A risk factor profile for placenta accreta spectrum in pregnancies conceived with assisted reproductive technology

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Objective: To identify independent risk factors for placenta accreta spectrum among pregnancies conceived with assisted reproductive technology.
Design: Retrospective cohort study.
Setting: Tertiary hospital.
Patient(s): Individuals who conceived with assisted reproductive technology and reached 20 weeks' gestation or later from 2011 to 2017.
Intervention(s): Patient and cycle data was abstracted from hospital records and supplemented with state-level data. Poisson regression was used for multivariate analyses and reported as adjusted relative risks (aRR).
Main Outcome Measure(s): Clinical or histologic placenta accreta spectrum.
Result(s): Of 1,975 qualifying pregnancies, 44 (2.3%) met criteria for accreta spectrum at delivery. In the multivariate model, significant risk factors included low-lying placenta at delivery (aRR, 15.44; 95% CI 7.76–30.72), uterine factor infertility or prior uterine surgery (aRR, 4.68; 95% CI, 2.72–8.05), initial low-lying placentation that resolved (aRR, 3.83; 95% CI, 1.90–7.73), and use of frozen embryos (aRR, 3.02; 95% CI, 1.66–5.48). When the fresh vs frozen variable was replaced with controlled ovarian hyperstimulation, the final model did not change (aRR, 2.40 for unstimulated cycles, 95% CI, 1.32–4.38). With frozen transfers, the accreta rate was 16% when the endometrial thickness was $<$ 6mm vs 3.8% with thicker endometrium ($P=.02$).
Conclusion(s): Among pregnancies conceived with assisted reproductive technology, accreta spectrum is associated with low placental implantation (even when resolved), uterine factor infertility and prior uterine surgery, and the use of frozen embryo transfer or unstimulated cycles. (Fertil Steril Rep® 2023;4:279–85. ©2023 by American Society for Reproductive Medicine.)
Key Words: Placenta accreta spectrum, IVF, uterine factor infertility, placenta previa

Placenta accreta spectrum (PAS) represents a relatively uncommon, although exceedingly morbid, placentation disorder. Defined by placental villi attaching directly to and sometimes invading the uterine myometrium, it is associated with high rates of blood transfusion and hysterectomy, making it an important contributor to severe maternal morbidity (1). Clinically the condition is defined by the abnormally adherent placenta, often with either visual signs of myometrial invasion or major hemorrhage when the placenta is removed (2, 3). Although most often described when a placenta previa implants on a prior cesarean scar, it is also found without these risk factors (4). The pathophysiology has been attributed to uterine scarring, which leads to abnormal decidualization and vascular remodeling (5, 6), although not all histologically-confirmed cases involve a uterine scar (4).

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Assisted reproductive technology (ART)—which includes in vitro fertilization and related techniques—was first identified as a PAS risk factor in 2011 (7), and multiple studies have since confirmed this association (8–11). Additional studies have attempted to identify specific ART processes that elevate the PAS risk and have shown an association with frozen embryo transfer (FET) cycles (12, 13) as well as transferring multiple frozen embryos (14), whereas embryo biopsy does not appear to be a risk factor (15, 16). Another recent study found an elevated risk in programmed or hormone-replacement cycles compared with natural (unmedicated) FET cycles (17).

Studies linking ART to PAS development remain subject to limitations. These include inconsistent definitions of PAS, with some including only histologic confirmations, generally from a hysterectomy specimen (10, 11), whereas others include a nonspecific clinical criterion of "adherence" (7–9), with other studies not giving a definition (12, 14). Furthermore, these studies are subject to residual confounding, with some lacking controls for patient factors, such as infertility diagnosis and surgical history.

A previous project published by this institution used an earlier, smaller cohort (2005–2011) and focused on a single risk factor (fresh vs. FET) (13). The objective of the current study was to examine multiple elements of ART cycles that may contribute to PAS risk, including laboratory data, baseline patient risk factors, and outcomes confirmed with a rigorous definition of PAS.

