PERINATAL JOURNAL

Original Article

Perinatal Journal 2023;31(3):186-191

The effects of abnormal placentation on fetal development

Şükran Doğru[1], Fatih Akkuş[1], Ali Acar[2]

[1]Necmettin Erbakan University, Medical School of Meram, Department of Obstetrics and Gynecology, Division of Perinatology, Konya, Türkiye
[2]Necmettin Erbakan University, Medical School of Meram, Department of Obstetrics and Gynecology, Obstetrics and Gyneacology, Konya, Türkiye

Abstract

Objective: This study aimed to evaluate the effects of placental adhesion anomalies on neonatal birth weights.

Methods: Pregnant women consisting of placenta previa (PP), placenta accreta with placenta previa (PPAS), and healthy Controls were included in the study retrospectively. Birth weights, delivery weeks, 5th-minute APGAR scores, neonatal intensive care admission (NICU), and mortality rates of all newborns were recorded.

Results: Two hundred fifty-seven patients were included in the study. Of these, 84 cases were PPAS, 91 were PP, and 82 were Control. Considering the fetal weight between all groups, the number of fetuses below the <10 percentile did not differ significantly. When PPAS and Control cases were compared, the number of fetuses with >90 percentile weight did not differ significantly, but it was significantly higher than the PP group (p=.007).

Conclusion: Premature births are still observed in cases of PP and PPAS, but PP and PPAS were not associated with poor newborn birth weight.

Keywords: Fetal development, placenta accreta spectrum, placenta previa

Introduction

The risk of Placenta Previa(PP) increases after delivery with a single cesarean section (CS). CS rates extend worldwide,[1] and PP complicates one out of 200 pregnancies. The increased number of CS correlates positively with the probability of PP in the subsequent pregnancy.[2] While the incidence of PP is 2% at the 20th gestational week, it decreases by 4-6% per 1000 live births between 34-39 weeks of gestation with placental migration.[3] Increasing CS rates also increase the risk for the placenta acreata spectrum. All studies to date have revealed that blastocysts can migrate to the scar site in the lower uterine segment after CS and that placental villi adhere or invade abnormally. The presence of PP is associated with a 3% PAS risk in women who had a previous single cesarean delivery, whereas the absence of PP is associated with a 0.03% PAS risk.[4] Risk factors for PP and PAS are common. Previous CS, uterine surgeries, maternal age, previous abortion history, in vitro fertilization, and Asherman syndrome are other risk factors.

The nutrient availability associated with the mother's diet, the uteroplacental blood supply, placental villous development, villous trophoblast, and the capability of fetal placental circulation to transport these nutrients are essential for fetal development. At birth, the fetoplacental weight ratio is a finding that retrospectively demonstrates the effect of the placenta on fetal growth[5]. It is known that the blood flow to the lower uterine segment is less than the fundus. Poor oxygenation and insufficient blood supply in the CS scar site affect placentation and

Correspondence: Şükran Doğru, Necmettin Erbakan University, Medical School of Meram, Department of Obstetrics and Gynecology, Division of Perinatology, Konya, Türkiye, **e-mail:** sukrandogru-2465@hotmail.com, **Received:** June 01, 2023, **Accepted:** August 10, 2023

How to cite this article: Doğru Ş, Akkuş F, Acar A. The effects of abnormal placentation on fetal development. Perinatal Journal 2023;31(3):186-191 DOI: 10.59215/prn.23.0313002

ORCID ID: Ş Doğru 0000-0002-3383-2837; F Akkuş 0000-0001-7037-9165; A Acar 0000-0002-9074-258X

CETUS Publishing

implantation by disrupting reepithelialization and decidualization in this region. This condition affects placental development and, subsequently, fetal development [6,7] one study has indicated growth retardation (SGA) in PP cases and lesions in the vessels feeding the placenta in these cases.[8] There is no decidua in the region where the placenta is located in PAS cases, and the remodeling of the spiral arteries is limited. Inadequate remodeling and vascular lesions have also been observed in cases of placenta-associated SGA.[9] Considering all this information in the coexistence of PP and PAS suggests that placental development and function will be affected.

