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MATERNO-FETAL MEDICINE

Critical analysis of risk factors and outcome of placenta previa

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Abstract
Objective To investigate risk factors and pregnancy outcome of patients with placenta previa.
Methods A population-based study comparing all singleton pregnancies of women with and without placenta previa was conducted. Stratified analysis using multiple logistic regression models was performed to control for confounders.
Results During the study period, there were 185,476 deliveries, of which, 0.42% were complicated with placenta previa. Using a multivariable analysis with backward elimination, the following risk factors were independently associated with placenta previa: infertility treatments (OR 1.97; 95% CI 1.45–2.66; $P < 0.001$), prior cesarean delivery (CD; OR 1.76; 95% CI 1.48–2.09; $P < 0.001$) and advanced maternal age (OR 1.08; 95% CI 1.07–1.09; $P < 0.001$). Placenta previa was significantly associated with adverse outcomes such as peripartum hysterectomy (5.3 vs. 0.04%; $P < 0.001$), previous episode of second trimester bleeding (3.9 vs. 0.05%; $P < 0.001$), blood transfusion (21.9 vs. 1.2%; $P < 0.001$), maternal sepsis (0.4 vs. 0.02%; $P < 0.001$), vasa previa (0.5 vs. 0.1%; $P < 0.001$), malpresentation (19.8 vs. 5.4%; $P < 0.001$), postpartum hemorrhage (1.4 vs. 0.5%; $P = 0.001$) and placenta accreta (3.0 vs. 1.3%; $P < 0.001$). Placenta previa was significantly associated with adverse perinatal outcomes such as higher rates of perinatal mortality (6.6 vs. 1.3%; $P < 0.001$), an Apgar score <7 after 1 and 5 min (25.3 vs. 5.9%; $P < 0.001$, and 7.1 vs. 2.6%, $P < 0.001$, respectively), congenital malformations (11.5 vs. 5.1%; $P < 0.001$) and intrauterine growth restriction (3.6 vs. 2.1%; $P = 0.003$). Using another multivariable logistic regression model, with perinatal mortality as the outcome variable, controlling for confounders, such as preterm birth, maternal age, etc., placenta previa was not found as an independent risk factor for perinatal mortality (weighted OR 1.018; 95% CI 0.74–1.40; $P = 0.910$).
Conclusions Infertility treatments, prior cesarean section, and advanced maternal age are independent risk factors for placenta previa. An increase in the incidence of these risk factors probably contributes to a rise in the number of pregnancies complicated with placenta previa and its association with adverse maternal and perinatal outcomes. Careful surveillance of these risk factors is recommended with timely delivery in order to reduce the associated complications.

Keywords Placenta previa · Fertility treatments · Cesarean section · Advanced maternal age · Perinatal mortality · Pregnancy outcome

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Introduction

Placenta previa is a condition in which the placenta lies in the lower uterine segment, completely or partially obstructing the internal os of the cervix [1]. The prevalence of placenta previa is about 0.28–1.5% [2–6]. Pregnancies complicated with placenta previa are prone for bleeding

during the second trimester [7] which increases the risk of adverse maternal and perinatal outcome as compared to the general population [3, 4, 8, 9]. These patients are particularly at an increased risk for peripartum hysterectomy [10, 11], usually performed due to uncontrolled bleeding, whose obvious result is the loss of future fertility.

Several studies attempted to define risk factors for placenta previa [2, 4–6], and pointed out an association with advanced maternal age, parity, maternal smoking, infertility treatments, previous cesarean deliveries, and recurrent abortions [2, 4–6]. Of the aforementioned risk factors, several have increased during the past decades including the rate of cesarean sections [12–16], advanced maternal age [17–20] and the number of women undergoing fertility treatments [21, 22]. Accordingly, the aim of the current study was to evaluate current risk factors and pregnancy outcome of women with placenta previa as compared with the general population.

