Original Article

Association Between Characteristics of Patients having A Previous Cesarean Delivery and the Presence of Placenta Accreta Spectrum: A Case-Control Study

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ABSTRACT

Objective: To assess the association between the characteristics of patients with previous cesarean delivery and placenta accreta spectrum (PAS).

Patients and Methods: This multicenter case-control study was conducted at Obstetrics and Gynecology Departments of Tanta and Zagazig Universities in the period from January, 1, 2017 to December, 31, 2021. One hundred twenty cases of placenta accreta were compared to 120 matched cases without placenta accretes at the time of delivery. Characteristics of previous cesarean delivery were recorded in PAS and control cases.

Results: Demographic data were matched in PAS and control cases. Presence of placenta accrete spectrum was associated with many risk factors in previous cesarean surgery. There was a significant difference between both groups regarding history of dilatation and curettage (OR=3.996, CI=2.276-7.017), operator experience, manual removal of the placenta (OR=4.923, CI=2.743-8.837), postpartum fever (OR=3.561, CI=2.038-6.224), IUD use before pregnancy (OR=6.889, CI=3.887-12.211), place of delivery and layers of suture of uterine incision (OR=3.609, CI=2.115-6.158).

Conclusion: Patients' characteristics at previous cesarean section and the postpartum events are very important determining factor for placental adhesive disorders; history of D&C, operator experience, manual removal of the placenta, postpartum fever and IUD use before pregnancy , place of delivery and layers of suture of uterine incision. The data and the finding of all cesarean deliveries should be accurately recorded to evaluate the future risk of PAS.

Key Words: Characteristics, postoperative complications, placenta accreta, previous cesarean delivery.

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INTRODUCTION

Placenta accreta spectrum, (PAS) refers to pathologic adhesion of placenta to uterine muscle or beyond. These conditions include placenta accreta, placenta increta, and placenta percreta. Endometrial–myometrial defect is the most accepted hypothesis in the pathogenesis of placenta accreta spectrum. That defect leads to deficiency or complete absence of normal decidua at the scar site and consequently deep invasion of anchoring villi and trophoblastic infiltration into myometrium[1].

The incidence of placenta accreta spectrum (PAS) is rising parallel to increased cesarean section rates. Evidence correlates the increased incidence of placenta accrete in patients with previous cesarean delivery and as the number of repeat cesarean delivery increase, the incidence of placenta accrete also increased[2].

The definite etiology for placenta accretes is still unknown. Several risk factors were proposed eg. Previous uterine surgery, previous uterine trauma, uterine anomalies and presence of uterine defect or niche. None of these factors explains all cases of placenta accrete spectrum. Patient identification and proper planning for safe delivery without major morbidity or mortality could be commenced after proper establishment of the risk factors implicated in the pathogenesis of placenta accreta spectrum[3].

Many biomarkers also were reported to be predictive for PAS such as elevated maternal serum α-fetoprotein, pregnancy-associated plasma protein A (PAPP-A), free β-hCG, natriuretic peptide, and human placental lactogen[4]. More recently, circulating trophoblasts (cTBs) in maternal blood were used in prediction of PAS with 79% accuracy[5].

In this study, the association of characteristics of previous cesarean delivery to incidence of PAS were evaluated in this retrospective study.

PATIENTS AND METHODS

Study design and settings: This case-control study was a multicenter study being conducted at Tanta and Zagazig

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Universities, Egypt. The study started at January, 2017 till December 2021.

Sample size

Over the duration of the study period, the anticipated cases (n=350) based on the developed experience at both Universities where the study was conducted and considering an estimated incidence of PAS to be 1 in 2500[5,6]. To detect odds ratios (ORs) between 1.6 and 2.3, in cases and controls respectively, the level of significance was 5% and the estimated power was 80%. The assumed prevalence range for potential risk factors was between 5% and 40% in the control women. Sample was calculated and was 120 in each group.

