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

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ABSTRACT

Objectives: To evaluate fetal growth in pregnancies complicated by placenta previa, both with and without PAS, compared to pregnancies with just a low-lying placenta.

Methods: This was a multicentre retrospective cohort study of singleton pregnancies complicated by placenta previa, both with and without placenta accreta spectrum (PAS), for which maternal characteristics, ultrasound estimated fetal weight and birthweight were available. The control group chosen was singleton pregnancies with a low-lying placenta (0.5-2cm from the internal os). For comparison, the study groups were matched for smoking status, ethnic origin and gestational age at delivery. The diagnosis of PAS and depth of invasiveness was confirmed at birth using both a pre-defined clinical grading score and histopathological examination. Four maternal-fetal medicine units participated in data collection of diagnosis, treatment, and outcomes.

Results: The study included 82 women with previa-PAS, subdivided into adherent previa-PAS (n= 35) and invasive previa-PAS (n= 47) and 146 women with a placenta previa. There were 64 controls with a low-lying placenta. There was no significant difference in the incidence of small-for-gestational age (SGA) and large-for-gestational age (LGA) between the study groups at the different percentiles cut-off values. The median gestational age at diagnosis was significantly (P=0.002) lower in the placenta previa than in the low-lying placenta group. No significant difference was found between previa-PAS and placenta previa groups for any of the variables.

The median EFW percentile was significantly higher in the adherent compared to the invasive subgroup (*P*= 0.048). The actual birthweight percentiles at delivery did not differ significantly (*P*= 0.804) between the subgroups.

Conclusions: No difference was seen in fetal growth for pregnancies with a previa-PAS when compared with placenta previa and low-lying placenta. There was also no increased incidence of either SGA or LGA babies when a placenta previa was complicated by PAS when compared to a previa which separated spontaneously at birth. Neonatal outcome in previa-PAS is linked to premature delivery and not to impaired fetal growth.

INTRODUCTION

The incidence of placenta previa increases after a single caesarean delivery, and still further with increasing numbers of caesarean deliveries[1,2]. The main factor leading to placenta accreta spectrum (PAS) disorder is a prior caesarean delivery and as for placenta previa, the risk of developing PAS in subsequent pregnancies increases with the number of previous caesarean deliveries[3]. Overall the epidemiological data suggest that the scar left by a caesarean delivery in the lower segment uterine myometrium encourages both implantation of the blastocyst in the area of the scar and the abnormal adherence or invasion of placental villi within the scar tissue. The two placental conditions are often combined and women with a prior history of caesarean section, presenting with a low-lying placenta or placenta previa, now represent the group with the highest risk of PAS disorder[4].

Poor vascularisation and tissue oxygenation in the area of a previous scar is associated with a local failure of re-epithelialization and decidualization which has an impact on both implantation and placentation[5-7] but also possibly on placental development and subsequently on fetal growth. Women with a previous caesarean delivery have been shown to have an increased uterine artery resistance in a subsequent pregnancy compared to women with a previous vaginal birth[8]. The main complication of placenta previa during pregnancy is antepartum hemorrhage which affects around 50% of cases[9]. In addition, recent studies have suggested that the fetuses of women presenting with placenta previa are at higher risks of small-for-

gestational-age (SGA) associated with a higher incidence of placental vascular supply lesions[10,11]. Placenta previa-PAS is also associated with higher risks of antepartum bleeding due to the placental position inside the uterine cavity but the main risk of major hemorrhage is during delivery, in particular, in cases that remain undiagnosed during pregnancy[12].

One of the primary characteristics of PAS placentation is the absence of decidua in the placentation area[6,7]. Several authors have found that the spiral artery remodeling is reduced in PAS[13-15]. Incomplete transformation of the spiral arteries and lesions associated with maternal vascular malperfusion is commonly found in placental-related disorders of pregnancy such as fetal growth restriction and preeclampsia[16], suggesting that PAS placentation in a placenta previa may have an even greater impact on placental development and functions. Placenta previa and placenta accreta spectrum (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 further examine the possible association between placentation anomalies and fetal growth restriction.