PP and PAS are linked with severe morbidity and mortality in neonates and mothers. However, there are very few studies on the effect of the coexistence of these two clinical entities on fetal development. This study aimed to evaluate the effects of placental adhesion anomalies on neonatal birth weights.

Methods

Pregnant women who underwent cesarean sections for PP, PPAS, or other reasons (Control) at Necmettin Erbakan University (NEU) Meram Medical Faculty Hospital between January 2017 and December 2022 were included in the retrospective study. Demographic and obstetric histories of the patients were obtained from their file records. PP cases were defined as whose cervical os was covered entirely by the placenta. PPAS cases were determined with prenatal abdominal or vaginal ultrasonography and doppler ultrasonography as the placenta localized in the lower segment, myometrial-bladder border disappeared, myometrial thickness below 1 mm, multiple and irregular lacunae, increased bladder border hypervascularity, myometrial-bladder border, cases with Previa with bridging or intraoperative observation of invasion into the serosa, bladder or parametrium and confirmed postpartum pathology (at least 3 of these criteria were required). Control cases constituted cases with presentation anomaly, cephalopelvic incompatibility, or a history of previous cesarean section. Twin pregnancies, pregnancies with fetal anomalies, diabetes diagnosis, hypertension, pregnant women with in vitro fertilization, history of thrombophilia, and smokers were excluded. The last menstruation dates of the patients were confirmed by first-trimester ultrasonography results. Demographic data of all patients were obtained from hospital records. Birth weights of all newborns were noted, and percentiles were calculated using the Fetal Medicine Foundation [10] birth scale. Below the 10% percentile was considered for those who were small according to gestational age (SGA) and above the 90% percentile for the large ones (LGA). Birth weights, weeks of birth, 5th-minute Apgar scores, neonatal intensive care admission (NICU), and death rates of all newborns were recorded. This study has been approved by the NEU Ethics Committee with decree number 2021/3535 (7964).

Statistical Analysis

While mean, standard deviation, median, minimum and maximum values were presented in the descriptive statistics of continuous variables, frequency (n) and percent (%) values were stated in the definition of categorical variables. Normality assumptions of the variables were examined with the Kolmogorov Smirnov test.

The Kruskal-Wallis test compared the non-normally distributed continuous variables between groups of three or more. If a statistically significant difference was obtained from the Kruskal-Wallis test, the Mann-Whitney test with Bonferroni correction was used to determine which groups the difference originated. In cases where the normality assumption was met, a one-way analysis of variance (ANOVA) was used in groups of three or more. If a significant difference was determined in the ANOVA analysis, Post-Hoc analysis was applied. Relationships between categorical variables were examined by Chi-square/Fisher exact analysis. IBM SPSS.25 program was used in all analyses, and $p<0.05$ was accepted as the significance level.

Results

A total of 351 patients were evaluated for the study. Among them, in vitro fertilization (IVF), hypertension (HT), Diabetes mellitus(DM), thrombophilia, smoking mothers were excluded (Figure 1). A total of 257 patients were included in the study, of which 84 (32.7%) were in the PPAS group, 91 (35.4%) were in the PP group, and 82 (31.9%) were in the Control group. Maternal age (p =.001), number of gravida (p =.002), the total number of deliveries (p =.001), number of cesarean sections (p =.001), and number of vaginal deliveries (p =.001) were statistically significant between the groups (Table1). The gravida number of the PPAS group was higher than the PP and Control groups. The total number of deliveries in the PPAS group was higher than the Control group (p=.001), the number of cesarean sections was significantly higher than the PP and Contol groups, and the number of vaginal deliveries was significantly lower than the PP and Control groups.

