Placenta previa $n = 452$ Mean ± SD % (n)	Cesarean delivery—no previa $n = 18{,}617$ Mean ± SD % (n)	p
Maternal age	31.7 ± 6.1	30.4 ± 6.3	<0.01
Parity	1.3 ± 1.5	1.4 ± 1.2	0.12
Gravidity	3.2 ± 2.0	3.1 ± 1.8	0.36
Prepregnancy weight (kg)	66.4 ± 15.5	72.9 ± 20.7	<0.01
Prepregnancy BMI (kg/m^2)	24.8 ± 5.7	27.6 ± 7.4	<0.01
Maternal race			<0.01
White	44.3 % (189)	41 % (7,279)	
Black	22.5 % (96)	30.5 % (5,461)	
Hispanic	22.3 % (95)	21.1 % (3,765)	
Other	11.0 % (47)	7.7 % (1,382)	
Pregestational diabetes	3.0 % (13)	4.9 % (865)	0.07

There were significant differences in the races and marital status of the two groups, $p < 0.01$. There was no difference in the education level or presence of diabetes between the two groups, $p = 0.75$ and $p = 0.12$.

Indications for cesarean delivery were analyzed for each group. More women in the cesarean delivery group had an elective cesarean delivery, 25 % compared to 0.66 % in the placenta previa group. There was no difference recorded in emergency cesarean deliveries or cesarean section for fetal anomalies between the two groups. More women in the cesarean delivery group had their cesarean deliveries performed for nonreassuring fetal heart rate tracings, 8.3 % compared to 1.3 %; $p \leq 0.01$.

The reason for admission between the two groups was significantly different; $p < 0.01$. Significantly more women in the cesarean delivery group were admitted for elective reasons, 53.2 %, compared to 34.7 % in the placenta previa group. Significantly fewer women in the cesarean delivery group were admitted for maternal indications, 4.0 % compared to 25.2 % in the placenta previa group. Other reasons for admission included fetal indications, 2.8 % in the cesarean delivery group and 6.2 % in the placenta previa group, labor, 11.5 % in the cesarean delivery group and 6.2 % in the placenta previa group, rupture of membranes, 3.8 % in the cesarean delivery group and 2.2 % in the placenta previa group. 24.2 and 24.3 % of cases in the cesarean delivery group and placenta previa group, respectively, were admitted for other/unknown reasons.

The neonatal outcomes for the study population were analyzed. The average gestational age at delivery for the placenta previa group was 36.2 weeks and the average gestational age for the cesarean delivery group was 38.1 weeks, a difference of 1.9 weeks, $p < 0.01$ (Table 2). The birth weights of the infants born to mothers with known placenta previa were less than the infants of those born to mothers in the cesarean delivery group; 2,806 g compared to 3,285 g, $p < 0.01$. NICU admissions were more likely in the placenta previa group, 39.2 % (177) compared to 18.6 % (3467), OR 2.8 (2.3–3.4), $p < 0.01$. There were significantly more adverse neonatal outcomes in the placenta previa group, including respiratory distress syndrome, intracerebral hemorrhage, need for mechanical ventilation and anemia, $p < 0.01$. There were no differences in the presence of congenital anomalies, 10.6 % (48) in the placenta previa group and 9.4 % (1,745) in the cesarean delivery group, OR 1.1 (0.8–1.6), $p = 0.37$. The presence of small for gestational age infants was not different in the two groups, 5.5 % (24) in the placenta previa group and 7.1 % (1,292) in the control group, $p = 0.19$. There were no neonatal deaths in the study group.

Because gestational age, birth weight and indication for cesarean delivery are so closely related to many of the neonatal variables that were assessed, a multivariable analysis was performed to adjust for these variables (Table 2). Frequency of NICU admission was no longer significantly different between the groups of neonates after correction for cofounders in the multivariable analysis, OR 1.0 (0.8–1.3). In addition, all other neonatal variables, including 5 min Apgar score, cord arterial pH, intracerebral hemorrhage, presence of anemia, need for mechanical ventilation and respiratory distress syndrome were no longer significantly different between the two groups. Congenital anomalies were not significantly different between the two groups, OR 0.8 (0.6–1.1), nor was small for gestational age infants, OR 0.9 (0.4–1.7).