METHODS

We conducted a retrospective, multicentre cohort study of 292 consecutive patients presenting with a singleton pregnancy diagnosed between 20 and 36 weeks of gestation with a placenta previa, both with and without PAS, or with a low-lying placenta over a 6-year period for which ultrasound and clinical outcome data were available. Four maternal-fetal medicine units and the hospitals (University College Hospitals London, The Fetal Medicine Research Institute, Nuffield Department of Women's and Reproductive Health and Saint Luc University Hospital) in which they practice, participated in data collection. All four units are part of regional referral centres and only patients who were referred prenatally were included in the study. Multiple pregnancies and pregnancies complicated by diabetes were excluded from the study. Local institutional ethical committee approval was obtained by the principal investigator in the different centres involved in the study. Retrospective patient consent was not required for this study as all ultrasound records were examined within the centre where it was undertaken, basic clinical data were collected using a standard clinical audit protocol and all data were fully anonymised before being submitted for central analysis.

In all cases, the fetal ultrasound measurements and diagnosis of abnormal placentation were obtained prenatally by expert maternal-fetal medicine physicians using both transabdominal and transvaginal ultrasound transducers. All pregnancies were dated using the last menstrual period and confirmed by crown-rump length before 14 weeks of gestation or biparietal diameter (BPD) from 14 weeks. Estimated

fetal-weight (EFW) and the corresponding percentiles were calculated using the Hadlock regression formulae including abdominal circumference, femur length, head circumference, biparietal diameter[17], at the time of referral to the specialist unit. 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 <0.5cm from the internal os or completely covering it, it was defined as placenta previa (marginal or complete)[18]. The diagnosis of placenta accreta spectrum disorder was made by maternal-fetal medicine physicians experienced with the condition using the standardised reporting pro-forma proposed by the 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 the birthweight and the secondary outcome was impact of the grade of PAS. Birthweight percentiles were calculated using the new intrauterine growth curves of the Fetal Medicine Foundation.[20] Small for gestational age (SGA) and Large for gestational age (LGA) were defined as birthweight centile below the 10th and above the 90th, respectively. The presence and severity of any 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 a partial myometrial resection was performed. In each unit, all pathologic examinations were undertaken by senior pathologists who have expertise in perinatal pathology. The cases of previa-PAS were then sub-divided

according of to the depth of villous invasiveness into adherent previa-PAS (clinical grade 1 or histopathological diagnosis of accreta) and invasive previa-PAS (clinical grades 2, 3a or 3b or histopathological diagnosis of increta or percreta).

StatGraphic-plus data analysis (Version 3; Manugistics, Rockville, MD) SPSS Statistics for Windows (The statistical software package IBM Corp, Version 25.0. Armonk, NY: IBM Corp) and MedCalc Statistical Software (Version 14.12.0 (MedCalc Software, Ostend, Belgium) were used for data analysis. Standard Kurtosis analysis indicated that some values were not normally distributed and are therefore presented as median and interquartile range (IQR). Categorical variables were compared between groups using the Pearson's chi-square test or Fisher's exact test when samples sizes were small. Continuous variables were compared using the ANOVA, Kruskal Wallis or Mann-Whitney (Wilcoxon) W rank test at the 95% confidence interval (CI). The data from the low-lying, placenta previa and previa-PAS groups were compared after matching on a 1:1 basis for maternal smoking status, ethnic origin and gestational age at delivery. Individual correlations between the ultrasound and birthweight percentiles were calculated by the least square method and their slopes tested for significance by the *F* ratio test. A *P* value <0.05 was considered significant. Univariate and multivariate binary logistic regression was used to assess the independent contributions of maternal age, parity, gestational age at diagnosis, ultrasound estimated fetal weight (EFW) and the three groups of women (Low-lying placenta, placenta previa and previa-PAS), coded in a

single nominal variable as “Group” for the prediction of small for gestational age (SGA).

RESULTS

The study included 82 women with previa-PAS, 146 with a placenta previa and 64 patients with a low-lying placenta. The previa-PAS study group included 35 cases of adherent previa-PAS and 47 cases of invasive previa-PAS (20 increta and 27 percreta). Around two-thirds of the corresponding women 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 co-morbidities 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 caesarean hysterectomy.

The clinical characteristics of the groups are displayed in Table 1. There was no significant difference between the study groups in the numbers of women of advanced maternal age (AMA), median maternal age, fetal sex ratio and the numbers of women who smoked during pregnancy. There was a significantly higher proportion of women from Asian origin in the placenta previa group than in the low-lying placenta group (P= 0.028) and previa-PAS group (P= 0.029). There were no primiparous in previa-PAS group was and the median parity in the previa-PAS group was 2 (IQR 1.0-3.0). One woman had a history of previous myomectomy, all the remaining women in that group had had one or more caesarean deliveries. The proportion of primiparous women was not significantly different between the previa-PAS and low-lying placenta groups. A significantly (P< 0.001) higher number of

women presenting with placenta previa-PAS were delivered prematurely for maternal symptoms compared to both the placenta previa and low-lying placenta groups. The median gestational age at delivery was lower in the cases of PAS compared to that of low-lying placenta ($P< 0.001$) or placenta praevia ($P< 0.001$). A significantly ($P= 0.002$) higher number of women in the placenta previa group were delivered before 37 weeks of gestation than in the low-lying placenta group.