Table 1. Comparison of Sociodemographic parameters according to groups

	PPAS (n= 84) Mean ± SD	PP (n=91) Mean ± SD	Control (n=82) Mean ± SD	p value
Age*	32.57 ± 5.14	32.59 ± 5.46	29.70 ± 5.42	.001
Gravida *	3.80 ± 1.63	3.05 ± 1.57	3.00 ± 1.41	.002
Birth*	2.07 ± 1.29	1.47 ± 1.17	1.44 ± 1.04	.001
Abortion*	.73 ± 1.08	.59 ± 1.11	.55 ± 1.00	.326
Cesarean section number*	1.89 ± 1.19	.77 ± .91	.72 ± .82	.001
Number of vaginal births*	.18 ± .49	.65 ± .92	.76 ± .88	.001
BMI (kg/m²)**	29.26 ± 4.31	29.48 ± 3.75	28.50 ± 4.52	.282

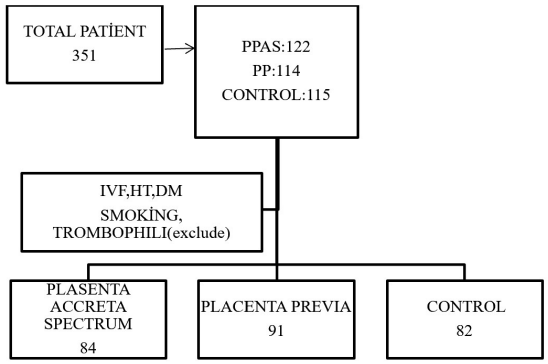
*Kruskal Wallis **One-Way ANOVA, BMI: Body mass index, PPAS: placenta accreta spectrum+ Placenta previa, PP: Placenta previa,

In Table 2, the week of birth (p =.001), birth weight (p =.001), and 5th-minute Apgar score (p =.001) were found to be statistically significantly different between the groups. It was found that birth weight differed significantly between the groups (p =.001). The birth weight of the PPAS group was lower than that of the Control group. There was no difference in birth weight between the PPAS and PP groups (p =.001). While the proportion of patients with PPAS birth weight percentiles above 90 was higher than in the PP group (p =.007), no significant difference was found in the Control group. When all groups were considered, no difference was found between <10 percentile rates defined as fetal SGA (figure 2).

Table 2. Comparison of fetal parameters in PPAS, PP, and Control group

	PPAS (n= 84) Mean ± SD	PP (n=91) Mean ± SD	Control (n=82) Mean ± SD	p value
Birth weight (gram)*	2623.21 ± 581.42	2848.57 ± 533.29	3234.63 ± 515.00	.001
Gestational week*	34.58 ± 2.38	36.12 ± 2.04	37.55 ± 1.66	.001
Birth weight(percentil)**	57.62 ± 33.25	49.27 ± 28.44	59.23 ± 30.44	.057
Apgar*(5.min)	5.80 ± 1.40	6.52 ± 1.05	6.60 ± 1.00	.001
	PPAS (84) n (%)	**PP (91) n (%)**	**Control (82) n (%)**	**p**
Gestational week ***				.001
28-33	26 (31)	7 (7.7)	11 (13.6)	
34-36	41 (48.8)	37 (40.7)	29 (34.6)	
≥37	17 (20.2)	47 (51.6)	42 (51.8)	
Fetal death***	0	0	0	
NICU				.001
No	55 (65.5)	80 (87.9)	74 (90.2)	
Yes	29 (34.5)	11 (12.1)	8 (9.8)	
Fetal gender ***				.763
Boy	48 (57.1)	47 (51.6)	44 (53.7)	
Girl	36 (42.9)	44 (48.4)	38 (46.3)	
Birth weight percentile***				.007
< 10	11 (13.1)	8 (8.8)	5 (6.1)	
10-90	51 (60.7)	76 (83.5)	61 (74.4)	
> 90	22 (26.2)	7 (7.7)	16 (19.5)	
Maternal age***				.059
<35	50 (59.5)	56 (61.5)	62 (75.6)	
≥35	34 (40.5)	35 (38.5)	20 (24.4)	