MATERIALS AND METHODS

Data Sources

This retrospective cohort study included pregnancies that were conceived with ART at a single, large teaching hospital in Massachusetts and delivered at the same hospital between 2011 and 2017 at $\geq$20 weeks gestation. Details of the ART cycles were obtained from the ART laboratory database, whereas obstetric data were collected from the hospital's electronic prenatal and delivery records. These data were collected as part of the Massachusetts Outcome Study of Assisted Reproductive Technology, which includes ART data linked to birth certificate data and hospital discharge data for all patients whose ART treatments, deliveries, and residences took place in Massachusetts between 2004 and 2017 (18). A single center (Brigham and Women's Hospital in Boston) was selected for both the ART procedures and deliveries included in the current study, as complete collection and confirmation of PAS outcomes were available for this center only. This is a tertiary referral center that sees a large mix of high- and low-risk obstetric patients. This study was approved by the institutional review boards of Mass General Brigham, the Massachusetts Department of Public Health, and Dartmouth-Hitchcock Health.

Outcome Variable

The outcome variable of interest was PAS, with either a clinical or histopathologic diagnosis being permitted. To minimize misclassification bias, the definitions proposed by the International Federation of Gynecology and Obstetrics (FIGO) were applied retrospectively (2). This included a clinical diagnosis involving both abnormal placental adherence and heavy bleeding with placental removal, necessitating surgical or mechanical intervention (arterial ligations, placental bed suturing, uterine tamponade, or arterial embolization), or histologic diagnosis obtained from a hysterectomy specimen.

Delivery and pathology reports were obtained for all pregnancies and were scanned using an electronic search function for the strings "creta" and "adhere" (referring to the placenta). Once identified, these delivery records were reviewed by two separate obstetricians to confirm the clinical and/or histologic diagnosis of PAS. If the reviewers gave discrepant results, then the cases were discussed by a larger group of obstetric providers, and the final categorization was determined by consensus. Because the significance of myometrial fibers adherent to the placental basal plate without a hysterectomy specimen is unclear, if a placental pathology report indicated this finding in the absence of clinical PAS findings, then the case was classified as non-PAS.

Covariates

Maternal age and body mass index were obtained from ART laboratory data, whereas gravidity, parity, number of gestations, and history of prior cesarean delivery (CD) were obtained from obstetric records.

Placental location was determined from a review of scanned radiology reports. During the study period, it was standard practice to describe the relationship between the placenta and the cervix at 16 weeks and beyond. If low placentation could not be clearly excluded with a transabdominal ultrasound, then a transvaginal ultrasound was performed. If the placenta was $\leq$ 2 cm of the cervical ostium at 16 weeks or later, then it was classified as "low-lying." If it remained $\leq$ 2 cm of the cervical ostium on the final documented ultrasound before delivery, then it was categorized for this study as "previa or low-lying placenta at delivery." If the placenta was documented on a subsequent ultrasound as $\geq$2 cm from the cervical os, it was called "low-lying placenta, resolved." If the placenta was never within two cm of the cervical ostium, then it was called "high placentation."

Infertility diagnosis, fresh versus FET, use of donor oocytes, embryo biopsy, intracytoplasmic sperm injection (ICSI), assisted hatching, number of embryos transferred, and number of initial sacs implanted were obtained from the laboratory database. Cycles with a transfer of both fresh and frozen embryos were excluded from those analyses comparing fresh to FET. Controlled ovarian hyperstimulation (COH), in which gonadotrophins were administered to stimulate the production of multiple oocytes, was a feature of all fresh, autologous cycles (including those where fresh and frozen embryos were transferred together), whereas all others (frozen-only and all fresh and frozen transfers with donor oocytes) were classified as nonCOH (ie, unstimulated). Endometrial thickness was routinely available for patients undergoing frozen embryo transfers but not all patients undergoing fresh transfers (including fresh donor cycles); therefore, this variable was analyzed for the frozen transfers only. The

TABLE 1

Associations between maternal, cycle, and implantation factors and placenta accreta spectrum at delivery.

