Obstetric Outcomes of Pregnant Women with Placenta Previa: A Retrospective Comparative Study

Plasenta Previalı Gebelerin Obstetrik Sonuçları; Retrospektif Karşılaştırmalı Çalışma

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ABSTRACT

Placenta previa (PP) is one of the leading causes of severe peripartum complications that resulting in serious maternal and perinatal morbidity such as peripartum hemorrhage and preterm delivery. Herein, we aimed to compare obstetric outcomes of pregnant women with PP versus pregnant women without PP in our hospital. This retrospective case-control study was conducted on 179 pregnant women in the study group (PP group) and 626 in the control group. Outcome measures included demographic and clinical characteristics of both groups, chief complaints on admission, gestational age at birth, postpartum hemorrhage, interventional modalities to treat postpartum hemorrhage and emergency peripartum hysterectomy. Maternal age ($p<0.001$), parity ($p<0.002$) and prior abortus ($p<0.001$) were greater in the PP group. The chief symptom present on admission was vaginal bleeding, 53% in the study group, and pelvic pain, 50% in the control group. Median birth week ($p<0.001$), median birth weight ($p< 0.001$), and mean hemoglobin level ($p=0.005$) were lower in the study group. Early preterm birth (<34 weeks) rate and late preterm birth (between 34 and 37 weeks) rate were greater in the study group (both $p<0.001$). Term birth rate (≥ 37 weeks) was greater in the control group ($p<0.001$). Postpartum hemorrhage rate ($p<0.001$), blood product transfusion rate ($p<0.001$), uterine atony rate ($p<0.001$), and emergency postpartum hysterectomy rate ($p<0.001$) were greater in the study group. PP leads to worsening of obstetric outcomes, particularly increased maternal morbidities and premature delivery. Obstetricians should be familiar with diagnoses, complications and management of PP for appropriate and timely intervention. Pregnant women with PP should be close follow-up to decrease maternal morbidity and mortality.

Keywords: Maternal morbidity, obstetric labor complications, peripartum hysterectomy, postpartum hemorrhage, preterm delivery**.**

ÖZ

Plasenta previa (PP), peripartum kanama ve erken doğum gibi ciddi maternal ve perinatal morbiditeye neden olan, ciddi peripartum komplikasyonların önde gelen nedenlerinden biridir. Burada hastanemizde PP'li gebelerle PP'siz gebelerin obstetrik sonuçlarını karşılaştırmayı amaçladık. Bu retrospektif vaka-kontrol çalışmasına Ordu Üniversitesi ve Zekai Tahir Burak Eğitim ve Araştırma Hastanesi, Ordu, Ankara'da doğum yapan gebeler dahil edildi. Çalışma grubunda 179, kontrol grubunda 626 gebe bulunmaktadır. Sonuç ölçütleri, her iki grubun demografik ve klinik özelliklerini, başvurudaki başlıca şikayetleri, doğumdaki gebelik yaşını, doğum sonu kanamayı, doğum sonu kanamayı tedavi etmek için girişimsel modaliteleri ve acil peripartum histerektomiyi içermiştir. Anne yaşı ($p<0,001$), parite ($p<0,002$) ve önceki abortus ($p<0,001$) PP grubunda daha fazlaydı. Başvuru sırasında mevcut olan başlıca semptom, çalışma grubunda %53 oranında vajinal kanama ve kontrol grubunda %50 oranında pelvik ağrıydı. Ortanca doğum haftası ($p<0,001$), ortanca doğum ağırlığı ($p< 0,001$) ve ortalama hemoglobin düzeyi ($p=0,005$) çalışma grubunda daha düşüktü. Erken erken doğum (<34 hafta) ve geç erken doğum (34-37 hafta) oranı çalışma grubunda daha fazlaydı (her ikisi de $p<0,001$). Dönem doğum oranı (≥ 37 hafta) kontrol grubunda daha fazlaydı ($p<0,001$). PP grubunda doğum sonu kanama oranı ($p<0,001$), kan ürünü transfüzyon oranı ($p<0,001$), uterus atoni oranı ($p<0,001$) ve acil doğum sonu histerektomi oranı ($p<0,001$) daha yüksektir. PP, özellikle artan maternal morbiditeler ve erken doğum olmak üzere obstetrik sonuçların kötüleşmesine yol açmaktadır. Doğum uzmanları, uygun ve zamanında müdahale için PP'nin tanılarına, komplikasyonlarına ve yönetimine aşina olmalıdır. PP'li gebeler maternal morbidite ve mortaliteyi azaltmak için yakın takip edilmelidir.