There was no significant ($P= 0.997$) difference in birthweight centile or the incidence of SGA (p=0.847) and LGA ($P= 0.846$) between the study groups at the different percentiles cut-off values (Figure 1). Only three of the 34 fetuses with a birthweight <10th percentile also had an ultrasound EFW <10th percentile. Seven of the 12 mothers were smokers.

Table 2 displays and compares the maternal characteristics and fetal growth parameters for the placenta previa (n= 60) and low-lying placenta (n= 60) groups matched for smoking status, ethnic origin, fetal sex ratio and gestational age at delivery. The median gestational age at diagnosis was significantly lower in the placenta previa than in the low-lying placenta group ($P= 0.002$). There was no significant difference seen for the other variables between the groups.

Tables 3 shows and compares maternal characteristics and fetal growth parameters between previa-PAS (n= 52) and placenta previa (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 presents and compares the maternal characteristics and fetal growth parameters between the adherent previa-PAS (n= 35) and invasive previa-PAS (n= 47) subgroups. The median EFW percentile was significantly higher in the adherent compared to the invasive subgroup (*P*= 0.048) although the actual birthweight percentiles at delivery (Figure 2) did not differ significantly (*P*= 0.804). No other significant difference was found between these subgroups.

In univariate binary logistic regression, significant predictors of SGA were maternal age (logit (SGA)= 0.94-0.9*Maternal age, p= 0.02, R^2= 0.03), ultrasound estimated fetal weight (logit (EFW)= -0.17-0.4*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 has demonstrated that independent contributors for SGA were maternal age and EFW (logit (SGA)=2.54-0.08*Maternal age-0.04*EFW, p< 0.001, R^2= 0.17).

DISCUSSION

Main findings of the study

The data of this study indicate that the risk of SGA is not increased in placenta previa and that after matching for smoking status, ethnic origin and gestational age at delivery that there is no difference in fetal growth between low-lying placenta and placenta previa and that the median ultrasound EFW and birthweight are around the 50 percentiles in both groups. It also demonstrates that there is no difference in fetal growth with previa-PAS when compared to both placenta previa and low-lying placenta. No difference was seen between fetal growth in adherent previa-PAS when compared with invasive previa-PAS.

Strengths and limitation of the study

Our study has a number of strengths compared to other contemporary published studies. It has captured cases from ultrasound and maternity hospital records, eliminating potential bias from exclusively database-captured or self-reported cases. The birthweight percentiles from the different centres were calculated using the new intrauterine growth curves of the Fetal Medicine Foundation[20] which overcome the issue of underestimating growth restriction birth. The relatively large number of cases in each study group has enabled the different variables 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 the study rests in its retrospective nature, although this was mitigated by the relatively hard outcome data collected. Cases were only included if there was documented ultrasound evidence of a measured distance of the placental edge from the internal os on transvaginal ultrasound examination. It could be argued that using placentas inserted elsewhere in the uterus, such as in the fundus, as a control group might have been better, however, the precise site of placental implantation is notoriously inaccurately reported on routine ultrasound scanning. Therefore, by using those reported as 'low-lying' on transvaginal ultrasound scanning we ensured that we were certain that the majority of the placenta in that group was implanted upwards and away from the lower segment. Using 'low-lying' placenta as a control group aims to remove confounding factors from the results that may be due to the site of implantation rather than to PAS itself