*Kruskal Wallis **One-Way ANOVA; ***Chi-Square, PPAS: placenta accreta spectrum+previa, PP: Placenta previa, NICU: neonatal intensive care unit



PPAS: placenta accreta spectrum, PP: placenta previa, IVF: in vitro fertilization, HT: hypertension, DM: Diabetes mellitus

Fig.1 Distribution of patients

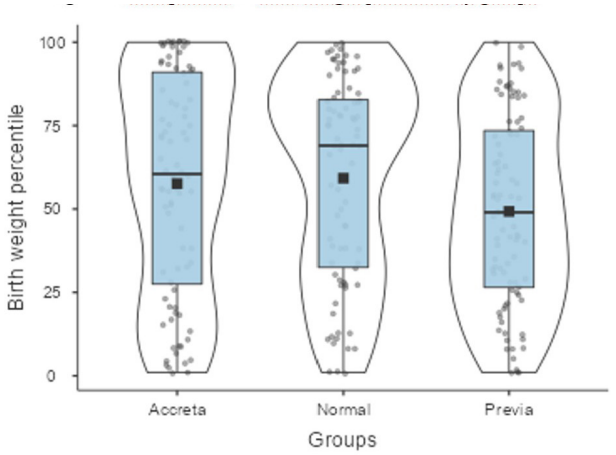


Fig. 2 Comparison of birth weight percentile by groups

The proportion of patients with a gestational age of ≥37 in the PP and Control groups was significantly higher than in the PPAS group. The proportion of patients admitted to the NICU was significantly higher in the PPAS group than in the Control group (p=.001).

Discussion

In this study, it was seen that there was no difference between the neonatal weight of all three groups when the percentiles were taken into account according to the fetal week. SGA infant rates were not different in all groups. While the LGA infant rate was not different in the PPAS and Control groups, it was lower in the PP group. Advanced maternal age (≥35 was not statistically different in all groups.

Placental pathologies can be used to explain the underlying pathology of poor obstetric outcomes. However, it is unclear what placental histopathological lesions are in the PP and PPAS patient groups. The reduction in volume, total area, and blood supply of intermediate and terminal villi that mediate maternal-fetal villi is one of the most important characteristics of the placenta in cases of fetal growth retardation (FGR).[11] Weaknesses in extravillous trophoblast invasion and disruptions in maternal arterial remodeling may be the cause of FGR via malperfusion of the placenta.[12] In pathological pregnancies, abnormal remodeling of the proximal radial arteries results in placental malperfusion.[13] One study found that developmental defects in the maternal placental stromal-vascular compartment result in placental dysfunction via malperfusion and loss of integrity. An abnormal implantation site has been linked to abnormal placental development, which may affect fetal development.[14] Weiner et al., in their study of the PP and control groups, stated that significantly lower placental weight was found in the PP group compared to the control group, and placental weight below the 10% percentile was more prevalent in the PP group. They stated that the number of cases with fetal weight <10 percentile and <5 percentile was more frequent in the PP group.[15] Balayla et al. reported in their meta-analysis that the risk of SGA increased by 19% in PP cases relatively.[3] After adjusting for confounder factors, Harper et al. found that the risk of SGA, defined as birth weight <10th percentile, was similar when compared with Controls without Previa. They concluded that the presence of bleeding, type of placenta, low lying PP, and complete or partial PP did not affect the risk of FGR.[16] Our study results support these findings. We did not determine any difference between the groups in terms of SGA.