Eligibility

Patients' files for cases admitted for elective cesarean delivery at Department of Obstetrics and Gynecology in both Universities were reviewed for potential enrollment in the current study. The inclusion criteria for PAS cases were: (a) age between 20-40 years, (b) previous cesarean delivery, (c) prenatally diagnosed PAS either by grey-scale ultrasound or by MRI or both, or histologically after delivery and (d) available complete data about previous cesarean delivery from operative records. The exclusion criteria were: (a) missing (>20%) or incomplete operative details of previous cesarean delivery, (b) emergency cesarean delivery. One hundred and twenty cases were included in the study group and similar number of matched cases was included in control group admitted for elective cesarean delivery without PAS.

Data extraction

Demographic data of enrolled patients including age, parity, number of previous cesarean deliveries, body mass index (BMI), and gestational age at the time of delivery in the current pregnancy were registered. Data of previous cesarean delivery were extracted from the operative card with each patient. The extracted data were site of previous delivery, operator experience, uterine closure in single or double layers; intraoperative complications as extension of uterine incision, or uterine artery laceration and any postoperative complications such as postpartum hemorrhage, wound sepsis, fever, or ugly scar.

Ethical issues

Privacy of patients' data was maintained all through the study. This study was exempt of ethical committee approval being retrospective in nature.

Statistical analysis

Statistical analyses were done using SPSS, version 25 (IBM Corp., Armonk, NY). The level of statistical significance was set at $P < 0.05$ was considered statistically significant. Shapiro-Wilk test and normality distribution was done. Student t-test was used to compare normal data and Mann-Whitney test for non-normal data. Binary and categorical data were presented as numbers and percentages and compared with the Chi-square [Fisher exact test when appropriate].

The logistic regression (LR) was used to predict the dichotomous outcome, the presence or absence of PAS. Non-significant variables in the univariate analysis were not included in the LR model. The dummy variables were used for categorical variables that consisted of more than three categories. Dichotomous variables were computed directly. Assumptions of LR were fulfilling (sufficient number of cases per each variable and negative test for collinearity). The model was run using the Enter method. The model summary showed that 68% of the outcome could be predicted (Nagelkerke R Square value was 0.681). The validity of regression model was tested using Hosmer and Lemeshow Test (it was non-significant). The regression coefficients were computed showing the B coefficient, the SE, Wald, df, p value, OR or [Exp(B)] and the 95% CI.

RESULTS

The total files examined were 155 who were primarily diagnosed as PAS. After application of eligibility criteria, 35 cases were excluded either due to missing data (n=23), or false diagnosis (n=12). Similarly, 120 control cases were enrolled.

Baseline data

Study and control groups are age - matched group as proved by the insignificant difference between both groups as regard the age .

There was significant difference between study and control group regarding gestational age (*p-value*= 0.001) with mean gestational age 35.55 weeks in study group, and 37.53 weeks in control group (Table 1).

There was significant difference between both groups regarding IUD use before pregnancy (*P-value*= 0.001), as 80 cases had IUD before pregnancy in study group compared by only 27 cases in control group (OR=6.889 with 95% confidence interval 3.887-12.211) as shown in (Table 1).

There was a significant difference between both groups regarding operator experience (*P-value*=0.001), as 58 cases was operated by a surgeon with less than 3 years' experience in study group compared by only 13 cases in control group (OR=7.700 with 95% confidence interval 3.909-15.167) as shown in (Table 3).

There was significant difference between both groups as regard the manual removal of placenta (*P-value*=0.001), as 63 cases were reported to have manual removal of placenta in last delivery in study group compared by only 22 cases in control group (OR = 4.923 with 95% confidence interval 2.743-8.837) (Table 1).

There was significant difference between both groups as regard the past history of D&C with P value 0.001 , as 63 cases were reported to have past history of D&C in study group compared by only 26 cases in control group (OR = 3.996 with 95% confidence interval 2.276- 7.017) (Table 1)

There was significant difference between both groups as regard the suturing layers with P value 0.001 , as 74 cases were reported to have double layer closure in last delivery in study group compared by only 37 cases in control group (OR = 3.609 with 95% confidence interval 2.115 -6.158) (Table 1)

there was significant difference between both groups as regard the occurrence of postpartum fever with P value 0.001 , as 61 cases were reported to suffer from postpartum fever after last delivery in study group compared by only 27 cases in control group (OR = 3.561 with 95% confidence interval 2.038 -6.224) (Table 1)