Implications for clinical practice and research

In a controlled study of 119 cases of placenta previa versus non-previa placenta matched for maternal complications, Weiner et al found that placenta previa were significantly smaller and presented with a higher incidence of vascular lesions secondary to maternal malperfusion and to fetal thrombo-occlusive diseases than controls. Although the mean birthweight of the placenta previa group was 700g higher than in the control group, the incidence of SGA $<10^{th}$ and $<5^{th}$ percentile was significantly higher in the placenta previa group[10]. In a secondary analysis of the placenta previa group, they found that the placental size was smaller and the

incidence of placental tissue vascular lesions was higher in symptomatic women compared to asymptomatic women[11]. They hypothesized that placentation in the lower segment of the uterus is associated with suboptimal vascular development of both the utero-placental and the umbilico-placental circulations. Compared to 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, fetal growth restriction and with a higher incidence of placental vascular lesions. Weiner et al did not match their cases and controls for maternal smoking status or for gestational age a delivery[10,11]. Their patients with placenta previa were delivered on average 3 weeks before their non-previa controls making the evaluation of placental weight and fetal birthweight inaccurate. Finally, they did not differentiate between low-lying and placenta previa which may have had an impact on pregnancy outcome and in particular on maternal symptoms and premature delivery rates.

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 birthweight was only slightly increased 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 retrospective large 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 birthweight <10th percentile was similar in placenta previa compared to non-previa controls. The presence of bleeding and the type of the placenta i.e. low-lying placenta (partial previa) and placenta previa (marginal or complete) did not impact the risk of FGR. These data and our data finding a similarly low rate of birthweight <10th percentile in both low-lying and placenta previa suggest that development of most of the placenta inside the lower uterine segment does not affect the normal development of the utero-placental circulation, the placenta and the fetus.

This study is the first to have evaluated fetal growth in placenta previa complicated by 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 caesarean section has shown that the uterine artery resistance is increased and the volume of uterine blood flow is decreased as a fraction of maternal cardiac output compared to women with a previous vaginal birth[8]. Several histopathologic studies[13-15] have shown a decreased proportion of remodelled spiral arteries vessels, with many vessels displaying partial physiologic change in PAS areas in both adherent and invasive cases. The incomplete transformation of the uterine-placental circulation is seen more in cases without local decidua, and vascular remodeling is sometimes completely absent in the PAS area[15]. This is a common feature of pregnancy complicated by preeclampsia and/or FGR[16] but in cases of invasive PAS there is a greater degree of remodelling in radial/arcuate arteries[13,14] suggesting that the

overall maternal blood volume entering the placenta is increased rather than decreased. Our data indicating a low incidence of birthweight below the 10th centile in previa-PAS and no difference in median birthweight between the adherent and invasive subgroups suggests that the histopathological findings of differences in the spiral arteries in the accreta area has no impact of 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 biologic function of the rest of the placental tissue.

In conclusion, women presenting with a non-PAS placenta previa, women diagnosed prenatally with previa-PAS are not at a higher risk of SGA. Overall, multiparous women are at lower risk of developing pregnancy complications such as preeclampsia than primiparous women and thus their management and, in particular the timing of delivery, will depend mainly on maternal symptoms, severity of their PAS and risk of antenatal haemorrhage. Serial fetal growth ultrasounds are therefore not indicated in women with placenta previa or previa-PAS for this indication alone and neonatal outcomes depend essentially on the complications of prematurity and unlikely to be influenced by impaired fetal growth.

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FIGURE LEGENDS

Figure 1. Dot plot for birthweight centile with bars denoting the median and 25-75 percentiles for low lying placenta, placenta praevia and placenta accreta spectrum (PAS).

Figure 2. Dot plot for birthweight centile with bars denoting the median and 25-75 percentiles for adherent and invasive placenta accreta spectrum (PAS).

Table 1. Clinical characteristics of low-lying placenta, placenta previa and previa-PAS.

Characteristics	Low-lying placenta (n=63)	Placenta previa (n=146)	Previa-PAS (n=82)	P
Maternal age	34.0 (30.0-38.0)	34.5 (31.0-38.0)	35.5 (31.7-38.0)	0.611
AMA ≥ 35 years old ≥ 40 years old	29 (46.0) 10 (15.9)	73 (50.0) 19 (13.0)	45 (54.9) 15 (18.3)	0.564 0.556
Smoker	5 (7.8)	12 (8.2)	10 (12.2)	0.560
Ethnic origin - Caucasian - Asian - Afro-Caribbean - Other	 52 (81.3) 4 (6.3) 7 (10.8) 1 (1.6)	 102 (69.9) 26 (17.8) 17 (11.6) 1 (0.7)	 56 (68.3) 6 (7.3) 18 (22.0) 2 (2.4)	
Primiparous	25 (39.7) ***	45 (30.8) †††	0 (0.0)	**<0.001**
Fetal sex	32M/31F	78M/68F	43M/39F	0.940
Gestational age at confirmed diagnosis (weeks)	27.6 (20.5-35.1)	22.4 (20.3-30.3) †††	29.3 (26.0-33.3)	**<0.001**
EFW on ultrasound (percentile)	45.0 (30.0-60.0)	48.0 (31.7-67.2)	50.0 (35.7-69.2)	0.538
Gestational age at delivery	38.3 (37.2-39.1) ***	38.0 (36.4-39.0) †††	36.2 (34.1-37.2)	**<0.001**
Delivery < 37 weeks	13 (20.5) ***	41 (28.1) †††	51 (62.2)	**0.002**
Birthweight centile	54.9 (16.2-80.2)	52.3 (22.5-75.2)	42.7 (22.1-81.2)	0.997
Birthweight ≤ 10th centile	16 (11.0)	7 (11.1)	34 (11.7)	0.842
Birthweight ≥ 90th centile	16 (11.0)	8 (12.7)	11 (13.4)	0.842