Variable	Total N = 1931	PAS N = 44 (%)	*P* value
Maternal Factors			
Maternal age (y)[a]			.47
<35	760	15 (2.0)	
≥35	1171	29 (2.5)	
BMI (kg/m^2)			
<22.0	666	17 (2.6)	.99
22.0–24.9	551	14 (2.5)	Ref
>24.9	703	13 (1.8)	.40
History of Cesarean Delivery			.09
No	1662	34 (2.0)	
Yes	269	– (3.7)	
Prior uterine surgery			<.01
No	1644	26 (1.6)	
Yes	287	18 (6.3)	
Gravidity			<.01
1	761	– (1.2)	
≥2	1170	35 (3.0)	
Parity			.01
0	1261	21 (1.7)	
≥1	670	23 (3.4)	
Infertility diagnosis			
Polycystic ovary syndrome	177	– (3.4)	.30
Ovulatory dysfunction	206	– (1.4)	.40
Diminished ovarian reserve	439	– (1.4)	.14
Uterine factor	53	– (15)	<.01
Tubal factor	151	– (4.6)	.04
Male factor	602	14 (2.3)	0.92
Endometriosis	120	– (6.7)	<.01
Unexplained	543	– (1.1)	.03
Uterine abnormality[b]			<.01
No	1627	25 (1.5)	
Yes	304	19 (6.3)	
Cycle and Embryo Factors			
Controlled ovarian hyperstimulation			<.01
No	785	29 (3.7)	
Yes	1146	15 (1.3)	
ICSI			.82
No	998	22 (2.2)	
Yes	932	22 (2.4)	
Assisted Hatching			.38
No	1303	27 (2.1)	
Yes	628	17 (2.7)	
Embryo biopsy			.96
No	1840	42 (2.3)	
Yes	91	– (2.2)	
Oocyte Source			.57
Autologous	1771	42 (2.4)	
Donor	160	– (1.3)	
Frozen-cycle endometrial thickness[c]			
<7 mm	81	– (4.9)	.76
≥7 mm	591	24 (4.0)	
Embryo transfer state[d]			<.01
Fresh	1237	15 (1.2)	
Frozen	690	29 (4.2)	
Embryo transfer timing			.18
Cleavage Stage	936	17 (1.8)	
Blastocyst	989	27 (2.7)	
Embryos transferred, number			.99
1	791	18 (2.3)	
≥2	1139	26 (2.3)	

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TABLE 1

Continued.

Variable	Total N = 1931	PAS N = 44 (%)	*P* value
Implantation characteristics			
Sac number on first ultrasound			.62
1	1341	30 (2.2)	
≥2	535	14 (2.6)	
Number of births			.52
1 (ref)	1523	33 (2.2)	
≥2	408	11 (2.7)	
Number of placentas			.86
1	1556	35 (2.2)	
>1	375	– (2.4)	
Placental location			
High placentation	1482	15 (1.0)	Ref
Low-lying placenta, resolved	371	16 (4.3)	<.01
Previa or low-lying at delivery	78	13 (17)	<.01

PAS, placenta accreta spectrum; BMI, body mass index; ICSI, intracytoplasmic sperm injection. Small cell numbers (< 11) are suppressed in accordance with Massachusetts Department of Public Health guidelines.

[a] At cycle start

[b] Includes either prior uterine surgery or uterine factor infertility

[c] Restricted to frozen cycles. Data missing for < 1% of pregnancies.

[d] Excludes cycles in which both Fresh and Frozen embryos were transferred (< 1% of subjects)

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transferred embryos were categorized as "cleavage stage" if transferred on days 2 to 4 and "blastocyst stage" if transferred on days 5 to 7. Placenta number was derived using chorionicity data, with monochorionic pregnancies combined with singleton pregnancies as single placentas, whereas dichorionic or higher order chorionicity was classified as multiple placentas.

A patient's past uterine surgical history (other than prior CD) was obtained from two sources. First, from the Massachusetts Outcome Study of Assisted Reproductive Technology, which contains International Classification of Disease (ICD) codes for hospital discharges, observational stays, and emergency department visits. Second, current procedural terminology and International Classification of Disease codes were obtained from the Mass General Brigham Research Patient Data Registry, which includes inpatient and outpatient codes for five hospitals providing gynecology services as far back as 1997. Supplementary Table 1 (available online) lists the specific diagnosis and procedure codes used and includes myomectomy by any route, any operative hysteroscopy (excluding polypectomy, which is less likely to damage the endometrial basal layer), endometrial ablation, uterine septum removal, and uterine artery embolization. If patients received any one of these codes before the ART cycle start date, then they were considered to have had "prior uterine surgery." This variable was combined with "uterine factor infertility" to create a single variable called "uterine abnormality" for the multivariate analyses because of much overlap between the two variables.

TABLE 2

Placenta accreta spectrum risk according to placental location and history of cesarean delivery.

	No prior cesarean delivery (N = 1662)		Prior cesarean delivery (N = 269)	
Placental location	**PAS (%)**	***P* value**	**PAS (%)**	***P* value**
High placentation	12 (0.9)	Reference	– (1.4)	Reference
Low-lying, resolved	13 (4.0)	< .01	– (7.0)	.06
Previa or low-lying at delivery	– (13)	< .01	– (36)	< .01

PAS = placenta accreta spectrum.
Small cell numbers (< 11) are suppressed in accordance with Massachusetts Department of Public Health guidelines.

