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Impact of placenta previa with placenta accreta spectrum disorder on fetal growth

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KEYWORDS: birth weight; fetal growth; increta; percreta; placenta previa accreta

CONTRIBUTION

What are the novel findings of this work?
Placenta previa accreta does not impact on fetal growth.

What are the clinical implications of this work?
As placenta previa accreta does not pose a risk to fetal development other than those linked to premature birth, serial ultrasound examinations should not be required to evaluate fetal wellbeing in the second half of pregnancy in women presenting with placenta previa accreta.

ABSTRACT

Objectives *To evaluate fetal growth in pregnancies complicated by placenta previa with or without placenta accreta spectrum (PAS) disorder, compared with in pregnancies with a low-lying placenta.*

Methods *This was a multicenter retrospective cohort study of singleton pregnancies complicated by placenta previa with or without PAS disorder, for which maternal characteristics, ultrasound-estimated fetal weight and birth weight were available. Four maternal–fetal medicine units participated in data collection of diagnosis, treatment and outcome. The control group comprised singleton pregnancies with a low-lying placenta (0.5–2 cm from the internal os). The diagnosis of PAS and depth of invasion were confirmed at delivery using both a predefined clinical grading score and histopathological examination. For comparison of pregnancy characteristics and fetal growth parameters, the study groups were matched for smoking status, ethnic origin, fetal sex and gestational age at delivery.*

Results *The study included 82 women with placenta previa with PAS disorder, subdivided into adherent (*n = *35) and invasive (*n = *47) PAS subgroups, and 146 women with placenta previa without PAS disorder. There were 64 controls with a low-lying placenta. There was no significant difference in the incidence of small-for-gestational age (SGA) (birth weight* $\leq 10^{th}$ *percentile) and large-for-gestational age (LGA) (birth weight* $\geq 90^{th}$ *percentile) between the study groups. Median gestational age at diagnosis was significantly lower in pregnancies with placenta previa without PAS disorder than in the low-lying placenta group (*P = *0.002). No significant difference was found between pregnancies complicated by placenta previa with PAS disorder and those without for any of the variables. Median estimated fetal weight percentile was significantly lower in the adherent compared with the invasive previa–PAS subgroup (*P = *0.047). Actual birth weight percentile at delivery did not differ significantly between the subgroups (*P = *0.804).*

Conclusions *No difference was seen in fetal growth in pregnancies complicated by placenta previa with PAS disorder compared with those without and compared with those with a low-lying placenta. There was also no increased incidence of either SGA or LGA neonates in pregnancies with placenta previa and PAS disorder compared with those with placenta previa with spontaneous separation of the placenta at birth. Adverse neonatal outcome in pregnancies complicated by placenta previa and PAS disorder is linked to premature delivery and not to impaired fetal growth.* Copyright © 2019 ISUOG. Published by John Wiley & Sons Ltd.

INTRODUCTION

The risk of placenta previa increases after a single Cesarean delivery and rises further with increasing number of Cesarean deliveries[1,2]. The main factor

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associated with placenta accreta spectrum (PAS) disorder is prior Cesarean delivery and, similar to placenta previa, the risk of developing PAS in subsequent pregnancies increases with the number of previous Cesarean deliveries[3]. Epidemiological data suggest that the scar left following a Cesarean delivery in the myometrium of the lower uterine segment encourages both implantation of the blastocyst in the area of the scar and abnormal adherence or invasion of placental villi within the scar tissue. Placenta previa and PAS disorder often occur together, and women with a history of Cesarean section and presenting with a low-lying placenta or placenta previa represent the group with the highest risk of PAS disorder[4].

Poor vascularization and tissue oxygenation in the area of a Cesarean scar is associated with local failure of re-epithelialization and decidualization, which has an impact on both implantation and placentation[5–7], as well as a possible effect on placental development and, subsequently, fetal growth. Women with a previous Cesarean delivery have been shown to have increased uterine artery resistance in a subsequent pregnancy compared with those with previous vaginal delivery only[8]. The main complication of placenta previa during pregnancy is antepartum hemorrhage, which affects around 50% of cases[9]. Furthermore, recent studies have suggested that pregnancies complicated by placenta previa are at higher risk of delivering a small-for-gestational-age (SGA) neonate and are associated with a higher incidence of placental vascular supply lesions[10,11]. Placenta previa with PAS disorder is also associated with a higher risk of antepartum bleeding due to the placental position inside the uterine cavity, but the main risk of major hemorrhage is during delivery, particularly in cases that remain undiagnosed during pregnancy[12].

