

Placenta Previa and Adverse Neonatal Outcomes in A Tertiary Center

Üçüncü Basamak Bir Merkezde Plasenta Previa ve Olumsuz Yenidoğan Sonuçları

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Abstract

Objective: Abnormal localization of the placenta with complete or partial closure of the cervix is called placenta previa. Placenta previa occurs in approximately 0.3-0.5% of pregnancies. In this study, we aimed to determine the risk factors and adverse fetal outcomes by comparing the neonatal outcomes of patients who underwent cesarean section for placenta previa with those of patients who underwent cesarean section for other indications.

Method: Patients with singleton pregnancies diagnosed with placenta previa were retrospectively analyzed. Placenta previa, risk factors, and adverse neonatal outcomes were estimated using multivariate logistic regression models.

Results: A total of 61,110 deliveries were analyzed, and 632 deliveries (288 patients, 344 controls) were included in the study. The prevalence of placenta previa was 0.47%. Advanced maternal age [odds ratio (OR)=3.03], multigravida (≥ 5) (OR=2.31), previous abortion (OR=1.58) and curettage (OR=2.32) were significant risk factors for placenta previa. However, these patients had an increased risk of 1st minute Apgar score < 7 (OR=1.59) and neonatal intensive care unit (NICU) admission (OR=2.15). At the same time, the risk of Apgar score < 7 at 1 min (OR=5.59) and 5 min (OR=3.94) and NICU admission (OR=28.47) increased in infants of patients with placenta previa < 34 weeks. Newborns in the > 37 weeks

Öz

Amaç: Plasentanın, serviksi tam ya da kısmen kapatarak anormal lokalizasyonda olmasına plasenta previa denir. Plasenta previa, gebeliklerin yaklaşık %0,3-0,5'inde görülür. Bu çalışmada plasenta previa nedeniyle sezaryan olmuş hastaların yenidoğan sonuçları ile başka endikasyonlarla sezaryan olmuş hastaların yenidoğan sonuçları karşılaştırılarak risk faktörleri ve olumsuz fetal sonuçları tespit etmeyi amaçladık.

Yöntem: Plasenta previa tanısı almış tekil gebeliği olan hastalar retrospektif olarak analiz edildi. Plasenta previa, risk faktörleri ve bu durumun oluşturabileceği olumsuz neonatal sonuçlar çok değişkenli lojistik regresyon modelleri ile tahmin edildi.

Bulgular: Toplam 61.110 doğum analiz edilmiş ve 632 doğum (288 hasta, 344 kontrol) çalışmaya dahil edilmiştir. Plasenta previa prevalansı %0,47 idi. İleri anne yaşı [olasılık oranı (OO)=3,03], multigravida (≥ 5) (OO=2,31), önceki abortus (OO=1,58) ve küretaj (OO=2,32) plasenta previa risk faktörleri için anlamlı bulunmuştur. Bununla beraber bu hastalarda 1. dakika Apgar skoru < 7 (OO=1,59) ve yoğun bakım ünitesine (YYBÜ) (OO=2,15) kabul riski artmıştır. Aynı zamanda < 34 hafta hafta olan plasenta previa bulunan hastaların bebeklerinde 1. dakikada (OO=5,59) ve 5. dakikada (OO=3,94) Apgar skorunun < 7 olması ve YYBÜ'ye kabul (OO=28,47) riski artmıştır. Plasenta previa bulunan > 37 haftalık gebelik yaşı grubundaki yenidoğanların daha düşük doğum ağırlığına (OO=4,21)

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Abstract

gestational age group with placenta previa were more likely to have a lower birth weight (OR=4.21) and an Apgar score <7 at 5 min (OR=1.89).

Conclusion: Pregnancies with a diagnosis of placenta previa were associated with an increased risk of serious fetal outcomes compared with cesarean deliveries for all other indications, regardless of delivery timing.