Increasing CS rates increase the probability of PAS with the presence of PP. While discussing the coexistence of PP and SGA, there are few studies on SGA rates in PAS cases. Histopathological studies have demonstrated that spiral remodeling is insufficient in PAS cases, and some vessels undergo inadequate transformation.[17] In most cases, the area of the abnormal PAS is limited to a few cotyledons. Therefore, the spiral arteries outside the area of the accreta undergo regular physiological changes, and the development and biological function of the rest of the placental tissue is not affected. In invasive PAS cases, remodeling mainly occurs in the radial and arcuate arteries. This condition causes an increase in maternal blood flow to the placenta. The fact that the remodeling is limited in the radial and arcuate arteries and the other placental regions are normal may explain the LGA ratio in PPAS cases being the same as in the Control group. The first study on this subject, by Jauniaux et al., showed that there was no difference in the incidence of low birth weight below the 10th percentile and the median birth weight in PPAS. They reported that the differences in

spiral arteries in the accreta region between adherent and invasive subgroups had no effect on fetal growth when their histopathological findings were evaluated. Although LGA numbers were higher in the PP and PPAS groups in the same study, the difference was not statistically significant.[18] In our study, when the groups were compared, the birth weight percentiles were similar, but LGA rates were higher in the PPAS group than in the PP group. We could not find any study in the literature to explain this situation.

Previous studies have shown that uterine artery resistance is increased and uterine blood flow volume is reduced in women who have had CS compared to women who have had a vaginal delivery.[19] In the study of Torabi et al., it was observed that in cases with CS in the first pregnancy, the presence of a placenta close to the uterine scar in the next pregnancy was associated with impaired placental function and circulation and adverse pregnancy outcomes.[20] Considering that most of the placenta is located in this region in PPAS cases, this information is valuable. Placental location is important. FGR is more frequently present in cases of lateral placentation. According to a case-control study, women who had FGR complications were roughly four times more likely to have lateral placentation at 16–20 weeks than anterior or posterior placentation.[21,9]

The limitations of our study are the retrospective nature, lack of prenatal Doppler studies, estimated fetal weights, pathological examinations of the placenta, the low number of patients, being single-centered, and not including the PAS group without PP. Not including maternal nutrition on fetal development, weight gained during pregnancy, medications taken during pregnancy, and medical conditions are our limitations.

Conclusion

PP and PPAS continue to carry a high risk of maternal and fetal morbidity and mortality. Premature births are still observed in cases of PP and PPAS, but PP and PPAS were not associated with poor newborn birth weight.