Mothers who delivered via cesarean delivery for placenta previa were significantly more likely to have postpartum hemorrhage and receive blood transfusions (Table 3). Placenta accreta was significantly more common in the placenta previa group; 8.3 % (19) compared to 0.3 %

Table 2 Neonatal outcomes of the study group, neonates born to women with placenta previa, and controls, neonates born to women without placenta previa delivered via cesarean delivery

	Placenta previa $n = 452$	Cesarean delivery—no previa $n = 18{,}617$	OR (95 % CI) or diff in means	p	Adjusted OR[a] (95 % CI)
Gestational age at delivery (weeks)	36.2 ± 2.9	38.1 ± 2.4	−1.9	<0.01	–
Birth weight (g)	2,806 ± 639	3,285 ± 652	−479	<0.01	–
Arterial pH	7.2 ± 0.1	7.2 ± 0.1	0	<0.01	–
5 min Apgar	8.69 ± 0.9	8.81 ± 0.7	−0.12	<0.01	–
NICU admission	39.2 % (177)	18.6 % (3,467)	2.8 (2.3–3.4)	<0.01	1.0 (0.8–1.3)
Respiratory distress syndrome	9.5 % (43)	3.5 % (645)	2.9 (2.1–4.1)	<0.01	1.0 (0.6–1.5)
Mechanical ventilation	8.5 % (38)	3.4 % (635)	2.6 (1.9–3.7)	<0.01	1.1 (0.7–1.6)
Intraventricular hemorrhage	0.7 % (3)	0.3 % (53)	2.3 (0.7–7.5)	0.14	1.4 (0.4–4.7)
Anemia	8.5 % (38)	2.7 % (500)	3.3 (2.4–4.7)	<0.01	1.4 (0.9–2.1)
Congenital anomalies	10.6 % (48)	9.4 % (1,745)	1.1 (0.8–1.6)	0.37	0.8 (0.6–1.1)
Small for gestational age	5.5 % (24)	7.1 % (1,292)	0.7 (0.5–1.2)	0.19	0.9 (0.4–1.7)
Neonatal death	0	0	–	–	–

[a] Adjusted for gestational age at birth, birthweight and indication for cesarean delivery

Table 3 Maternal outcomes in the study group, women with placenta previa, and controls, women without placenta previa delivered via cesarean delivery

	Placenta previa $n = 452$	Cesarean delivery—no previa $n = 18{,}617$	OR or diff in means (95 % CI)	p	Adjusted OR[a] (95 % CI)
Postpartum hemorrhage	4.2 % (12)	0.7 % (80)	6.4 (3.5–11.9)	<0.01	4.8 (1.9–12.6)
Blood transfusion	8.8 % (19)	1.9 % (184)	5.1 (3.1–8.3)	<0.01	4.6 (2.3–9.4)
Cesarean hysterectomy	2.7 % (12)	0.2 % (36)	14.1 (7.3–27.2)	<0.01	8.6 (2.7–26.9)
Placenta accreta	8.3 % (19)	0.3 % (23)	36.8 (19.7–68.5)	<0.01	71.9 (22.9–225.5)
Intensive care unit admission	1.3 % (4)	0.5 % (67)	2.7 (1.0–7.6)	0.04	3.9 (1.2–12.0)
Maternal death	0	0.03 % (5)	0.1 (0.01–999)	0.72	0.1 (0.01–999)

[a] Adjusted for previous cesarean delivery, prepregnancy BMI and indication for cesarean delivery

(23) in the control group, OR 36.8 (19.7–68.5). Twelve women, 2.7 %, in the placenta previa group had a cesarean hysterectomy, compared to 0.2 % (36) in the cesarean delivery group; OR 14.1 (7.3–27.2), $p < 0.01$. Intensive care unit admissions were also higher in the placenta previa group; 1.3 % (4) versus 0.5 % (67) in the cesarean delivery group, OR 2.7 (1.0–7.6). After correction for confounding factors, all maternal outcomes had a higher odds for patients undergoing cesarean delivery for known placenta previa (Table 3). There were five maternal deaths, all in the cesarean delivery without placenta previa group.