AMA= advance maternal age; EFW= estimated fetal weight; M= Male; F= Female
Numerical data are presented as median (interquartile range) and categorical data as n (%).
The p-values denote the overall significance for the Kruskal-Wallis or ANOVA (for numerical data)and the overall Chi-square tests (for categorical data). Comparison between subgroups is represented with the following symbols:

- Low-lying placenta and Previa-PAS: * P <0.05, ** P < 0.01, *** P <0.0001
- Placenta praevia and Previa-PAS: † P <0.05, †† P < 0.01, ††† P <0.0001

Table 2. Comparison of maternal characteristics and fetal growth parameters between low-lying placenta (n= 60) and placenta previa (n= 60) groups matched for smoking status, ethnic origin and gestational age at delivery.

Variable	**Low-lying Placenta**	**Placenta previa**	**P**
Maternal age (years)	34.0 (30.0;38.0)	34.0 (32.5;37.0)	0.695
AMA $\geq$ 35 years old $\geq$ 40 years old	28 (46.7) 9 (15.0)	29 (48.3) 8 (13.3)	0.855 0.793
Parity	1.0 (0.0;1.5)	1.0 (0.0;2.0)	0.054
Gestational age at confirmed diagnosis (weeks)	27.0 (20.4;34.9)	20.4 (20.1;29.3)	**0.002**
EFW on ultrasound (percentile)	47.5 (30.2;60.7)	53.5 (29.0;68.0)	0.386
Gestational age at delivery	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
Birthweight (percentile)	51.9 (16.3;81.2)	58.5 (24.4;78.8)	0.639
BW $\leq$ 10th centile	6 (10.0)	4 (6.7.)	0.509
BW $\geq$ 90th centile	8 (13.3)	9 (15.0)	0.793

AMA: advance maternal age, EFW: estimated fetal weight

Numerical data are presented as median (interquartile range) and categorical data as n (%).

Table 3. Comparison of maternal characteristics and fetal growth parameters between placenta previa (n= 52) and previa-PAS (n= 52) groups matched for smoking status, ethnic origin and gestational age at delivery.

Variable	**Not PAS**	**PAS**	***P***
Maternal age (years)	36.0 (31.2;39.0)	35.0 (31.2;38.0)	0.696
AMA $\geq$ 35 years old $\geq$ 40 years old	30 (57.7) 9 (17.3)	27 (51.9) 10 (19.2)	0.544 0.800
Parity	1.5 (1.0;2.0)	2.0 (1.0;3.0)	0.061
Gestational age at confirmed diagnosis (weeks)	29.6 (21.1;32.5)	30.0 (26.2;34.0)	0.072
EFW on ultrasound (percentile)	47.0 (34.0;68.7)	50.5 (36.0;68.7)	0.730
Gestational age at delivery	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
Birthweight (percentile)	38.8 (21.5;65.9)	49.6 (22.7;81.8)	0.158
BW $\leq$ 10th centile	7 (13.5)	8 (15.4)	0.780
BW $\geq$ 90th centile	1 (1.9)	6 (11.5)	0.113