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Statistical analysis

Potential risk factors for PAS were evaluated using Chi-square or Fisher Exact statistics (alpha = 0.05). Age was dichotomized (< 35, ≥ 35 years) (19), whereas BMI was stratified into tertiles, with the middle group used as the reference. This was done to balance the patient numbers within groups and because the World Health Organization BMI categories were not created with obstetric risks as outcomes of interest (20). Gravidity, number of embryos transferred, number of sacs on initial scan, and number of births were similarly dichotomized at (1, 2+), whereas parity was dichotomized at (0, 1+). An endometrial thickness cutoff (<7mm, 7+mm) was selected based on a prior publication of obstetric outcomes with FET cycles. (21) Given that the best cutoff for PAS risk with FET is undefined, we also performed a sensitivity analysis comparing three different levels (<6 mm, 6–7 mm, ≥7 mm). Additional potential risk factors for PAS are listed in Table 1.

Multivariate analyses were conducted using Poisson regression with a log function to derive relative risk ratios and 95% CI. Generalized estimating equations were used to account for individual patients contributing data to more than one delivery. Risk factors were selected for adjusted analyses if they were significantly associated with PAS with a *P* value of.05 or less and were retained in the final model if the adjusted *P* value was ≤ .05. Maternal age (≤ 34, 35+ years) and history of CD (Yes, No) were tested in the adjusted analyses a priori. Analyses were performed using the SAS software, version 9.4 (SAS Institute, Cary, NC). In accordance with theMassachusetts Department of Public Health guidelines, patient counts of < 11 were not displayed in the tables.

RESULTS

A total of 1975 pregnancies met the study's inclusion criteria. Of these, 44 (2.3%) met diagnostic criteria for PAS at delivery, with 77% classified at FIGO Grade 1 and the remainder at FIGO Grade 2. Table 1 shows the associations among individual patient, cycle, and implantation factors and the PAS outcome. Significant relationships were found between gravidity (3.0% PAS for those ≥2), parity (3.4% PAS for those ≥1), prior uterine surgery (6.3% PAS), diagnoses of uterine factor infertility (15% PAS) and endometriosis (6.7% PAS), with a *P* value ≤ .01 for all variables when compared with those without the variable. Those with tubal factor infertility also had more PAS than those without (4.6%, *P*=.04). When history of prior uterine surgery was added to uterine factor infertility as a single risk factor (uterine abnormality), the risk of PAS was 6.3% (*P*<.01 compared with those without this history). Advanced maternal age, BMI, history of CD, and other infertility diagnoses were not significantly associated with PAS, whereas a diagnosis of "unexplained" infertility had a negative association with the outcome (1.1% PAS, *P*=.03 compared with those with an infertility diagnosis).

ART cycle factors, including a non-COH cycle protocol (3.7% PAS, *P*<.01) and FET (4.2% PAS, *P*<.01), were associated with PAS, whereas the use of ICSI, assisted hatching, embryo biopsy, or donor oocytes as well as stage of embryo development and the number of embryos transferred were not significantly associated with PAS.

Endometrial thickness < 7mm among those with FET was not a risk factor (4.9% PAS for EM < 7mm and 4.0% for those > 7mm, *P*=.76). However when comparing EM < 6 mm, 6 to 7 mm and ≥7 mm the overall comparison was significant (16%, 0%, and 4.0%, respectively, *P*<.01). A binary cutoff of 6 mm was most discriminatory in this sensitivity analysis (16% vs 3.7%, *P*=.02).

Regarding implantation factors, neither the presence of multiple sacs on initial ultrasound, multiple placentas implanted, nor multiple fetuses at delivery was associated with PAS. However, initial low placental implantation was highly associated with the outcome, with 29 of 44 PAS cases (66%) having a low-lying placenta in mid-pregnancy and 13 of 44 (30%) having a previa or low-lying placenta at delivery. Patients with an initial low implantation that resolved before delivery had a 4.3% risk of PAS, and those with persistent low implantation had a 17% risk (*P*< .01 for both when compared with those with high placental implantation). With a history of prior cesarean, persistent previa or low implantation had a 36% PAS risk (*P*<.01), whereas the risk with resolved low implantation was 7% (*P*=.06), compared with 1.4% for those with an initial higher implantation (Table 2). This pattern held in the group without a prior cesarean as well; those with a persistent previa or low implantation had a 13% risk of PAS (*P*<.01), wheras those with a resolved low implantation had a 4.0% risk, compared with 0.9% risk of PAS with high implantation (*P*<.01 for both comparisons).