Keywords: Neonatal, outcome, placenta previa

Öz

ve 5. dakikada <7 Apgar skoruna (OR=1,89) sahip olma olasılığı daha yüksektir.

Sonuç: Plasenta previa tanısı konan gebelikler, doğum zamanlamasından bağımsız olarak, diğer tüm endikasyonlar için sezaryen ile yapılan doğumlara kıyasla ciddi fetal sonuç riski ile ilişkilendirilmiştir.

Anahtar kelimeler: Neonatal, plasenta previa, sonuç

Introduction

In obstetrics, implantation of the placenta in an abnormal location close to the uterine isthmus, just above or near the internal os, is called placenta previa (1). This condition can be observed in approximately 0.3-0.5% of all pregnancies, and this rate has increased in the last 30 years (2). Although there are different opinions regarding the etiology, the exact cause has not been established. However, it has been associated with well-established demographic factors such as advanced maternal age (3), multiparity (4), smoking, and cocaine use (5) as well as clinical features such as one or more cesarean deliveries (6), previous uterine incision (7), placenta previa in previous pregnancy (8), multiple pregnancy (9) and use of assisted reproductive techniques (10).

Pregnant women with placenta previa may have adverse maternal complications such as death, maternal hypovolemia, blood transfusion, and emergency hysterectomy due to severe bleeding (11), and their newborns have an increased risk of low birth weight (LBW), fetal anomalies, stillbirth, and early neonatal death (12). Women with placenta previa are managed according to their clinical condition; however, almost all women with placenta previa and no bleeding undergo planned prophylactic preterm cesarean delivery, which balances the risks of maternal antepartum bleeding and fetal immaturity. The Society for Maternal Fetal Medicine (SMFM) recommends waiting until 36-37 6/7 weeks of gestation for delivery, especially in stable patients without bleeding and other obstetric complications (Level of Evidence: Grade 1B) (13).

In our study, we aimed to investigate whether placenta previa alone is a risk factor for neonatal outcomes by comparing the neonatal outcomes of patients who were followed up for placenta previa and who underwent cesarean delivery with those of patients who underwent cesarean delivery for all other indications; both groups included preterm deliveries.

Understanding this will allow us to better manage and prevent adverse neonatal outcomes.

Materials and Methods

This was a retrospective cohort study of women with singleton pregnancies who delivered between January 2012 and December 2015 at our institution, a tertiary referral hospital. Data were retrieved from the local perinatal database, medical documentation system, or patient files. This study was approved by the institutional review board. Ethical approval was obtained from the Ethics Committee University of Health Sciences Turkey, İstanbul Kanuni Sultan Süleyman Training and Research Hospital (date: 02.05.2015, number: 2014/10). Written informed consent was obtained from all patients and controls.

We recruited all patients with a definitive diagnosis of placenta previa who underwent cesarean section due to placenta previa. Placenta previa was defined as the placenta covering all or part of the internal os, as diagnosed through ultrasound during the second or third trimester, and the diagnosis was confirmed at cesarean delivery. The control group comprised healthy pregnant individuals without placenta previa who underwent elective cesarean section for all other indications. Patients with incomplete data in their medical files, multiple pregnancies, chronic disease, and fetuses with major congenital anomalies were excluded.

Demographic data including maternal age, obstetric history (gravidity, parity, prior cesarean section/vaginal delivery/abortion/curettage), and neonatal outcome variables [gestational age at delivery, birth weight, Apgar score at minute 1, Apgar score at minute 5, and neonatal intensive care unit (NICU) admission] were recorded. Gestational age was based on the last menstrual period, first-trimester ultrasound, or both. LBW was defined as a birth weight of 2500 g (up to and including 2499 g). The Apgar score was

defined as a measure of the physical condition of a newborn infant. The Apgar score has maximum ten points, with two points possible for each heart rate, muscle tone, response to stimulation, and skin coloration. Apgar scores between 0 and 6 were recorded as low Apgar scores. NICU admission was considered when infants were intubated.