Lastly, there was significant difference between both groups regarding the place of delivery in last pregnancy *(P-value*=0.012), as 58 cases were reported to have cesarean delivery in private hospital in last delivery in study group compared by 39 cases in control group (OR = 1.943 with 95% confidence interval 1.151 -3.280) (Table 3)

The significant risk factors associated with increased risk of PAS were collected (Table 2) and then ranked in descending order from the highest risk to the lowest risk , and the highest is operator experience with OR 7.7 , and the lowest is place of last delivery with OR 1.943 . the other risk factors are the presence of IUD before pregnancy , manual removal of placenta , past history of D&C , number of suturing layer and postpartum fever. (Table 3)

There were no significant difference between both groups as regard the age , number of previous cesarean , type of CS , ugly scar , postpartum hemorrhage , wound sepsis and postoperative complications especially uterine artery laceration and extension of incision scar.

Risk assessment

Logistic regression analysis of the ranked risk factors was presented in table 4 where it was found that PAS was strongly correlated to operator experience (23 times increase), IUD (10 times), prior D&C (6 times), manual removal of placenta (6 times) and private hospital delivery (5 times). Suturing uterus in one layer also increases the risk of PAS (4 times). And the lest association was the Postpartum fever with increased risk of PAS (3 times) (Table 4).

Table 1: Univariate analysis of all potential risk factors for development of PAS

Table 1: Univariate analysis of all potential risk factors for development of PAS		The presence of Placenta Accreta spectrum		Chi-Square (χ^2=)	*P value*	OR	95% Confidence Interval	
		0	1				Lower	upper
Patient age (Mean Rank)		114.78	126.23	U=6531	0.20			
Gest. age (Mean Rank)		164.79	76.21	U=1885.5	0.0001			
Number of previous CS	1	6	5	6.097	0.192			
	2	26	41					
	3	67	58					
	4	21	15					
	5	0	1					
Operator experience	<3 years	13	58	41.374	0.0001*			
	3-5 years	40	25					
	5-10 years	54	27					
	> 10 years	13	10					
Place of last delivery	Private hospital	39	58	6.985	0.0304*			
	General hospital	59	41					
	University hospital	22	21					
Past H of D&C	No	94	57	24.448	0.0001*	3.996	2.276	7.017
	Yes	26	63					
IUD before pregnancy	No	93	40	47.373	0.0001*	6.889	3.887	12.211
	Yes	27	80					
Type of CS	Elective	80	79	0.019	0.891	1.038	0.608	1.773
	Emergency	40	41					
Ugly scar	No	103	105	0.144	0.704	0.866	0.411	1.824
	Yes	17	15					
Suturing layers	Double	83	46	22.946	0.0001*	3.609	2.115	6.158
	Single	37	74					
Manual removal of placenta	No	98	57	30.622	0.0001*	4.923	2.743	8.837
	Yes	22	63					
Postpartum hemorrhage	No	97	85	3.274	0.070	1.737	0.952	3.168
	Yes	23	35					
Postpartum fever	No	93	59	20.742	0.0001*	3.561	2.038	6.224
	Yes	27	61					
Wound sepsis	No	104	106	0.152	0.696	0.858	0.399	1.848
	Yes	16	14					
Intraoperative complications	No	100	106	1.233	0.267	1.51	0.73	3.16
	Yes	20	14					
Extension of uterine scar	No	111	115	1.213	0.27	1.86	0.61	5.74
	Yes	9	5					
Laceration of uterine artery	No	109	111	0.218	0.64	1.24	0.5	3.12
	Yes	11	9					

CS: cesarean section; IDU: intrauterine device

NB: U = Mann-Whitney U and χ^2= Chi-Square

Table 2: Collective significant risk factors associated with either increased or decreased OR of PAS