Materials and methods

A retrospective cohort study comparing pregnancies of women with and without placenta previa was conducted. The deliveries occurred between 1988 and 2009 at the Soroka University Medical Center. This is the sole hospital in the Negev, the southern part of Israel, and thus provides care for nearly all of the region's obstetrical population. Data were collected from the computerized perinatal database and the hospital's computerized charts. The obstetrical information is entered immediately after birth by an obstetrician, and is routinely checked for inaccuracies. Only four skilled medical secretaries examine the information before entering it into the database. Coding is done after assessing the medical prenatal care records, as well as the routine hospital documents. These procedures assure maximal completeness and accuracy of the database. The definition of placenta previa included all singleton pregnancies with placental attachment totally or mostly in the lower uterine segment which covered completely or partially the internal os in the second and third trimester, as diagnosed by ultrasound. Pregnancies with multiple fetuses and pregnancies without adequate prenatal surveillance were excluded from the study.

The following clinical characteristics were evaluated: maternal age, ethnicity (Bedouin Arab vs. Jewish), parity, gestational age, birth weight, and fetal gender. The following obstetrical risk factors were examined: smoking, previous cesarean deliveries, infertility treatments, recurrent abortions (two or more consecutive spontaneous abortions), and hypertensive disorders (pre-eclampsia, eclampsia and chronic hypertension). The following maternal complications were assessed: second trimester bleeding, preterm deliveries, cesarean deliveries, placenta accrete, placental abruption, vasa previa, postpartum hemorrhage, hysterectomy, maternal sepsis and maternal packed cell transfusions. The following neonatal complications and birth outcomes were assessed: intrauterine growth restriction (IUGR), Apgar score at 1 and 5 min less than 7, congenital malformations, and perinatal death. The local ethics institutional review board approved the study.

Statistical analysis was performed with the SPSS package (SPSS, Chicago, IL). Statistical significance was calculated using the Chi-square test for differences in qualitative variables and the *t* test for differences in continuous variables. Multivariable logistic regression model, with backward elimination, was constructed in order to find independent risk factors and complications associated with placenta previa, and another model was constructed to evaluate the association between placenta previa and perinatal mortality, while controlling for confounders. Odds ratios (OR) and their 95% confidence interval (CI) were computed. $P < 0.05$ was considered statistically significant.

Results

Placenta previa complicated 0.42% ($n = 771$) of all pregnancies. The clinical characteristics of pregnancies complicated with placenta previa are shown in Table 1. Placenta previa was significantly associated with advanced maternal age, Jewish ethnicity and lower gestational age.

Obstetric risk factors are presented in Table 2. There were higher rates of infertility treatments, prior cesarean delivery, smoking and a history of recurrent abortions

Table 1 Clinical characteristics of women with and without placenta previa

Characteristic	Placenta previa ($n = 771$)[a]	No placenta previa ($n = 184{,}705$)[a]	*P* value
Maternal age			<0.001
<20 years	1	4.1	
20–29 years	32.5	55.8	
30–34 years	29.0	23.6	
35+ years	37.4	16.5	
Ethnicity			<0.001
Bedouins	35.3	46.1	
Jews	64.7	53.9	
Gestational age			<0.001
<34 weeks	23.5	2.1	
34–36 weeks	28.4	5.6	
37–41 weeks	47.1	87.6	
42+ weeks	1.0	4.7	

[a] Values are in percentage

Table 2 Obstetric risk factors of women with and without placenta previa

	Placenta previa (n = 771)[a]	No placenta previa (n = 184,705)[a]	OR	CI	P value
Infertility treatment	6.4	1.9	3.6	2.7–4.8	<0.001
Prior cesarean section	26.3	11.6	2.7	2.3–3.2	<0.001
Smoking	2.9	1.3	2.2	1.4–3.3	<0.001
Habitual abortions	10.5	5.4	2.1	1.6–2.6	<0.001
Hypertensive disorders	5.3	6.0	0.88	0.64–1.20	0.416

[a] Values are in percentage

among parturients with placenta previa as compared with the comparison group. There were no significant differences between the placenta previa and the control group regarding hypertensive disorders. We checked the number of previous cesarean sections of women within the placenta previa group, and revealed a relatively large group of women with a history of multiple previous cesarean deliveries within the placenta previa group: 161 (20.9%) women had one previous cesarean delivery, 43 women (5.6%) had two previous cesarean deliveries, 25 women (3.2%) had three previous cesarean deliveries, 17 women (2.2%) had four previous cesarean deliveries, and three women (0.4%) had five previous cesarean deliveries.