The study population was initially divided into two groups: Those born by cesarean section because of placenta previa (patient group) and those born by cesarean section for all other indications (control group). Both groups were further stratified into three subgroups based on the gestational age because studies (14) have consistently shown higher neonatal mortality and morbidity in preterm infants: <34 weeks, 34-36 weeks, and ≥ 37 weeks. The incidence of adverse neonatal outcomes was examined in each group.

Statistical Analysis

NCSS 10 statistical software (Kaysville, Utah, USA) was used for data recording and statistical analysis. Statistical analyses were performed using descriptive statistics, independent samples t-test, and Mann-Whitney U test, when appropriate, applying a significance level of $p < 0.05$. Categorical variables were analyzed using the chi-square test and Yates's chi-square test. Covariance analysis was performed, and the variables found to differ were reanalyzed because the age variable was different between the groups. Variables are given as mean, standard deviation, median, minimum, maximum, frequency, and percentage.

Results

In our study, a total of 61,110 deliveries were evaluated, and 288 of them (0.47%) were diagnosed with previa. placenta Apart from this group, 344 control patients were included in the study, and the total number of patients participating in the study was 632. The mean age of pregnant women complicated with previa was significantly higher than that

of the control group. Similarly, gravida, parity, previous curettage, and curettage rates were also found to be significantly higher ($p=0.001$, $p=0.048$, $p=0.014$ and $p=0.007$, respectively). The percentage of previous cesarean section was significantly higher in the control group ($p < 0.001$); however, the mean number of cesarean sections was similar for both groups (1.2 ± 1.01 for the patient group and 1.1 ± 0.73 for the control group, $p=0.869$). Demographic data and risk factors of all patients and the control group participating in the study are shown in Table 1.

In our study, it was observed that patients complicated with placenta previa were older than those who underwent cesarean section for all other reasons. Pregnancies complicated with placenta previa were significantly more common in multigravida women in the <34 weeks and ≥ 37 weeks gestational age groups and higher in the 34-36 weeks group. Previous miscarriage was significantly more frequent in the <34 weeks group and previous curettage was significantly more frequent in the 34-36 weeks group. As in the main groups, previous cesarean section was more common in all control groups, reaching statistical significance in the <34 weeks and ≥ 37 weeks groups ($p=0.004$ for each). However, the mean number of cesarean sections was not significantly higher in either previa group (1.4 ± 1.25 vs. 1.1 ± 0.61 , $p=0.193$ in the <34 weeks group and 1.11 ± 0.962 vs. 1.09 ± 0.656 , $p=0.843$ in the ≥ 37 weeks group). The demographic characteristics and risk factors of the subgroups in our study are shown in Table 2.

After adjusting for the factors that may cause differences between the two groups, advanced maternal age (≥ 35 years) [odds ratio (OR) =3.03; 95% confidence interval (CI): 1.99-4.59], multigravida (≥ 5) (OR=2.31; 95% CI: 1.43-3.73), previous abortion (OR=1.58; 95% CI: 1.10-2.25) and previous curettage (OR=2.32; 95% CI: 1.26-4.29) were found to be significant risk factors for placenta previa. History of vaginal delivery or previous cesarean section was not

Table 1. Maternal characteristics in pregnancies with and without placenta previa

	Placenta previa group (n=288)	Control group (n=344)	p
Maternal age at index birth (years)	31.5 \pm 5.14	28.5 \pm 5.19	<0.001
Gravidity	3.1 \pm 1.45	2.8 \pm 1.25	0.001
Parity	1.5 \pm 1.11	1.4 \pm 0.98	0.048
Previous cesarean section	69.4%	82.8%	<0.001
Previous vaginal delivery	20.5%	16.3%	0.180
Previous abortion	30.9%	22.1%	0.014
Previous curettage	10.8%	4.9%	0.007