One of the primary characteristics of PAS disorder placentation is the absence of decidua in the placentation area[6,7]. Several authors have found that spiral artery remodeling is reduced in PAS[13–15]. Incomplete transformation of the spiral arteries and lesions associated with maternal vascular malperfusion are commonly found in placenta-related disorders of pregnancy, such as fetal growth restriction (FGR) and pre-eclampsia[16], suggesting that PAS placentation in a pregnancy complicated by placenta previa may have an even greater impact on placental development and function. Placenta previa and PAS disorder are both associated with high risks of prenatal and perinatal maternal complications but there are limited data available on their possible impact on fetal growth. The aim of this study was therefore to examine further the possible impact of placenta previa with and without PAS disorder on fetal growth.

METHODS

This was a retrospective, multicenter cohort study of 292 consecutive patients presenting with a singleton pregnancy, diagnosed between 20 and 36 weeks of gestation with placenta previa with or without PAS, or with a low-lying placenta, during a 6-year period, for which ultrasound and clinical outcome data were available. The maternal–fetal medicine units of four hospitals (University College Hospitals London, King's College Hospital, University of Oxford and Saint Luc University Hospital) participated in data collection. All four units are part of regional referral centers and only patients who were referred prenatally were included in the study. Multiple pregnancies and those complicated by diabetes were excluded from the study. Local institutional ethics committee approval was obtained by the principal investigator in each of the centers. Retrospective patient consent was not required for this study as all ultrasound records were examined within the center at which the examination was performed, basic clinical data were collected using a standard clinical audit protocol and all data were fully anonymized before being submitted for central analysis.

In all cases, fetal ultrasound measurements and diagnosis of abnormal placentation were obtained prenatally by expert maternal–fetal medicine physicians using both transabdominal and transvaginal ultrasound. All pregnancies were dated using the last menstrual period with confirmation by crown–rump length before 14 weeks of gestation or biparietal diameter from 14 weeks. Estimated fetal weight (EFW) and corresponding percentiles were calculated at the time of referral to the specialist unit using the Hadlock regression formula incorporating abdominal circumference, femur length, head circumference and biparietal diameter[17]. Using transvaginal ultrasound examination, a placenta was recorded as 'low lying' when the edge was 0.5–2 cm from the internal os of the uterine cervix. When the placenta was < 0.5 cm from the internal os or completely covering it, it was defined as placenta previa (marginal or complete)[18]. The diagnosis of PAS disorder was made by maternal–fetal medicine physicians experienced with the condition, using the standardized reporting pro-forma proposed by the abnormally invasive placenta (AIP) international expert group[19].

The women were managed according to their local unit protocol. Pregnancy and delivery data were collected from hospital records. The primary outcome was birth weight and the secondary outcome was the impact of the grade of PAS disorder. Birth weight percentiles were calculated using the new intrauterine growth curves of the Fetal Medicine Foundation[20]. SGA and LGA were defined as birth weight $\leq 10^{th}$ and $\geq 90^{th}$ percentiles, respectively. The presence and severity of a PAS disorder was assessed at delivery by an attending obstetrician with experience of PAS, according to the current FIGO-recommended clinical grading system[21] and from histopathological results if a hysterectomy or partial myometrial resection was performed. In each unit, all pathological examinations were undertaken by senior pathologists with expertise in perinatal pathology. The cases of placenta previa with PAS were then subdivided, according to the depth of villous invasion, into adherent PAS (clinical Grade 1 or histopathological diagnosis of accreta) and invasive PAS (clinical Grade 2, 3a or 3b or histopathological diagnosis of increta or percreta).