Anahtar Kelimeler: Maternal morbidite, Obstetrik doğum komplikasyonları, Peripartum Histerektomi, Postpartum Hemoraji, Preterm Doğum.

Ethical approval was obtained (Date: 16.01.2019, Decision No:12/2019) from Dr. Zekai Tahir Burak Education and Research Hospital.

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INTRODUCTION

Peripartum hemorrhage and preterm delivery are important conditions that result in increased maternal and fetal morbidity and mortality. Placenta previa (PP) is one of the leading causes of peripartum hemorrhage and preterm delivery, both resulting in serious maternal and perinatal morbidity, even maternal and fetal mortality[1,2,3]. The prevalence of PP is about 0.3-0.5% among pregnant women[3]. It is defined as implantation of the placenta on the internal cervical os or the lower placental edge lying within 20 mm from the internal cervical os after 20 weeks of pregnancy[1,2].

PP leads to massive maternal bleeding before the beginning of labor, during labor or in the postpartum period[4]. Thus, in the presence of persistent PP at the time of delivery, cesarean delivery is indicated due to the risks of placental detachment from the implantation site and postpartum hemorrhage at the time of vaginal delivery[5]. PP is associated with peripartum hemorrhage which often requires medical and surgical interventions that includes use of uterotonic medication, urgent cesarean section, need for blood and blood product transfusion, surgical intervention such as uterine/ internal iliac artery ligation, emergency peripartum hysterectomy (EPH), admission to the intensive care unit, and even maternal death[5]. The maternal mortality rate of women due to PP is approximately 0.03% and perinatal mortality is 8.1% in the developed world[6]. EPH is a life-saving measure when uterine conservative therapies are insufficient to cease challenging postpartum hemorrhage[7]. Antepartum bleeding and uterine contraction due to PP usually result in preterm cesarean delivery that leads to increased risk of neonatal morbidity and mortality because of prematurity[1,2].

Furthermore, PP has two important risk factors for the subsequent pregnancy. First, PP is a recurrent pregnancy complication with a recurrence rate of 2.3-3.2%. Second, a patient who has preterm birth due to PP has an independent risk factor for a recurrent spontaneous preterm delivery in the subsequent pregnancy[3].

The objective of the present study was to compare obstetric outcomes of pregnant women with PP versus pregnant women without PP in our hospital.

MATERIALS AND METHODS

This retrospective case controlled study included pregnant women who delivered between between January 1, 2010 and August 31, 2019 at the Ordu University Education and Research Hospital, Ordu and Zekai Tahir Burak Education and Research Hospital, Ankara which both are tertiary medical centers in, Turkey. The hospital's local ethic committee approved was obtained (Date:17.07.2018, Decision No:36/2018).The diagnosis of women with PP was identified from the labor ward registry, and then patient data was collected from each patient's file. The control group was selected with the following procedures: pregnant women who delivered by cesarean section were listed first according to the date of giving birth, then pregnant women who were delivered transvaginally according to their date of giving birth were listed next to the cesarean section list. For each study group patient, 2 normal and 2 cesarean section patients without PP were selected. Those control patients were randomly determined by a computer program. In this manner, cesarean deliveries and vaginal deliveries were equally allocated in the control group to be representative of the hospital population.

PP was defined as a placenta that covered the internal cervical os, or when the lower placental edge was within 20 mm from this point. The three types of PP (total, partial and marginal, where the placenta was adjacent to the internal os within 20 mm) were evaluated together in the study group. PP was diagnosed in the antenatal period and confirmed on admission at the time of

delivery by transvaginal ultrasonography, and verified during the cesarean section.