All values are expressed as mean \pm SD and percentage, where appropriate, SD: Standard deviation

significantly associated with placenta previa. Neonates in the patient group were more likely to have a 1st minute Apgar score below 7 (OR=1.59; 95% CI: 1.05-2.41) and to be admitted to the neonatal intensive care unit (OR=2.15; 95% CI: 1.53-3.02). Apgar score below 7 in 5 min and LBW were not associated with placenta previa (Table 3). In the <34 weeks placenta previa group, the probability of having a 1st minute Apgar score below 7 (OR=5.59; 95% CI: 2.32-13.48), the probability of having a 5th minute Apgar score below 7 (OR=3.94; 95% CI: 1.17-13.28) and the probability of being admitted to the NICU increased (OR=28.47; 95% CI: 7.7-105.28). In the >37 weeks placenta previa group, LBW (OR=4.21; 95% CI: 1.36-13.08) and 5th minute Apgar score below 7 were more likely (OR=1.89; 95% CI: 1.71-2.09) (Table 4).

Discussion

In our study, we compared the neonatal outcomes after cesarean section performed in patients complicated by placenta previa with the neonatal outcomes of patients who underwent cesarean section for all other indications. We found statistically significantly higher maternal age,

gravidia, previous abortion, and curettage rates in the patient group. We found that neonates in the patient group had a lower 1st minute Apgar score and a higher risk of NICU admission. This demonstrated that placenta previa is a negative risk factor for neonatal outcomes regardless of gestational week, especially in the <34 weeks gestation group. A 5-min Apgar score below 7 and LBW neonatal outcomes were not associated with placenta previa in the study groups. Although there are some differences, these data are complementary and contribute to studies evaluating perinatal outcomes in pregnancies complicated with placenta previa.

Abnormal localization of the placenta and partial or complete closure of the cervical canal is called placenta previa. Although some studies have shown the incidence to be 1% (16), most studies have shown the incidence to be 0.3-0.5% in general (2,15), and we found 0.47% in our study, which is consistent with the literature. Although a published meta-analysis showed that the previa rate was affected by regional differences (17), another study with a longer duration and a larger scope showed a prevalence similar to that in our study (16).

Table 2. Maternal characteristics in pregnancies with and without placenta previa based on gestational age at delivery

	<34 weeks			34-36 weeks			≥37 weeks		
	Placenta previa (n=47)	Controls (n=50)	p	Placenta previa (n=80)	Controls (n=113)	p	Placenta previa (n=161)	Controls (n=181)	p
Maternal age at index birth (years)	30.4±5.48	28.1±4.37	0.029	31.7±5.22	28.5±5.37	<0.001	31.8±5.00	28.6±5.31	<0.001
Gravidity	3.1±1.62	2.5±0.81	0.020	3.3±1.51	2.9±1.52	0.097	3.1±1.39	2.8±1.16	0.018
Parity	1.7±1.33	1.3±0.77	0.109	1.6±1.24	1.4±1.19	0.177	1.4±0.97	1.4±0.88	0.527
Previous cesarean section	68.1%	92.0%	0.004	68.8%	77.9%	0.183	70.2%	83.4%	0.004
Previous vaginal delivery	21.3%	24.0%	0.811	23.8%	14.2%	0.128	18.6%	15.5%	0.472
Previous abortion	27.7%	8.0%	0.015	27.5%	25.7%	0.869	33.5%	23.8%	0.054
Previous curettage	4.3%	4.0%	>0.999	17.5%	5.3%	0.008	9.3%	5.0%	0.139

Table 3. Neonatal outcomes in pregnancies with and without placenta previa

	Placenta previa group (n=288)	Control group (n=344)	p
Gestational age at delivery, weeks	35.9±2.97	35.9±2.40	0.788
Sex, male			-
Birth weight (g)	2745.7±709.21	2980.3±711.12	<0.001
Low birth weight	29.5%	25.0%	0.209
Apgar score at minute 1	7.3±1.67	7.5±1.60	0.153
Apgar-score <7	20.5%	14.0%	0.033
Apgar score at minute 5	8.8±1.14	9.1±0.98	<0.001
Apgar-score <7	5.2%	3.5%	0.326
Neonatal intensive care unit admission	41.0%	24.4%	<0.001