StatGraphics Plus (Version 3; Manugistics, Rockville, MD, USA), SPSS Statistics for Windows (Version 25.0., IBM Corp., Armonk, NY, USA) and MedCalc Statistical Software (Version 14.12.0, MedCalc Software, Ostend, Belgium) were used for data analysis. Standard kurtosis analysis indicated that some variables were not normally distributed, and these are therefore presented as median and interquartile range (IQR). Categorical variables were compared between groups using Pearson's chi-square test or Fisher's exact test when sample sizes were small. Continuous variables were compared using ANOVA, the Kruskal–Wallis test or the Mann–Whitney (Wilcoxon) *W* rank test. Data from pregnancies with a low-lying placenta and those complicated by placenta previa with PAS disorder and those without were compared after matching on a 1 : 1 basis for maternal smoking status, ethnic origin, fetal sex and gestational age at delivery. Individual correlations between ultrasound EFW percentile and birth-weight percentile were calculated using the least squares method and their slopes were tested for significance using the *F*-ratio test. A *P*-value of < 0.05 was considered significant. Univariate and multivariate binary logistic regression analyses were used to assess the independent contributions to the prediction of SGA of maternal age, parity, gestational age at diagnosis, ultrasound EFW and study group (low-lying placenta, placenta previa with PAS or placenta previa without PAS), coded in a single nominal variable as 'Group'.

RESULTS

This study included 82 women with placenta previa with PAS disorder, 146 with placenta previa without PAS disorder and 64 with a low-lying placenta. The placenta previa with PAS group included 35 cases of adherent PAS and 47 cases of invasive PAS (20 of increta and 27 of percreta). Around two-thirds of the women included in the study were referred for prenatal care and delivery by other units with no multidisciplinary surgical team and/or access to neonatal intensive care. There were no maternal hypertensive comorbidities or pre-existing thrombophilias in any of the study groups. No increase in placental lesions associated with maternal vascular malperfusion, such as maternal floor infarctions and atherosis of the spiral arteries, was reported in PAS cases managed by primary Cesarean hysterectomy.

The clinical characteristics of the groups are displayed in Table 1. There was no significant difference between the study groups in the proportion of women of advanced maternal age, median maternal age, fetal sex ratio and the proportion of women who smoked during pregnancy. There was a significantly higher proportion of women of Asian origin in the placenta previa without PAS group than in the low-lying placenta group ($P = 0.028$) and placenta previa with PAS group ($P = 0.029$). In the placenta previa with PAS group, there were no primiparous women and median parity was 2 (IQR, 1.0–3.0). In this group, one woman had a history of myomectomy and the remaining women had all had one or more previous Cesarean deliveries. The proportion of nulliparous women was not significantly different between the placenta previa without PAS and low-lying placenta groups. A significantly higher number of women presenting with placenta previa and PAS were delivered prematurely for maternal symptoms, compared with both the placenta previa without PAS and low-lying placenta groups ($P < 0.001$ for both). Median gestational age at delivery was lower in the cases of placenta previa with PAS compared with in

Table 1 Clinical characteristics of 292 pregnancies, according to diagnosis with low-lying placenta or placenta previa with or without placenta accreta spectrum (PAS) disorder

Characteristic	*Low-lying placenta* (n = *64*)	*Placenta previa without PAS* (n = *146*)	*Placenta previa with PAS* (n = *82*)	P
Maternal age (years)	34.0 (30.0–38.0)	34.5 (31.0–38.0)	35.5 (31.7–38.0)	0.611
AMA ≥ 35 years	29 (45.3)	73 (50.0)	45 (54.9)	0.564
AMA ≥ 40 years	10 (15.6)	19 (13.0)	15 (18.3)	0.556
Smoker	5 (7.8)	12 (8.2)	10 (12.2)	0.560
Ethnic origin				
Caucasian	52 (81.3)	102 (69.9)	56 (68.3)	
Asian	4 (6.3)	26 (17.8)	6 (7.3)	
Afro-Caribbean	7 (10.9)	17 (11.6)	18 (22.0)	
Other	1 (1.6)	1 (0.7)	2 (2.4)	
Nulliparous	25 (39.1)*	45 (30.8)*	0 (0.0)	< 0.001
Fetal sex ratio (M : F)	32 : 31	78 : 68	43 : 39	0.940
GA at confirmed diagnosis (weeks)	27.6 (20.5–35.1)	22.4 (20.3–30.3)*	29.3 (26.0–33.3)	< 0.001
Ultrasound EFW percentile	45.0 (30.0–60.0)	48.0 (31.7–67.2)	50.0 (35.7–69.2)	0.538
GA at delivery (weeks)	38.3 (37.2–39.1)*	38.0 (36.4–39.0)*	36.2 (34.1–37.2)	< 0.001
Delivery < 37 weeks	13 (20.3)*	41 (28.1)*	51 (62.2)	0.002
Birth-weight percentile	54.9 (16.2–80.2)	52.3 (22.5–75.2)	42.7 (22.1–81.2)	0.997
Birth weight ≤ 10th percentile	7 (10.9)	16 (11.0)	11 (13.4)	0.842
Birth weight ≥ 90th percentile	8 (12.5)	16 (11.0)	11 (13.4)	0.842