To compare the groups, maternal age, body mass index (BMI), gravidity, parity, gestational age at delivery (according to the date of the last menstrual period), hemoglobin level on admission, the lowest hemoglobin level during delivery, at postpartum second or sixth hour (usually evaluated in our hospital), mode of delivery, birth weight, medications to prevent postpartum hemorrhage, such as oxytocin flacon (synpitan 5 IU/ml Deva Holding A.S Karaagac, Cerkezkoy Tekirdag, Turkey), metilergobazin flacon or pill (metiler 0.2mg/ml Adeka Ilaç ve Ticaret A.S Samsun, Turkey), misoprostol pill (cyctotec 200 mcg, Primal Healtcare, UK limited/England), balloon tamponade, postpartum hemorrhage, uterine atony, artery ligation (uterine or internal iliac), transfusion of red blood cell, fresh frozen plasma, whole blood, platelet suspension, EPH (defined as a hysterectomy performed within 24 hours of delivery), and duration of hospital stay were retrieved from each patient's file and evaluated as measures of obstetric outcomes.

Routinely blood sample was taken from each patient on admission, at the time of delivery if needed and at postpartum second and sixth hours to evaluate Hb and Htc in our hospital for early detection of postpartum hemorrhage and timely management. Postpartum hemorrhage was defined as any blood loss exceeding 1000 cc for cesarean delivery, and 500 cc for vaginal delivery. The amount of postpartum blood loss for each patient was estimated using the following equation "EBL= (BV)X (HCTO-HCTf) / HCTave" where: EBL = Estimated Blood Loss, BV: Blood Volume= Body Weight (kg) X 65 cc, HCTO = Initial Hematocrit, HCTf = Final Hematocrit, HCTave = (HCTO + HCTF)/2, which was developed by Brecher and Colleagues[8,9]. Initial Hematocrit (HTCO) value was described as the HTC on admission, and Final Hematocrit (HCTf) value was described the lowest HTC after fetal delivery.

Birth weeks of fetuses were subdivided into three groups according to gestational week. Early preterm birth was defined as delivery <34 weeks of gestation, late preterm birth was defined as delivery between 34 and 36 weeks of gestation, and term birth was defined as ≥ 37 weeks.

Statistical analysis was performed with the SPSS package program version 22 (SPSS Inc., Chicago, USA). Student t-test and Mann-Whitney U test were used for comparison of continuous variables; Chi-square test was used to compare categorical variables. A two tailed P value less than 0.05 was considered significant. The results of Student t test are presented with mean ± standard deviation (SD), Mann-Whitney U test median with interquartile ranges (IQR), and Chi-square with percentile.

RESULTS AND DISCUSSION

Table 1. Demographic and Clinical Characteristics of The Groups

Variables	Patient (N=179)	Control (N=626)	p
Age (year)	29.5 (25.2-34)	25 (22-29.5)	<0.001*
BMI	29.2 (26.6-31.2)	28 (25.3-31.2)	0.062*
Gravidity	2 (1-3)	2 (1-3)	0.065*
Parity	1 (0-2)	1 (0-1)	0.002*
Prior live birth	1 (0-2)	1 (0-1)	0.068*
Prior abortus	39 (21.8 %)	95 (15.2%)	<0.001**
Prior D&C	13 (7.3%)	57 (7.1%)	0.936**

BMI: Body Mass Index
D&C: dilatation and curettage, * Mann-Whitney U test, ** Chi square test"

In this time interval there were approximately 79,150 deliveries in the hospital registry. The data of a total of 179 patients with PP were retrieved from patient files. We collect data of 626 patients in the control group, and a total of 805 pregnant women. When the two groups were compared for demographic and clinical features, the groups were different from each other and the results are presented in Table 1. The study group had a greater maternal age than the control group. In the PP group, the parity number and the percent of previous abortus were greater than the control group.

Table 2. Chief Complaints of Pregnant Women At The Time of Admission to the Hospital

The Chief Present Symptom on Admission	Patient (N=179)	Control (N=626)	p
Vaginal bleeding	95 (53%)	3 (0.5%)	<0.001**
PPROM	15 (8.3%)	84 (13.4%)	0.063**
Pelvic pain	23 (14%)	313 (50%)	<0.001**
Without symptom	40(22.4%)	214(34.2%)	0.004**
Others symptom	6 (3.4%)	12 (2%)	0.256**

** Chi square test, PPROM: Preterm Premature Rupture of Membrane

When the groups were compared according to their chief complaints on admission to the hospital, vaginal bleeding was the chief compliant in the study group, and pelvic pain in the control group. The chief complaints of both groups on admission were presented in Table 2.