The association between prior CD and PAS was further examined with a stratified analysis and a logistic model with an interaction term for low-lying placenta and prior

TABLE 3

Crude and adjusted analyses for predictors of placenta accreta spectrum at delivery.

Risk Factor	RR (95% CI)	aRR (95% CI)
Significant Factors: Final model		
Previa or low-lying placenta at delivery[a]	16.36 (8.08, 33.10)	15.44 (7.76, 30.72)
Uterine abnormality[b]	5.11 (2.87, 9.12)	4.68 (2.72, 8.05)
Low-lying placenta, resolved[a]	4.15 (2.02, 8.49)	3.83 (1.90, 7.73)
Frozen embryo transfer[c]	3.43 (1.86, 6.32)	3.02 (1.66, 5.48)
Nonsignificant Factors[d]		
Endometriosis	3.35 (1.50, 7.51)	2.19 (0.99, 4.84)
Gravidity ≥2	2.61 (1.26, 5.39)	1.94 (0.96, 3.95)
Maternal age ≥35 y[e]	1.33 (0.70, 2.52)	0.81 (0.43, 1.53)
History of cesarean delivery	1.89 (0.94, 3.80)	1.36 (0.70, 2.64)

[a] Compared with pregnancies with high placentation
[b] Includes either history of uterine surgery or uterine factor infertility
[c] Excludes cycles with both fresh and frozen embryo transfers (<1% of cycles)
[d] Each controlled for the four significant factors and the variables listed above that factor
[e] At cycle start

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CD. Among the 449 pregnancies with an initial low placental implantation, 13% of those with prior CD developed PAS, versus 5.5% of those without this history (OR, 2.53; 95% CI, 1.02–6.23). Alternatively, if the placenta was never low-lying, the PAS rates were 1.4% and 0.9%, respectively (OR, 1.48; exact 95% CI, 0.27–5.55). Although the absolute PAS rates were much higher in the setting of low placentation, the interaction term was not statistically significant ($P=.49$).

Table 3 shows the results of the multivariate analysis, with the four risk factors retained in the final model. The strongest independent risk factor for PAS was a previa or low-lying placenta at delivery (aRR 15.44, 95% CI 7.76–30.72) followed by a diagnosis of uterine factor infertility or history of prior uterine surgery (aRR 4.68, 95% CI 2.72–8.05) and an initial low-lying placenta that resolved (aRR 3.83, 95% CI 1.90–7.73). FET remained significant when controlling for these patient and obstetric factors with an aRR of 3.02 (95% CI 1.66–5.48). Both endometriosis (aRR 2.19, 95% CI 0.99-4.84) and gravidity ≥ 2 (aRR 1.94, 95% CI 0.96–3.95) approximately doubled the risk for PAS, but their confidence intervals just crossed unity in the adjusted analysis. Advanced maternal age and history of CD were not significant risk factors in the model. This model was re-run using the COH variable in place of FET (aRR 2.4, 95% CI 1.32–4.38 for nonCOH compared with COH cycles), and the same pattern of results was obtained.

DISCUSSION

The current study uses detailed ART and obstetric data to identify independent risk factors for PAS in ART-conceived pregnancies. The multivariate analysis shows that patient, ART cycle, and placental implantation factors all contribute to this risk. Previa or low placental implantation was the strongest contributor to PAS risk, and it conferred a high relative risk even when the low implantation resolved over the course of the pregnancy. That uterine factor infertility or a history of uterine surgery was a strong risk factor is not surprising, based on the known association with uterine surgery in the general pregnant population (22). This study confirms that both FET and the use of unstimulated cycles (which combines fresh transfers in donor egg recipients with all frozen transfers) are also independent risk factors for accreta spectrum.

Research in the general obstetric population has consistently shown an association between placenta previa and PAS, which is strongest in the presence of a prior CD scar (23). The current study confirmed this association both with and without a prior cesarean scar and showed that initial low implantation that resolves is also an independent risk factor in the ART population. The ART pregnancies are known to have an increased risk for placenta previa, with an overall odds ratio of 3.76 in one meta-analysis (24). Although the low placental implantation may be on the causal pathway between ART and PAS development, our multivariate analysis shows that it is not the only contributor to PAS development in this population.