Data are given as median (interquartile range) or *n* (%). *P*-values denote overall significance using Kruskal–Wallis test or ANOVA (for continuous data) and chi-square test (for categorical data). *$P < 0.001$ on pairwise comparison *vs* group with placenta previa and PAS. AMA, advanced maternal age; EFW, estimated fetal weight; F, female; GA, gestational age; M, male.

the low-lying placenta and placenta previa without PAS groups ($P < 0.001$ for both). A significantly higher proportion of women in the placenta previa without PAS group were delivered before 37 weeks of gestation than in the low-lying placenta group ($P = 0.002$).

There was no significant difference in birth-weight percentile or the incidence of SGA and LGA between the study groups (Figure 1 and Table 1). Only three of the 11 fetuses of pregnancies with placenta previa and PAS with birth weight $\leq 10^{th}$ percentile also had ultrasound EFW $\leq 10^{th}$ percentile.

Table 2 shows maternal and pregnancy characteristics and fetal growth parameters in the placenta previa without PAS ($n = 60$) and low-lying placenta ($n = 60$) groups matched for smoking status, ethnic origin, fetal sex ratio and gestational age at delivery. Median gestational age at diagnosis was significantly lower in the placenta previa without PAS group than in the low-lying placenta group ($P = 0.002$). There was no significant difference between the groups for the other variables.

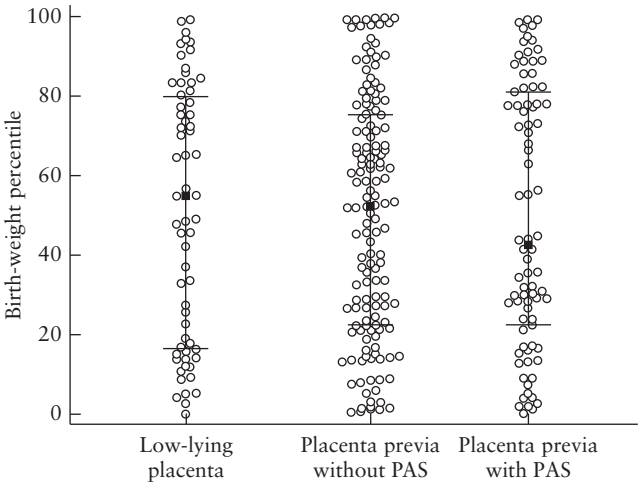

Figure 1 Birth-weight percentile in 292 pregnancies, according to diagnosis with low-lying placenta or placenta previa with or without placenta accreta spectrum (PAS) disorder. Bars are interquartile range and ■ is median.

Table 3 shows maternal and pregnancy characteristics and fetal growth parameters in the placenta previa with PAS ($n = 52$) and without PAS ($n = 52$) groups matched for smoking status, ethnic origin, fetal sex ratio and gestational age at delivery. No significant difference was found between the groups for any of the variables.

Table 4 shows maternal and pregnancy characteristics and fetal growth parameters in the adherent ($n = 35$) and invasive ($n = 47$) PAS subgroups. Median EFW percentile was significantly lower in the adherent compared with the invasive subgroup ($P = 0.047$), although birth-weight percentile did not differ significantly ($P = 0.804$) (Figure 2). No other significant difference was found between these subgroups.

On univariate binary logistic regression analysis, significant predictors of SGA were maternal age (logit (SGA) $= 0.94 - 0.9 \times$ maternal age; $P = 0.02$; $R^2 = 0.03$) and ultrasound EFW (logit (EFW) $= -0.17 - 0.4 \times$ EFW; $P < 0.001$; $R^2 = 0.15$), but not parity ($P = 0.5$), gestational age at diagnosis ($P = 0.7$) or group ($P = 0.6$). Multivariate binary logistic regression analysis demonstrated that independent contributors to the prediction of SGA were maternal age and EFW (logit (SGA) $= 2.54 - 0.08 \times$ maternal age $- 0.04 \times$ EFW; $P < 0.001$; $R^2 = 0.17$).