Table 4. Maternal characteristics in pregnancies with and without placenta previa based on gestational age at delivery

	<34 weeks			34-36 weeks			≥37 weeks		
	Placenta previa (n=47)	Controls (n=50)	p	Placenta previa (n=80)	Controls (n=113)	p	Placenta previa (n=161)	Controls (n=181)	p
Gestational age at delivery, weeks	30.3±2.61	31.2±1.97	0.078	35.4±0.82	35.4±0.68	0.923	37.7±0.95	37.6±0.63	0.084
Sex, male									
Birth weight (g)	1650.9±533.16	2004.8±354.08	<0.0001	2681.8±526.79	2690.4±531.40	0.912	3097.0±452.89	3430.8±482.27	<0.001
Low birth weight	93.6%	100%	0.110	33.8%	28.3%	0.432	8.7%	2.2%	0.013
Apgar score at minute 1	5.5±1.96	7.3±1.56	<0.001	7.3±1.62	7.1±1.95	0.483	7.9±1.16	7.8±1.27	0.758
Apgar-score <7	63.8%	24.0%	<0.001	17.5%	19.5%	0.852	9.3%	7.7%	0.698
Apgar score at minute 5	7.4±1.61	8.5±0.93	<0.001	8.9±0.88	8.9±1.18	0.753	9.2±0.66	9.4±0.75	0.010
Apgar-score <7	25.5%	8.0%	0.028	3.8%	6.2%	0.527	0%	0.6%	>0.999
Neonatal intensive care unit admission	93.6%	34.0%	<0.001	42.5%	32.7%	0.176	24.8%	16.6%	0.062

Each woman with placenta previa is managed according to her clinical characteristics; however, most women with placenta previa undergo elective prophylactic preterm cesarean section. In stable patients, the SMFM recommends waiting for delivery until 36-37 6/7 weeks of gestation (13). After 37 weeks, approximately 40-50% of deliveries are planned after this week because the concern of prematurity disappears (18). In our study, this rate was found to be 55.9%, which is higher than the literature.

Our study findings are compatible with the literature regarding risk factors for placenta previa, including advanced maternal age, increased gravidity, and previous abortion and curettage (1). It has been suggested that advanced maternal age has an effect on the risk of placenta previa formation (2) independent of other known risk factors due to age-related insufficient perfusion and insufficient vascularization (1). In contrast to our results, some other studies have reported that advanced maternal age was not associated with placenta previa (19). Many opinions have been put forward to demonstrate the relationship between gravida, parity, curettage, abortion history, and previa. During pregnancy, the endometrium in which the gestational material is implanted may be damaged, and vascularization may change, which may lead to inadequate

nutrition of the placenta by creating unsuitable regions for implantation and increase the possibility of implantation in the lower segment (20). Some studies found that the risk of previa increased 2.3-fold with multigravida (≥5) (19), some found no association (21,22), and some found that although there was an association, the risk did not increase significantly (23). In our study, we did not find a significant association between placenta previa and multiparity.

According to data from previous studies, there is a significant association between the number of previous cesarean sections and placenta previa (24). Interestingly, unlike previous studies (6,25), the number of previous cesarean sections was more common in the control group; however, in this study, the mean number of cesarean sections was similar for both groups and the history of previous cesarean section was not associated with placenta previa, similar to some other studies (19).

It has been reported that women reporting one or more abortions are 30% more likely to encounter placenta previa than women without a history of abortion (26). In our study, the abortion rate was significantly higher in patients with placenta previa (30.9% vs. 22.1%, $p=0.014$) (OR=1.58), which was consistent with previous data (27). The rate of

prior curettage in the patients in our study was similar to that in other studies (10.8% vs. 4.9%, $p=0.007$) (OR=2.32) (28).