Table 3. Comparison of The Two Groups in Terms of Birth Week, Fetal Birth Weight, Hemoglobin Level on Admission, and Subdivision of Birth Week

Variables	Patient(N=179)	Control (N=626)	p
Median birth weeks	37 (34-39)	39(37-40)	<0.001*
Median birth weight (gram)	2900 (2150-3260)	3180 (2837-3542)	<0.001*
Mean hemoglobin level on admission (mg/dL)	12.1 (11.1-12.9)	12.4 (11.5-13.2)	0.005***
Cesarean delivery	179 (100%)	154 (24%)	<0.001**
Early preterm birth (<34 weeks)	40 (22%)	33 (5%)	<0.001**
Late preterm birth (34-37 weeks)	35 (20%)	93 (15%)	<0.001**
Term birth (≥ 37 weeks)	103 (58%)	500 (80 %)	<0.001**

* Mann-Whitney U test, ** Chi square test, *** Student t test"

The median birth week, fetal birth weight and mean hemoglobin level on admission in the PP group were smaller than in the control group (p<0.001). The percentiles of early preterm birth, and late preterm birth in the study group were higher than in the control group (P<0.001), and term birth was higher (P<0.001) in the control group. The results are presented in Table 3.

Table 4. Comparison of the Groups in Requirements for Medical and/or Surgical Interventions."

Variables	Patient (N=179)	Control (N=626)	p
Oxytocin (Unit)	30 (25-45)	30(20-40)	0.069*
Ergometrine flacon	2 (1-3)	1(1-1)	<0.001*
Ergometrine pill	2 (0-3)	2(0-3)	0.873*
Misoprostol pill (number of patients, total pill)	32 (17.1%); 98	5(0.8%); 12	<0.001**
Postpartum hemorrhage	160(89.4 %)	144(23%)	<0.001**
Blood product transfusion	39 (21.8 %)	8(1.3 %)	<0.001**
Red cell concentrate (number of patient; total units)	39(21.8%); 153 U	8(1.3%); 24 U	<0.001**
Fresh blood transfused (number; total units)	7 (1.6%); 22 U	0 (0.0%); 0 U	<0.001**
Fresh frozen plasma (number; total units)	13(7.3%); 42 U	1(0.2%); 4 U	<0.001**
Platelet transfusion (number; total units)	3 (1.7%); 8 U	0(0.0%) U	0.011****
B-Lynch suture	2 (1.1 %)	0(0.0%)	0.049****
Hydrostatic balloon tamponade	10 (5.6 %)	(0.0 %)	<0.001**
Uterine atony	13 (7.3 %)	8(1.3 %)	<0.001**
Artery ligation	4 (2.2 %)	0 (0.0%)	0.002****
EPH	7 (3.9 %)	0 (0.0%)	<0.001**
Duration of hospital stay (days)	2 (2-3)	2 (2-3)	0.196*

BMI: Body Mass Index, D&C: Dilatation And Curettage, EPH: Emergency Postpartum Hysterectomy * Mann-Whitney U Test, ** Chi Square Test, *** Student T Test, **** Fisher's Exact Test."

We also compared the two groups according to the requirement for medical and/or surgical intervention for ceasing postpartum hemorrhage, blood product transfusion, and management of uterine atony. PP was significantly associated with severe pregnancy complications, which often requires medication, blood product transfusion and surgical intervention to cease postpartum hemorrhage and/or uterine atony. The comparison of the two group requirement for intervention to prevent/treat postpartum hemorrhage and uterine atony was presented in Table 4.