DISCUSSION

Main findings

The results of this study indicate that the risk of SGA is not increased in pregnancies complicated by placenta previa with or without PAS disorder and that, after matching for smoking status, ethnic origin, fetal sex and gestational age at delivery, there is no difference in fetal growth between pregnancies with a low-lying placenta and those with placenta previa without PAS disorder, and median ultrasound EFW and birth weight are around the 50th percentile in both groups. This study also demonstrates that there is no difference in fetal growth between pregnancies with placenta previa with PAS disorder and both those with

Table 2 Characteristics and fetal growth parameters in pregnancies with low-lying placenta and those with placenta previa without placenta accreta spectrum (PAS) disorder, matched for smoking status, ethnic origin, fetal sex and gestational age at delivery

Variable	*Low-lying placenta* (n = *60*)	*Placenta previa without PAS* (n = *60*)	P
Maternal age (years)	34.0 (30.0–38.0)	34.0 (32.5–37.0)	0.695
AMA ≥ 35 years	28 (46.7)	29 (48.3)	0.855
AMA ≥ 40 years	9 (15.0)	8 (13.3)	0.793
Parity	1.0 (0.0–1.5)	1.0 (0.0–2.0)	0.054
GA at confirmed diagnosis (weeks)	27.0 (20.4–34.9)	20.4 (20.1–29.3)	0.002
Ultrasound EFW percentile	47.5 (30.2–60.7)	53.5 (29.0–68.0)	0.386
GA at delivery (weeks)	38.2 (37.2–39.1)	38.1 (37.1–39.1)	0.729
Delivery < 37 weeks	12 (20.0)	12 (20.0)	1.00
Birth-weight percentile	51.9 (16.3–81.2)	58.5 (24.4–78.8)	0.639
Birth weight ≤ 10th percentile	6 (10.0)	4 (6.7)	0.509
Birth weight ≥ 90th percentile	8 (13.3)	9 (15.0)	0.793

Data are given as median (interquartile range) or *n* (%). AMA, advanced maternal age; EFW, estimated fetal weight; GA, gestational age.

Table 3 Characteristics and fetal growth parameters in pregnancies with placenta previa with and those without placenta accreta spectrum (PAS) disorder, matched for smoking status, ethnic origin, fetal sex and gestational age at delivery

Variable	*Placenta previa without PAS (n = 52)*	*Placenta previa with PAS (n = 52)*	P
Maternal age (years)	36.0 (31.2–39.0)	35.0 (31.2–38.0)	0.696
AMA ≥ 35 years	30 (57.7)	27 (51.9)	0.544
AMA ≥ 40 years	9 (17.3)	10 (19.2)	0.800
Parity	1.5 (1.0–2.0)	2.0 (1.0–3.0)	0.061
GA at confirmed diagnosis (weeks)	29.6 (21.1–32.5)	30.0 (26.2–34.0)	0.072
Ultrasound EFW percentile	47.0 (34.0–68.7)	50.5 (36.0–68.7)	0.730
GA at delivery (weeks)	36.5 (35.2–37.4)	36.5 (35.3–37.3)	0.578
Delivery < 37 weeks	27 (51.9)	27 (51.9)	1.000
Birth-weight percentile	38.8 (21.5–65.9)	49.6 (22.7–81.8)	0.158
Birth weight ≤ 10th percentile	7 (13.5)	8 (15.4)	0.780
Birth weight ≥ 90th percentile	1 (1.9)	6 (11.5)	0.113

Data are given as median (interquartile range) or *n* (%). AMA, advanced maternal age; EFW, estimated fetal weight; GA, gestational age.