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		The presence of placenta accreta spectrum		Chi-Square (χ^2=)	*P value*	OR	95% Confidence Interval	
		0	1				Lower	upper
Operator experience	<3 years	13	58	41.374	0.0001*			
	3-5 years	40	25					
	5-10 years	54	27					
	> 10 years	13	10					
Place of last delivery	Private hospital	39	58	6.985	0.0304*			
	General hospital	59	41					
	University hospital	22	21					
Past History of D&C	No	94	57	24.448	0.0001*	3.996	2.276	7.017
	Yes	26	63					
IUD before pregnancy	No	93	40	47.373	0.0001*	6.889	3.887	12.211
	Yes	27	80					
Suturing layers	Double	83	46	22.946	0.0001*	3.609	2.115	6.158
	Single	37	74					
Manual removal of placenta	No	98	57	30.622	0.0001*	4.923	2.743	8.837
	Yes	22	63					
Postpartum fever	No	93	59	20.742	0.0001*	3.561	2.038	6.224
	Yes	27	61					

Table 3: Ranked risk factors associated with increased OR of PAS

		The presence of placenta accreta spectrum		Chi-Square (χ^2=)	*P value*	OR	95% Confidence Interval	
		0	1				Lower	upper
Operator experience	<3 years vs others	13	58	40.503	0.0001*	7.700	3.909	15.167
IUD before pregnancy	No	93	40	47.373	0.0001*	6.889	3.887	12.211
	Yes	27	80					
Manual removal of placenta	No	98	57	30.622	0.0001*	4.923	2.743	8.837
	Yes	22	63					
past H of D&C	No	94	57	24.448	0.0001*	3.996	2.276	7.017
	Yes	26	63					
Suturing layers	Double	83	46	22.946	0.0001*	3.609	2.115	6.158
	Single	37	74					
Postpartum fever	No	93	59	20.742	0.0001*	3.561	2.038	6.224
	Yes	27	61					
Place of last delivery	Private hospital vs others	39	58	6.246	0.012*	1.943	1.151	3.280

Table 4: Logistic regression analysis using the interaction of the whole variables in a single model

Sorted risk factors	B	S.E.	Sig.	Exp (B) = OR	95% C.I for EXP(B)	
					Lower	Upper
Less than three years	3.137	0.588	0.000	23.043	7.279	72.949
IUD before pregnancy	2.312	0.447	0.000	10.096	4.206	24.237
Past H of D&C	1.924	0.456	0.000	6.849	2.802	16.744
Manual removal of placenta	1.822	0.450	0.000	6.187	2.564	14.932
Private hospitals vs others	1.766	0.482	0.000	5.849	2.274	15.045
Suturing layers	1.514	0.425	0.000	4.544	1.975	10.456
Postpartum fever	1.312	0.443	0.003	3.715	1.559	8.850
Constant	-4.954	0.674	0.000	0.007		

DISCUSSION

Many risk factors were investigated for occurrence of PAS. The investigated risk factors included advanced maternal age, placenta previa, prior cesarean delivery, conception by assisted reproductive technologies, and prior uterine surgery. One of the most important determinant factors for future possibility of placental adhesive disorders is the characteristics and circumstances of the previous cesarean delivery, as most of cases are related to the previous cesarean scar[4,7].

One of the most important determinant factors for future possibility of placental adhesive disorders is the characteristics and circumstances of the previous cesarean delivery, as most of cases are related to the previous cesarean scar. So we try to determine the factors in the previous cesarean deliver which may be related to increase risk of future placental adhesive disorders[8].

Placenta accreta spectrum rate is increasing due to the increase in cesarean delivery worldwide. The rate of PAS was 1 in 4,017 in 1970s and 1 in 2,510 in 1980s reported by observational studies. The rate became 1 in 533 from 1982 to 2002[9]. A recent study conducted in 2016 in United States reported an overall rate of 1 in 272 which is higher than published rates[5-8]. This increasing rate of PAS was linked to rising rates of cesarean section[10,11].

Our study was case controlled study , depending on the recorded data and files of the previous delivery , it was done in Tanta and Zagazig universities , it was difficult to trace the previous data as many patients' data was not available , absent or deficient , the study group (120 patients) with diagnosed o have placental adhesive disorders either by ultrasound Doppler or MRI or both , and control group (120 patients) with normal placenta .

After proper statistical analysis we found that Placenta adhesive disorders was related to certain data at previous pregnancy including g history of D and C, operator experience, manual removal of the placenta, postpartum fever and IUD use before pregnancy , place of delivery and layers of suture of uterine incision .