AMA: advance maternal age, EFW: estimated fetal weight

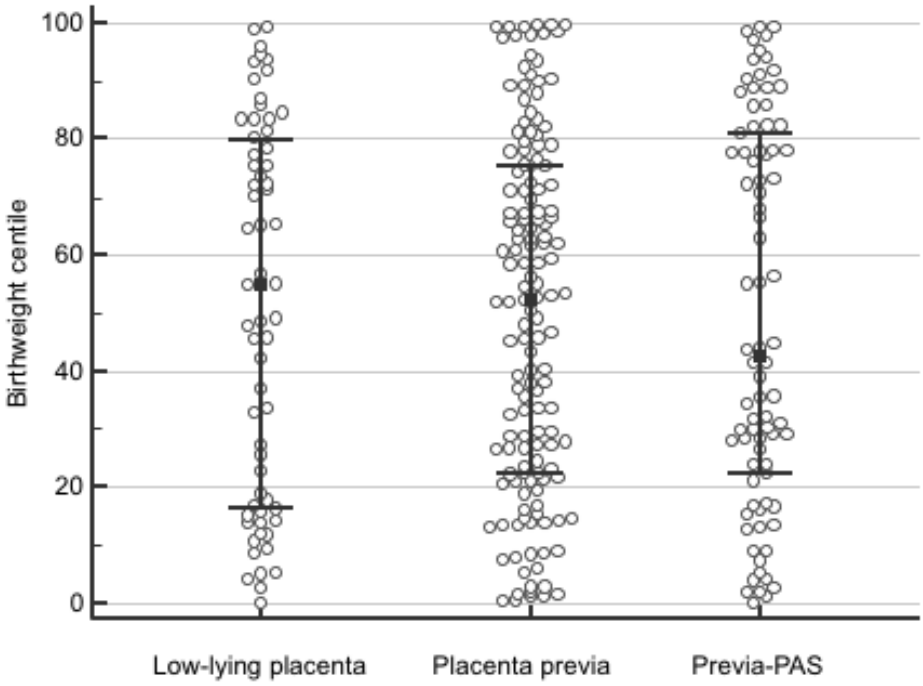
Numerical data are presented as median (interquartile range) and categorical data as n (%).

Table 4. Comparison of maternal characteristics and fetal growth parameters between adherent previa-PAS (n= 35) and invasive previa-PAS (n= 47) subgroups.

Variable	**Adherent PAS**	**Invasive PAS**	***P***
Maternal age (years)	36.0 (31.0;39.0)	35.0 (32.0;38.0)	0.914
AMA ≥ 35 years old ≥ 40 years old	20 (57.1) 6 (17.1)	25 (53.2) 9 (19.1)	0.722 0.816
Parity	2.0 (1.0;3.0)	2.3 (1.0;3.0)	0.465
Gestational age at confirmed diagnosis (weeks)	29.2 (25.3;34.0)	30.0 (26.1;33.1)	0.888
EFW on ultrasound (percentile)	44.0 (25.0;63.0)	57.0 (38.0;70.0)	**0.047**
Gestational age at delivery	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
Birthweight (percentile)	41.7 (16.4;82.2)	43.8 (26.3;78.1)	0.804
BW ≤ 10^{th} centile	5 (14.3)	6 (12.8)	0.842
BW ≥ 90^{th} centile	5 (14.3)	6 (12.8)	0.842

AMA: advance maternal age, EFW: estimated fetal weight

Numerical data are presented as median (interquartile range) and categorical data as n (%).



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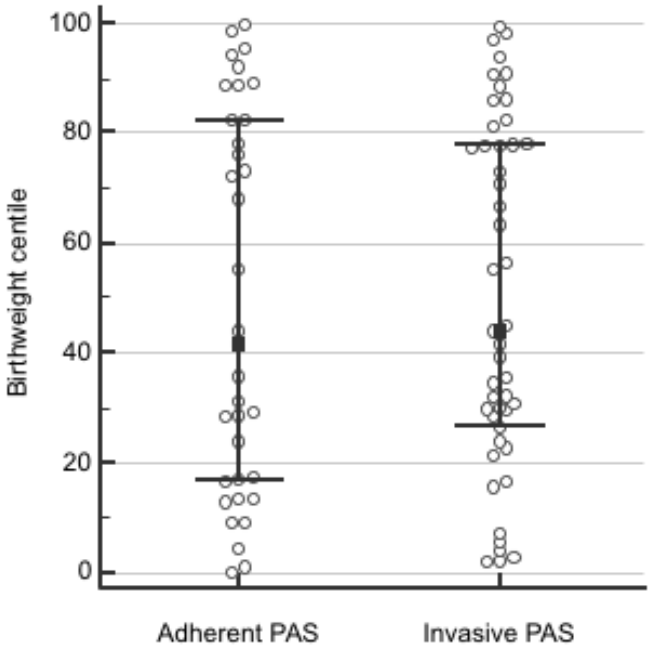

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