Table 4 Characteristics and fetal growth parameters in pregnancies with placenta previa and placenta accreta spectrum (PAS) disorder, according to classification as adherent or invasive placenta

Variable	*Adherent PAS (n = 35)*	*Invasive PAS (n = 47)*	P
Maternal age (years)	36.0 (31.0–39.0)	35.0 (32.0–38.0)	0.914
AMA ≥ 35 years	20 (57.1)	25 (53.2)	0.722
AMA ≥ 40 years	6 (17.1)	9 (19.1)	0.816
Parity	2.0 (1.0–3.0)	2.3 (1.0–3.0)	0.465
GA at confirmed diagnosis (weeks)	29.2 (25.3–34.0)	30.0 (26.1–33.1)	0.888
Ultrasound EFW percentile	44.0 (25.0–63.0)	57.0 (38.0–70.0)	0.047
GA at delivery (weeks)	36.0 (34.5–37.3)	35.5 (34.0–37.0)	0.075
Delivery < 37 weeks	19 (54.3)	32 (68.1)	0.202
Birth-weight percentile	41.7 (16.4–82.2)	43.8 (26.3–78.1)	0.804
Birth weight ≤ 10th percentile	5 (14.3)	6 (12.8)	0.842
Birth weight ≥ 90th percentile	5 (14.3)	6 (12.8)	0.842

Data are given as median (interquartile range) or *n* (%). AMA, advanced maternal age; EFW, estimated fetal weight; GA, gestational age.

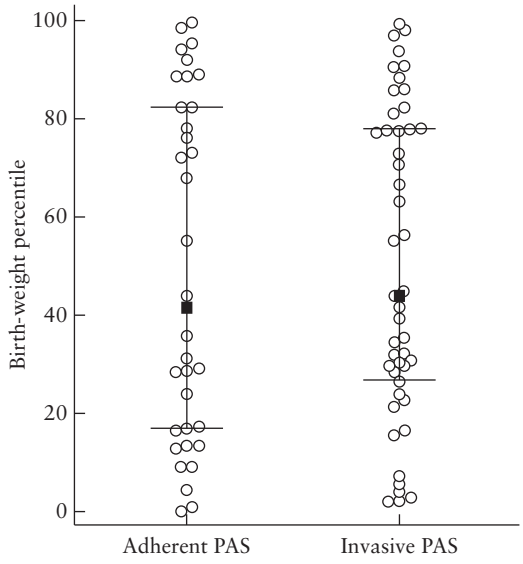

Figure 2 Birth-weight percentile in 82 pregnancies complicated by placenta previa with placenta accreta spectrum (PAS) disorder, according to classification as adherent or invasive placenta. Bars are interquartile range and ■ is median.

placenta previa without PAS and those with a low-lying placenta. No difference was seen in fetal growth between the adherent and invasive PAS disorder subgroups.

Strengths and limitations

Our study has a number of strengths compared with other contemporary published studies. It captured cases from ultrasound and maternity hospital records, eliminating potential bias from exclusively database-captured or self-reported cases. Birth-weight percentile was calculated at the different centers using the new intrauterine growth curves of the Fetal Medicine Foundation[20] that overcome the issue of underestimating growth restriction in preterm birth. The relatively large number of cases in each study group enabled them to be matched for maternal ethnic origin, fetal gender, smoking status and gestational age at delivery, thus controlling for the main factors affecting fetal growth.

The weakness of this study is its retrospective design, although this was mitigated by the relatively hard outcome data collected. Cases were included only if there was documented transvaginal ultrasound evidence

of a measured distance between the placental edge and internal os. It could be argued that including cases with a placenta inserted elsewhere in the uterus, such as in the fundus, as a control group might have been more appropriate; however, the precise site of placental implantation is notoriously inaccurate when reported on routine ultrasound scanning. Therefore, by using those reported as 'low-lying' on transvaginal ultrasound examination, we ensured that we were certain that the majority of the placenta in that group was implanted upwards and away from the lower segment. We used pregnancies with a low-lying placenta as the control group in order to remove confounding factors, ensuring that any differences were due to the presence of PAS disorder rather than the site of implantation.