Schneiderman and Balayla (29) suggested, as we planned to do, that to fully understand the neonatal outcomes of pregnant women complicated with placenta previa, they should not be compared with the outcomes of patients who had vaginal deliveries but with those of patients who had cesarean deliveries for all other indications. In addition, because neonatal morbidity can be greatly affected by gestational age, we also performed a subgroup analysis based on gestational age. Thus, in our study, we could determine whether placenta previa could be a risk factor for newborns regardless of gestational age.

Studies have examined the relationships among prematurity, LBW, postpartum respiratory depression, respiratory distress syndrome (RDS), low Apgar scores, and placenta previa (30,31). Prematurity is a risk factor for unfavorable outcomes. In our study, the rate of prematurity was found to be 44.1% (gestational week <37 weeks). We believe that this is related to elective planned preterm delivery. Although studies have shown that fetal oxygenation and growth are affected by abnormal placental positioning, some studies have conflicting results between placenta previa and fetal development. Although there are reports of intrauterine growth retardation related to the link between these two conditions (15,32), this link has not been demonstrated in some reports (12,33).

Regarding fetal weight, although mean newborn body weights were higher in the patient group ($p<0.001$), LBW was not associated with placenta previa in the entire study group; we found significantly higher LBW rates in the >37 weeks gestational age group with an OR of 4.21 (8.7% vs. 2.2%, $p=0.013$). This finding contradicts the idea that placenta previa negatively affects newborn weight after adjusting for gestational age (34). In the group of patients with previa, neonatal Apgar scores are more likely to be below 7 (12).

In this study, significant differences were found between the two groups in the rates of Apgar score <7 at 1 min and mean Apgar score at 5 min. However, Apgar score <7 at 5 min was not associated with placenta previa in the whole study group. When subgroups were evaluated, in pregnancies below 34 weeks of gestation, the probability of having a 1st minute Apgar score below 7 (OR=5.59) and the probability of having a 5th minute Apgar score below 7 increased in the group complicated with placenta previa

(OR=3.94). Neonates with a gestational age >37 weeks had a higher probability of having a 5th minute Apgar score below 7 (OR=1.89).

According to a published meta-analysis, NICU admission is five times higher in pregnant women complicated with placenta previa than in other pregnant women (35). It is thought that the intrauterine conditions of the newborn predispose the newborn to hypoxia and anemia, thus increasing the incidence of RDS and NICU admission (30). In our study, it was found that neonates of pregnant women complicated with placenta previa were more likely to be admitted to the NICU (OR=2.15); likewise, the likelihood of neonatal admission to the NICU increased in deliveries of these patients before the 34th gestational week (OR=28.47).

Study Limitations

The retrospective nature of our study and the lack of information about complicated cases, infertility treatment, and their outcomes are the limitations of our study. Prospective studies that minimize these limitations may contribute to the literature. The greatest strength of the study is the comparison of neonatal outcomes of pregnant women complicated with placenta previa with cesarean deliveries for all other indications, thus ruling out the higher risk of adverse neonatal outcomes with cesarean delivery compared with vaginal delivery, and the subgroup analysis based on gestational week because neonatal morbidity can be greatly affected by gestational week.

Conclusion

We conclude that pregnancies with a diagnosis of placenta previa are associated with an increased risk of serious fetal outcomes compared with cesarean deliveries for all other indications, regardless of the timing of delivery.

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Ethics

Ethics Committee Approval: This study was approved by the institutional review board. Ethical approval was obtained from the Ethics Committee University of Health Sciences Turkey, İstanbul Kanuni Sultan Süleyman Training and Research Hospital (date: 02.05.2015, number: 2014/10).

Informed Consent: Written informed consent was obtained from all patients and controls.

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Concept: M.B., İ.P., Design: M.B., V.A.T., A.E., A.B., O.K., D.Y.,
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