References

1. Thurn L, Lindqvist PG, Jakobsson M, Colmorn LB, Klungsoyr K, Bjarnadóttir RI, et al. Abnormally invasive placenta-prevalence, risk factors and antenatal suspicion: results from a large population-based pregnancy cohort study in the Nordic countries. BJOG : an international journal of obstetrics and gynaecology. 2016; 123:1348-55. [PubMed][CrossRef]
2. Getahun D, Oyelese Y, Salihu HM, Ananth CV. Previous cesarean delivery and risks of placenta previa and placental abruption. Obstetrics & Gynecology. 2006; 107:771-8. [PubMed][CrossRef]
3. Balayla J, Desilets J, Shrem G. Placenta previa and the risk of intrauterine growth restriction (IUGR): a systematic review and meta-analysis. Journal of perinatal medicine. 2019; 47:577-84. [PubMed][CrossRef]
4. Jauniaux E, Bunce C, Grønbeck L, Langhoff-Roos J. Prevalence and main outcomes of placenta accreta spectrum: a systematic review and meta-analysis. American journal of obstetrics and gynecology. 2019; 221:208-18. [PubMed][CrossRef]
5. Burton GJ, Fowden AL, Thornburg KL. Placental origins of chronic disease. Physiological reviews. 2016; 96:1509-65. [PubMed][CrossRef]
6. Jauniaux E, Burton GJ. Pathophysiology of placenta accreta spectrum disorders: a review of current findings. Clinical obstetrics and gynecology. 2018; 61:743-54. [PubMed][CrossRef]
7. Jauniaux E, Collins S, Burton GJ. Placenta accreta spectrum: pathophysiology and evidence-based anatomy for prenatal ultrasound imaging. American journal of obstetrics and gynecology. 2018; 218:75-87. [PubMed][CrossRef]
8. Weiner E, Miremberg H, Grinstein E, Schreiber L, Ginath S, Bar J, et al. Placental histopathology lesions and pregnancy outcome in pregnancies complicated with symptomatic vs. non-symptomatic placenta previa. Early human development. 2016; 101:85-9. [PubMed][CrossRef]
9. Burton GJ, Jauniaux E. Pathophysiology of placental-derived fetal growth restriction. American journal of obstetrics and gynecology. 2018; 218:S745-S61. [PubMed][CrossRef]
10. Nicolaides K, Wright D, Syngelaki A, Wright A, Akolekar R. Fetal Medicine Foundation fetal and neonatal population weight charts. Ultrasound in Obstetrics & Gynecology. 2018; 52:44-51. [PubMed][CrossRef]
11. Egbor M, Ansari T, Morris N, Green C, Sibbons P. Pre-eclampsia and fetal growth restriction: how morphometrically different is the placenta? Placenta. 2006; 27:727-34. [PubMed][CrossRef]
12. Brosens I, Pijnenborg R, Vercruysse L, Romero R. The "Great Obstetrical Syndromes" are associated with disorders of deep placentation. American journal of obstetrics and gynecology. 2011; 204:193-201. [PubMed][CrossRef]
13. Ong SS, Baker PN, Mayhew TM, Dunn WR. Remodeling of myometrial radial arteries in preeclampsia. American journal of obstetrics and gynecology. 2005; 192:572-9. [PubMed][CrossRef]
14. Redline RW. Classification of placental lesions. American journal of obstetrics and gynecology. 2015; 213:S21-S8. [PubMed][CrossRef]
15. Weiner E, Miremberg H, Grinstein E, Mizrachi Y, Schreiber L, Bar J, et al. The effect of placenta previa on fetal growth and pregnancy outcome, in correlation with placental pathology. Journal of perinatology : official journal of the California Perinatal Association. 2016; 36:1073-8. [PubMed][CrossRef]

16. Harper LM, Odibo AO, Macones GA, Crane JP, Cahill AG. Effect of placenta previa on fetal growth. American journal of obstetrics and gynecology. 2010; 203:330. e1-. e5. [PubMed] [CrossRef]

17. Hannon T, Innes BA, Lash GE, Bulmer JN, Robson SC. Effects of local decidua on trophoblast invasion and spiral artery remodeling in focal placenta creta - an immunohistochemical study. Placenta. 2012; 33:998-1004. [PubMed][CrossRef]

18. Jauniaux E, Dimitrova I, Kenyon N, Mhallem M, Kametas NA, Zosmer N, et al. Impact of placenta previa with placenta accreta spectrum disorder on fetal growth. Ultrasound in Obstetrics & Gynecology. 2019; 54:643-9. [PubMed] [CrossRef]

19. Flo K, Widnes C, Vårtun Å, Acharya G. Blood flow to the scarred gravid uterus at 22–24 weeks of gestation. BJOG: An International Journal of Obstetrics & Gynaecology. 2014; 121:210-5. [PubMed][CrossRef]

20. Torabi S, Sheikh M, Fattahi Masrour F, Shamshirsaz AA, Bateni ZH, Nassr AA, et al. Uterine artery Doppler ultrasound in second pregnancy with previous elective cesarean section(). The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet. 2019; 32:2221-7. [PubMed][CrossRef]

21. Kalanithi LE, Illuzzi JL, Nossov VB, Frisbaek Y, Abdel-Razeq S, Copel JA, et al. Intrauterine growth restriction and placental location. Journal of Ultrasound in Medicine. 2007; 26:1481-9. [PubMed][CrossRef]