Comparison with previous studies and clinical implications

In a controlled study of 119 cases with *vs* 199 without previa placenta matched for maternal complications, Weiner *et al.* found that placenta previa was associated significantly with delivery of a SGA neonate, a smaller placenta and a higher incidence of vascular lesions secondary to maternal malperfusion and fetal thrombo-occlusive disease[10]. Although mean birth weight in the placenta previa group was 700 g higher than in the control group, the incidence of SGA with birth weight $< 10^{th}$ and $< 5^{th}$ percentiles was significantly higher in the placenta previa group[10]. In a secondary analysis of the placenta previa group, they found that placental size was smaller and the incidence of placental tissue vascular lesions was higher in symptomatic women compared with asymptomatic women[11]. They hypothesized that placentation in the lower segment of the uterus is associated with suboptimal vascular development of both the uteroplacental and umbilicoplacental circulations. Compared with the present study, their rate of active smokers was more than double and 13% of their patients had thrombophilia[10,11]. Both maternal smoking[22] and thrombophilia[23] are associated with poor placental development, FGR and a higher incidence of placental vascular lesions. Weiner *et al.* did not match their cases and controls for maternal smoking status or gestational age at delivery[10,11]. Their patients with placenta previa were delivered on average 3 weeks before the controls without placenta previa, making the evaluation of placental weight and fetal birth weight inaccurate. Finally, they did not differentiate between low-lying placenta and placenta previa, which may have had an impact on pregnancy outcome and, in particular, maternal symptoms and premature delivery rate.

In a population-based, retrospective cohort study of singleton live births in women diagnosed with placenta previa, Ananth *et al.*[24], reported a higher rate of low birth weight due to preterm delivery and, to a lesser extent, FGR. The authors concluded that the risk of lower birth weight was increased only slightly among women presenting with placenta previa, but this association may be of little clinical significance when adjusted for gestational age at delivery. In a recent large retrospective cohort study of 724 women diagnosed prenatally with partial or complete placenta previa, Harper *et al.*[25] found that, after adjusting for confounding factors such as race, the risk of FGR, defined as a birth weight $< 10^{th}$ percentile, was similar in pregnancies with placenta previa compared with controls without placenta previa. The presence of bleeding and the type of placenta (i.e. low-lying placenta (partial previa) or placenta previa (marginal or complete)) did not impact the risk of FGR. The finding of a similarly low rate of birth weight $< 10^{th}$ percentile in both pregnancies with a low-lying placenta and those with placenta previa in both the study of Harper *et al.* and the current study suggests that development of most of the placenta inside the lower uterine segment does not affect the normal development of the uteroplacental circulation, the biological function of the placenta and the growth of the fetus.

This study is the first to have evaluated fetal growth in pregnancies complicated by placenta previa and PAS. Myofiber disarray, tissue edema, inflammation and elastosis have all been observed in uterine wound healing after surgery[26]. A Doppler ultrasound study of the uterine circulation in women with a previous Cesarean section showed that uterine artery resistance is increased and the volume of uterine blood flow is decreased as a fraction of maternal cardiac output compared with in women with previous vaginal delivery only[8]. Several histopathological studies[13–15] have shown a decreased proportion of remodeled spiral arteries, with many vessels displaying partial physiological change in PAS disorder areas in both adherent and invasive cases. Incomplete transformation of the uteroplacental circulation is seen more often in cases without local decidua, and vascular remodeling is sometimes completely absent in the PAS disorder area[15]. This is a common feature of pregnancy complicated by pre-eclampsia and/or FGR[16] but, in cases of invasive PAS disorder, there is a greater degree of remodeling in radial/arcuate arteries[13,14], suggesting that the overall maternal blood volume entering the placenta is increased rather than decreased. Our data, which indicate a low incidence of birth weight $\leq 10^{th}$ centile in the placenta previa with PAS group and no difference in median birth weight percentile between the adherent and invasive subgroups, suggest that the histopathological findings of differences in the spiral arteries in the accreta area has no impact on fetal growth. In most cases, the abnormal PAS area is limited to a few cotyledons and, thus, it does not affect the normal physiological changes of the spiral arteries outside the accreta area and the development and biological function of the rest of the placental tissue.

Conclusions

Women presenting with placenta previa without PAS disorder and those diagnosed prenatally with PAS are not at increased risk of SGA. Overall, parous women are at lower risk of developing pregnancy complications such as pre-eclampsia than are nulliparous women and, thus, their

management and, in particular, the timing of delivery will depend mainly on maternal symptoms, severity of the PAS disorder and risk of antenatal hemorrhage. Serial ultrasound examinations for fetal growth are therefore not indicated in women with placenta previa with or without PAS for this indication alone, and adverse neonatal outcome is primarily due to the complications of prematurity and unlikely to be influenced by impaired fetal growth.

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