CONCLUSION AND RECOMMENDATIONS

The prevalence of PP was 0.23 % in our study, which is lower than the reported approximately 0.3-0.5%[3]. We expected that the prevalence of PP should have been higher than calculated. This may be due to the type of our study which was retrospective that we could not retrieve all patient files with PP. The diagnosis of PP should be performed by ultrasonography. Transvaginal sonography (TVS) gives images of the cervix precisely and is widely preferred to transabdominal sonography (TAS)[10]. In the present study diagnosis of PP was based on TVS, and confirmed during delivery. There are many theories to explain risk factors for PP. Advanced maternal age, multiparity, previous cesarean deliveries, history of previous abortions, uterine surgical procedures, and the presence of PP in the previous pregnancy are some of the risk factors for PP. However the precise etiology of PP remains uncertain[3,7]. In the present study, maternal age, live birth rate, and history of previous abortus rate in the case group were higher than in the control group, and these findings are consistent with previous research.

PP is one of the frequent causes of peripartum hemorrhage, especially postpartum hemorrhage (PPH), which usually requires medical and surgical intervention. The mechanisms of hemorrhage due to PP during pregnancy are not known clearly. The presence of a slight uterine contraction and effacement can easily cause placental detachment from the decidua basalis and result in active hemorrhage[4]. An important degree of uterine contractility has been observed in patients with symptomatic PP[5]. The degree of uterine activity is directly associated with the acute event of clinical vaginal bleeding in the prepartum period[6]. An important percentage of women with PP related hemorrhage will experience subclinical uterine contractions before the onset of overt vaginal bleeding[6]. The lack of musculature in the lower uterine wall that inhibits the ability of contraction to perform hemostatic action on the placental insertion site causes hemorrhage[11]. PP often requires cesarean section due to uncontrollable prepartum hemorrhage or uterine contraction. Hasegawa et al reported that according to their experience, 66.7% of patients who had antenatal bleeding required emergency cesarean section due to uncontrollable hemorrhage[4]. Additionally, in the 3.2% of patients who had no episode of antenatal bleeding, an emergency cesarean section was performed due to uncontrollable uterine contractions before the date of the planned cesarean section[12]. In our study, there was a total of 96 pregnant women with vaginal bleeding symptoms on admission who were delivered with cesarean section after a short time interval, in the study group 93 (52.5%) and 3 (0.5%) in the control group. This demonstrates that vaginal bleeding is the most frequent symptom of patients with PP, which often requires delivery in an emergency condition.

PP is a serious complication of late pregnancy, which is further complicated by placenta accreta or percreta, that could unexpectedly lead to massive intractable bleeding and PPH that necessitate surgical intervention, such as EPH, and even maternal death[13].Daglar et al.[14] suggested that placenta invasion anomaly, advanced maternal age, increased number of previous CS, and increased need for blood transfusion are important risk factors for EPH in patients with PP totalis. Therefore, the type of PP is also important for the maternal and fetal outcomes.

PPH is the leading cause of maternal morbidity and mortality in developed countries with an overall incidence of approximately 5% currently and accounts for about one in every four maternal deaths worldwide[15,16]. Advanced maternal age, history of a previous cesarean section, inadequate uterine contraction which is defined uterine atony, adherent placenta, PP, uterine rupture or maternal coagulopathy produce increased blood loss during delivery and could be cause PPH[4,17,18]. PPH is the leading cause of hypovolemic shock, disseminated intravascular coagulopathy (DIC), EPH, multiorgan failure and even maternal death[19]. During cesarean section, PP might cause massive bleeding because the lower uterine segment has poor smooth muscle for compressing uterine vessels to stop the bleeding[4,11,20]. Predisposing factors for massive hemorrhage during cesarean section in patients with PP are; advanced maternal age, high parity, history of previous cesarean section and adherent placenta[4,20]. In the present study, maternal age, history previous live births and abortus were higher in the study group than the control group. The postpartum hemorrhage rate was 89.4 % in the study group and 23% in the control group in presented study. The results are consistent with previous literature knowledge. The results demonstrate that PP is one of the significant causes of PPH.

Many intervention modality were descript to treat PPH. Uterine conservative intervention is the first choice treatment option for PPH. Interventions include management with uterotonic drugs such as oxytocin and misoprostol, external compression with uterine sutures such as B-Lynch, intrauterine hydrostatic balloon placement, intrauterine tamponade packing to press the uterine vessel to stop uterine

hemorrhage, and selective devascularization by ligation or embolization of the uterine artery or internal iliac artery[11,17,21]. The uterine conservative intervention rate in the study group was much higher than in the control group. The uterin conservative interventions were presented at table 4. The result is in accordance with previously reported studies.