A history of prior uterine surgery has also been shown in multiple studies to be associated with PAS, both with (22) and without placenta previa (4). This is felt to be related to placental implantation on an area of damaged endometrium (6). Correspondingly, uterine factor infertility, which generally includes congenital anomalies, polyps, fibroids, adenomyosis, and Asherman syndrome (25), was a strong risk factor for PAS development in this study and showed a high degree of overlap with prior surgery. However, while endometriosis had a strong univariate association with PAS, it did not reach significance in the adjusted analysis. Although several published studies have identified an association (26, 27), this may be confounded by placenta previa (28) and previous uterine surgeries, which may be performed at the time of a surgical endometriosis diagnosis. Nevertheless, future large studies focusing on confirmed endometriosis may support this association.

A history of CD alone was not a significant risk factor, reflecting the low incidence of this risk factor in our cohort and very low rates of PAS when the placenta is implanted away

from the cesarean scar. In fact, a prior CD was a significant factor when restricting to pregnancies with low placental implantation. Our adjusted analysis shows that this factor has a smaller role in PAS development than the other risk factors. This is congruent with a recent prospective PAS study showing that 87% of IVF patients with PAS did not have a previa with a prior CD (29) and suggests a unique PAS pathology among this population.

Our institution previously reported an association between PAS and the use of FET (13). The current study confirms this association in a more contemporary cohort that was more likely to use vitrification for embryo freezing and to have increased use of embryo biopsy and donor oocytes. The prior study showed a significant negative association between peak endometrial thickness and PAS development, which was demonstrated in the current study when examining FET cycles only. Here we showed that those with a very thin endometrium (< 6 mm) experienced a high rate of PAS, suggesting that highly deficient or absent decidua may promote PAS development in this group.

Future research should prospectively validate the predictive value of these risk factors for PAS. This group can be the focus of imaging and biomarker studies that may improve antepartum diagnosis for this under-diagnosed subgroup. The relationship between PAS and endometriosis warrants further exploration as well, with larger studies that factor in staging, diagnostic confirmation, and possible treatment of the disease. Importantly, ongoing research should evaluate the ability to prevent PAS using ART cycle modifications, such as the use of natural (unmedicated) cycles with frozen embryo or donor egg pregnancies. The current study identified factors that warrant identification and adjustment as potential confounders in future studies of ART and PAS.

Major strengths of the current study include the use of a large cohort with detailed chart review for multiple obstetric variables, including resolved low-lying placentation, which has not been previously evaluated. It also allowed for simultaneous adjustment for multiple risk factors. The outcome variable was carefully assessed by two reviewers and, in line with recent publications, included hemorrhagic morbidity in addition to significant placental adherence. This should reduce the inclusion of simple retained products of conception and provide a clinically relevant outcome. Allowing both clinical and pathologic PAS diagnoses was important, as uterine conservation may have been prioritized for this largely nulliparous cohort.

Study limitations include its retrospective design and the potential for uncontrolled confounding. Infertility diagnoses, including endometriosis, were not retrospectively verified, and prior surgical procedures performed outside of Massachusetts and the specified hospital system would have been missed. Such misclassification would bias the results toward null findings, which was not the case here. The deliveries all occurred at a referral center for PAS pregnancies, which will inflate the absolute rate of the outcome for this group. However, this should not change the observed associations between the risk factors and outcome. Finally, although the study uses a relatively contemporary cohort of ART pregnancies, there were very few "natural" (unmedicated) cycles, precluding evaluation of this variable.

CONCLUSIONS

This study identifies a subset of ART patients at the highest risk for PAS. Although PAS is best defined and most easily diagnosed in patients with placenta previa and a prior cesarean scar, 70% of PAS cases in this cohort did not have a previa at delivery, which can lead to under-recognition before delivery (4). Although ART has been previously identified as a risk factor for PAS, this study shows that ART-specific factors—FET, particularly with very thin endometrial measurements, and use of nonCOH cycles—contribute to this risk even with adjustment for patient factors. Additionally, whereas low-lying placentation at delivery is an expected PAS risk factor, a resolved low implantation also shows a strong association and should be considered in risk stratification. Future research should prospectively evaluate the relative contributions of these factors, providing a practical tool for patient triaging and safe delivery planning.

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