The results of the current study showed that the Study group had a matched age (P= 0.20) with control group (Table 1) and this is not in accordance with the result of a study by Elbery *et al*., 2020 as their results conducted critical increment in maternal age among cases with Morbidly Adherent Placenta than cases without Morbidly Adherent Placenta[12]. These outcomes concurred with numerous creators Fitzpatrick *et al*. who read chance variables for PAS issue and found that high maternal age, earlier cesarean conveyance and placenta previa were considered as huge hazard factors[8]. Another study revealed that more established maternal age, earlier cesarean area, placenta previa and high equality were autonomous hazard factors for PAS issue[13].

The difference of the results is attributed to the design of our study which include the matched patients in both study and control groups as regard the age of the patients .

Cheng and lee 2015, compared cases with PAS and previous cesarean section to controls with unscarred uterus. The risk of PAS was significantly increased in presence of placenta previa and previous scar (P<0.01). Other additional risk factors for PAS were non-significant between cases and controls. The investigated additional risks were maternal age, parity, gestational age at delivery, and the number of surgical evacuations or previous surgical termination of pregnancy[14].

But the results of current research correlate the Past history of dilatation and curettage and IUD use before pregnancy and the incidence was significantly higher in the Study group (P<0.001). This was confirmed by a study by Cooper 2012 as the rate percreta, it was worsen significantly after uterine instrumentation particularly myomectomy, curettage, and other invasive procedures, as well as endometrial ablation[15].

Out of the expected in the current there were no differences in the type of the CS and the number of previous CS between groups. In contrary to the results in the current study Elbery *et al*., 2020 demonstrated that, there was measurably critical increment in Number of Previous CS among cases with Morbidly Adherent Placenta than cases without Morbidly Adherent Placenta[12].

Our study is in agreement with Gil Zeevi etal (2018) who evaluated risk factors for PAS following primary cesarean section. They included all deliveries between 1991 and 2015 in Soroka University Medical Center. The number of primary cesarean delivery was 13,727 women. They found that there is no influence on risk of placenta accrete as regard to The stage of trial of labour in which previous cesarean was done , number of pregnancy , number of previous deliveries , but the risk is increase in unplanned cesarean section which they explained that by the increase incidence of intraoperative and postpartum complications in those patients[16].

Bremen De Mucio *et al* (2019) assessed the risk of placenta accrete in relation to the number of previous cesarean deliveries by met analysis studies , and their result disagree with ours as they both groups were also matched according to the number of cesarean section and there was no significant difference between both group as regard the number of cesarean section[17].

Also same results was obtained by Kathryn *et al* (2012) as regards the risk of placenta accrte in realtion to the number of cesarean deliveries by a case control study , and they determined the number of cesarean scar as a risk factor for future placenta adhesive disorders[18].

On the contrary, Bowman *et al* (2014) conducted a large prospective cohort study included 196 patients with diagnosed PAS. They investigated maternal demographics, parity, body mass index, tobacco use, number of prior cesarean deliveries, interval between deliveries, and coexisting hypertension or diabetes. They found positive association between PAS and number of prior CS while no correlation to maternal demographic data was present[19]. While others reported that demographic risk factors such as advanced maternal age and high parity may be potential risk factors[20].

Hyo Kyozuka *et al* (2019) had assessed the risk of placenta adhesive disorders in relation to number of previous cesarean scar, presence of previous gynecological problems and some other general factors especially smoking . 202 cases were enrolled in their study had placental adhesive disorders .and they concluded that number of previous cesarean scars is an important risk factors for placenta adhesive disorders in association with other gynecological problems like uterine anomalies and adenomyosis[21].

Limitations of our study were the difficulty to obtain full data of previous cesarean delivery in some cases due to missing data. Another limitation was that the study did not evaluate the impact of the previous cesarean characteristics in the outcome of placenta accreta management so we advise for future research on this point.

CONCLUSION

Characteristics of previous cesarean section and the events postpartum are very important determining factor for placental adhesive disorders including history of D and C, operator experience, manual removal of the placenta, postpartum fever and IUD use before pregnancy, place of delivery and layers of suture of uterine incision. The data of all cesarean deliveries should be recorded to evaluate the future risk.

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CONFLICT OF INTERESTS

There are no conflicts of interest.

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