When uterine conservative treatment fails to stop hemorrhage, EPH is often required as a life saving measure. EPH is a radical intervention that remains the most common surgical procedure to manage intractable PPH in obstetrics practice and causes permanent infertility[18,22]. EPH defined as hysterectomy is performed in the time interval after 20 weeks of gestation and within the first 6 weeks of the postpartum period for uncontrollable uterine bleeding[23]. Risk factors for EPH have been defined as maternal age ≥35 years, parity≥ 3 and a history of caesarean delivery, PP and adherent placenta[24]. The rate of EPH is 0.2–0.8/1000 in all deliveries in European Countries[24]. Awan et al reported that the EPH rate due to PP was about 19.4%[23]. The EPH rate was 7 (3.9%) in the study group, none in the control group and 0.8 % in the study cohort. The EPH rate was higher in our hospital than reported in the literature. One reason of the this high rate might be due to our hospital being a tertiary center. Another reason might be the all patient with PP were in the study cohort. It is well known that PP is important cause of EPH.

Fortunately, there was no maternal death among our study patients. This should be because of our specialists are well experienced in the management of PPH and uterine atony, since our hospital is a tertiary center and the staff is often faced with such cases. Despite medical and surgical options for the management of PPH, substandard care accounts for about 60% of maternal deaths[11].

In the presence of PP, cesarean delivery is indicated. Antepartum vaginal bleeding due to PP is the most common indication for an emergency cesarean section[23]. Cesarean delivery has been associated with higher maternal and neonatal complications and healthcare costs than vaginal delivery[22]. Increasing rates of caesarean delivery have resulted in a rising incidence of abnormal placental implantation and invasion and the requirement for cesarean section in subsequent pregnancy are risk factors for peripartum obstetric hemorrhage and EPH[18].

PP is one of the risk factors for preterm birth that often requires iatrogenic preterm birth (PTB) before 34 weeks due to maternal bleeding or spontaneous preterm labor, which contributes to about 5% of all preterm deliveries[3,5,25]. A significant degree of uterine contractility has been observed in pregnant women with symptomatic PP and the degree of uterine activity is directly associated with the acute event of clinical vaginal bleeding[6]. With the presence of vaginal bleeding in a pregnant patient, after 34 weeks they are often likely to be promptly delivered because catastrophic bleeding can occur and is not predictable on the basis of clinical factors[5]. PP was recorded in 2.8 per 1000 live births, and neonatal mortality rate was 10.7 with PP, compared with 2.5 per 1000 among other pregnancies[25]. Among surviving infants who are delivered from patients with PP, there are high rates of prematurity, high associated morbidity, and low birth weight described[25]. As reported in a U.S. population based study of live births, approximately 16.9% of women with PP delivered at <34 weeks, 27.5% delivered at 34-37 weeks, and 55.6% at >37 weeks[25]. In our study, approximately 22% of women with PP delivered preterm at <34 weeks, 20% delivered at 34-37 weeks, and 58% at >37 weeks. These findings are in accordance with results of aforementioned study.

In addition, PP has two important risk factors for subsequent pregnancy. First, preterm birth due to PP is an independent risk factor for a recurrent spontaneous preterm delivery in the subsequent pregnancy[3]. Preterm delivery in patients with PP, especially if it occurs before 34 weeks of gestation, is a recurrent event in the subsequent pregnancy, supporting the notion

that a preterm delivery in women with PP has the epidemiologic characteristic of spontaneous preterm birth[4]. Thus, patients who had an early preterm delivery due to PP may need to be treated as patients with a previous spontaneous preterm birth in terms of perinatal counseling and preventive measures in their subsequent pregnancies[4]. Second, PP is also a recurrent pathology, similar to spontaneous preterm birth. The recurrence rate of PP in a subsequent pregnancy in different populations varies from 2.3% to 3.2%[3].

In conclusion, our study in accordance with previous studies demonstrates that PP is one of the leading causes of obstetric complications that affect both maternal and fetal outcomes. Obstetricians should be familiar with diagnoses, complications and management of PP for appropriate timely intervention,

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