Discussion

Placenta previa was present in 0.2 % of patients in the Consortium on Safe Labor database. Interestingly, the morbidity was all maternal, without any increased neonatal morbidity or mortality present in the placenta previa group, once correction for the confounding variable of gestation age was performed. As risk factors for placenta previa have been well defined in prior studies, we focused on the outcomes associated with the condition. Women with a diagnosis of placenta previa, not surprisingly, are at an increased risk of postpartum hemorrhage, OR 4.8, ICU admission, OR 3.9, and blood transfusions, OR 4.6. Placenta previa is also associated with placenta accreta; 8.3 % of women undergoing cesarean delivery for placenta previa were also diagnosed with placenta accreta. As would be expected, patients with known placenta previa were delivered earlier than our control group, by approximately 1.9 weeks. In our univariate analysis, we noted that all these associated neonatal outcomes were more prevalent with previa. However, after adjustment for gestational age, birth weight and indication for cesarean delivery our neonatal outcomes were no longer significantly different from

the controls, suggesting that these were most likely secondary to the lower gestational age and lower birth weight of our infants born to mothers with known placenta previa.

The purpose of this paper was to address the complications associated with the diagnosis of placenta previa in a contemporary obstetrics population, specifically focusing on neonatal outcomes, as these are not as well described as the maternal morbidities associated with placenta previa. A strength of our work was the large number of patients included. We were able to obtain patient information from a contemporary, diverse population, thus, making it applicable to many obstetric practices. Often times, when using a retrospective database, the definition and ability to obtain medical diagnoses can be difficult. In our case, placenta previa was a straightforward diagnosis that would be obvious to the clinician at the time of cesarean delivery. Our study is unique in that our comparison group was a group of women undergoing cesarean delivery without previa. This group comparison accounted for the fact that all women with placenta previa undergo cesarean delivery, thus, all the patients in our study underwent the surgical component and thereby decreased confounding, especially for maternal outcomes. In addition, women with placenta previa typically are delivered prior to ensuing labor, so this would make our groups more equal, than comparing placenta previa patients to the general population. In addition, the diagnosis of placenta previa was made at the time the patient presented for admission to labor and delivery, unlike studies that used an antenatal diagnosis of placenta previa. This ensured that patients with resolved placenta previa, diagnosed at the time of their anatomy or a growth ultrasound, were not included, as these patients were unlikely to have the same outcomes as women who have a placenta previa at term. However, because we used this strict timing in the definition of placenta previa, this may have caused the total percentage of women with placenta previa to be lower than reported in previous studies. The number of women in our study with placenta previa was 0.2 %, and only included women who had a placenta previa diagnosed at the time of delivery, and not at any other time in their antenatal course.

The limitations of this study include the retrospective nature. As the data were previously collected, and many times answered in a yes or no fashion, we cannot extract further information regarding some of the variables. In addition, since some variables were coded as yes or no, i.e., congenital anomalies, it is possible that the number of these was higher than the actual number of neonates with congenital anomalies. As some of the neonatal morbidities shown can be associated with operator inexperience or incision to delivery times and this was not accounted for in our study, this could have introduced some bias. There were five maternal deaths in the cesarean delivery group. Further information was unable to be elucidated as we used an existing database, and this remains a limitation of such work. Our findings for increased risk of postpartum hemorrhage, ICU admission and blood transfusions in the placenta previa group are similar to previously reported studies. In a study by Zlatnik et al. [7], an adjusted odds ratio for postpartum hemorrhage of 5.9 (4.1–8.4) and adjusted odds ratio for blood transfusion 9.3 (4.8–18.1) were analogous to our findings. Similarly, in a population-based study of women with known placenta previa, with an incidence of 0.42 %, there were higher rates of blood transfusion and postpartum hemorrhage [3]. In addition, placenta previa is a known risk factor for placenta accreta. Placenta accreta confers greater blood losses, blood transfusions, and possibly cesarean hysterectomies [4]. In a patient with a known placenta previa, the chance of having a placenta accreta with one prior cesarean delivery is 3.3 % and rises steadily with each additional cesarean delivery, up to 11 % with two prior cesarean deliveries and to 61 % with four prior cesarean deliveries [13]. In a case study of women with placenta previa, the rates of placenta accreta were even higher, 1.9 % with no prior cesarean deliveries, and up to 50 % with five prior cesarean deliveries [4]. The accreta rate for our patients with known placenta previa was 8.3 %, regardless of the number of prior cesarean deliveries. We did not track the number of cesareans in either group, but our rate was closer to those with two previous cesarean deliveries, as reported in a prior study. When placenta accreta is diagnosed antenatally and confirmed surgically, typically, a hysterectomy is performed, with the placenta left in situ [13]. The significantly increased rate of placenta accreta in our previa group most likely accounts for the significant increase in cesarean hysterectomy between the two groups; 2.7 % in the placenta previa group, compared to 0.2 % in the control group, OR 8.6 (2.7–26.9). We have confirmed these previously reported findings of adverse maternal sequelae known to be associated with placenta previa, even when comparing them to a control group of women undergoing surgical delivery.

Our neonatal findings were similar to prior studies, in that women with placenta previa delivered 2.1 weeks earlier than women without placenta previa [8]. Since these neonates are born at earlier gestational ages, they had higher rates of neonatal complications associated with prematurity, as we found with our univariate analysis. In the multivariable analysis, these findings were no longer significant. In both the univariate and multivariable analyses, the presence of small for gestational age infants was not significantly associated with placenta previa in our study. In addition, the total number of SGA infants in the entire Consortium on Safe Labor database was 10 %, which is similar to the control group, suggesting it is not

elevated by the control group which was selected. 10 % of SGA infants in the entire Consortium on Safe Labor database is significantly higher than that in our placenta previa group of 5.5 %, $p < 0.01$. As this was a retrospective database, ultrasound information and specific data on intrauterine growth restriction were not available so instead, a surrogate marker, small for gestational age, was utilized to assess this. Three recent studies, one from 2011, a population-based study, one from 2012, a literature review, and one from 2013, a population-based cohort study, found that placenta previa was associated with intrauterine growth restriction; one noted an 3.20-fold increased risk (2.50–4.10) [3, 12, 14]. Even with term deliveries, it was demonstrated that infants born to mothers with placenta previa were significantly smaller [6, 8]. One prior study reported no effect of placenta previa on fetal growth restriction [10]; however, they defined placenta previa as the presence of placenta previa diagnosed at routine anatomy ultrasound, typically around 20 weeks gestation. We believe that our comprehensive nationwide large database, with cases of placenta previa noted to be present at the time of delivery, a precise, well-defined small for gestational age variable, defined as <10 % birthweight for gestational age, and similar number of placenta previa in our group compared to other investigators is a good depiction of a standard obstetric population. We demonstrated no difference in the rates of small for gestational age infants born to mothers with known placenta previa.

Finally, we demonstrated no increased risk of congenital anomalies, OR 0.8 (0.6–1.1) in the placenta previa group. Interestingly, however, our rate of congenital anomalies, 10.6 %, was similar to previously reported rates of neonates with congenital anomalies born to women with placenta previa, up to 11.5 % [3]. Prior studies have suggested there is an increased incidence of congenital anomalies in neonates born to mothers with placenta previa, possibly doubling the risk, from 5.1 to 11.5 % [3]. Two additional studies reported OR of 1.77 and 2.6 for congenital anomalies in infants born to mothers with placenta previa [6, 15]. As the rates of congenital anomalies reported were high in the entire Consortium on Safe Labor database, it is difficult to make accurate comparisons or draw conclusions, regardless of the groups used. As placenta previa is a condition of placental implantation, and most significant in the late second to third trimester, it would make clinical sense that the risk of congenital anomalies was not affected by this condition, as organogenesis is mostly complete by the end of the first trimester. Our findings support this hypothesis.

Placenta previa is a problem for obstetricians and neonatologists, in part due to the rising cesarean delivery rate. Because it is seen relatively frequently, an awareness of the complications associated with this condition is important in counseling patients. We designed an investigation with decreased confounding factors and clear definitions. The outcomes addressed in the paper are pertinent not only for educational reasons, but will serve clinicians well in practice. Maternal risks have been confirmed and were again demonstrated in our study. Neonates born to mothers with placenta previa at the time of cesarean delivery are more likely to be delivered preterm, have lower birthweights and are more likely to require neonatal intensive care unit admission. As our multivariate analysis demonstrated, this increased morbidity appears to be more likely related to the gestational age and birthweight of the neonate, as opposed to the maternal condition of placenta previa. Increased awareness of the expected complications allows physicians to adequately prepare themselves, their teams and their patients for the best possible outcomes.

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Conflict of interest We declare that we have no conflict of interest.

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