Placenta previa was significantly associated with several adverse pregnancy outcomes, such as peripartum hysterectomy, second trimester bleeding, maternal blood transfusion, maternal sepsis, vasa previa, malpresentation, postpartum hemorrhage, and placenta accrete (Table 3).

The clinical characteristics and perinatal outcomes of neonates are shown in Table 4. Neonates born after a pregnancy complicated with placenta previa had significantly lower birth weight, but did not differ from the comparison group in regard to their gender. Adverse perinatal outcomes include higher rates of neonatal mortality, an Apgar score <7 after 1 and 5 min, congenital malformations and intrauterine growth retardation in the placenta previa group.

In order to assess which of the aforementioned factors is independently associated with placenta previa, a multivariable analysis with backward elimination was conducted. The following conditions were found to be significantly associated with placenta previa: a previous episode of second trimester bleeding, preterm delivery, infertility treatments, prior cesarean section, smoking, habitual abortions, and advanced maternal age (Table 5).

Using another multivariable logistic regression model, with perinatal mortality as the outcome variable, controlling for pre-term birth, intrauterine growth restriction, maternal age, and congenital malformations, placenta previa was not found as an independent risk factor for perinatal mortality (weighted OR 1.018; 95% CI 0.74–1.40; P = 0.910, data not shown).

Discussion

This is one of the largest studies investigating risk factors for placenta previa, from a single medical center. The incidence of placenta previa was 0.42%, in accordance with other reports [2–6], but higher than the 0.38% incidence that was previously reported in our institution for the period between 1990 and 1998 [4]. Such an increase could be explained by changing trends of known risk factors for placenta previa.

As our medical center is the sole tertiary hospital providing care for the entire population of southern Israel, our data allows us to investigate the incidence of these risk factors, as well as to assess their impact on the adverse outcomes associated with placenta previa. The study strengthens the association between placenta previa and risk factors, such as increased maternal age, prior cesarean

Table 3 Pregnancy outcomes and labor complications of women with and without placenta previa

	Placenta previa (n = 771)[a]	No placenta previa (n = 184,705)[a]	OR	CI	P value
Cesarean hysterectomy	5.3	0.036	154.8	104.2–229.8	<0.001
Second trimester bleeding	3.9	0.046	99.7	64.9–153.1	<0.001
Maternal blood transfusion	21.9	1.2	22.8	19.1–27.1	<0.001
Maternal sepsis	0.4	0.017	22.5	6.9–73.8	<0.001
Vasa previa	0.5	0.1	4.8	1.8–13.0	<0.001
Malpresentation	19.8	5.4	4.4	3.7–5.2	<0.001
Post partum hemorrhage	1.4	0.5	2.7	1.4–4.9	<0.001
Placenta accrete	3.0	1.3	2.4	1.6–3.6	<0.001

[a] Values are in percentage

Table 4 Perinatal outcome of women with and without placenta previa

Characteristic	Placenta previa ($n = 771$)[a]	No placenta previa ($n = 184{,}705$)[a]	OR	CI	*P* value
Birth weight					<0.001
<2,500 g	42.8	8.1			
2,500–4,000 g	46.1	77.5			
>4,000 g	1.2	4.6			
Gender					0.351
Female	47.1	48.7			
Male	52.9	51.3			
Perinatal mortality	6.6	1.3	5.6	4.2–7.4	<0.001
Antepartum fetal death	1.6	0.7			
Intrapartum death	0.5	0.1			
Post partum death	4.5	0.5			
Apgar scores at 1 min < 7	25.3	5.9	5.4	4.6–6.3	<0.001
Apgar scores at 5 min < 7	7.1	2.6	2.9	2.2–3.8	<0.001
Congenital malformation	11.5	5.1	2.4	1.9–3.0	<0.001
IUGR	3.6	2.1	1.8	1.2–2.6	0.003

[a] Values are in percentage

Table 5 A back-step multiple logistic regression model for independent conditions associated with placenta previa

Condition	OR	CI	*P* value
Second trimester bleeding	33.11	20.29–54.02	<0.001
Preterm birth	11.07	9.55–12.83	<0.001
Infertility treatment	1.97	1.45–2.66	<0.001
Prior cesarean section	1.76	1.48–2.09	<0.001
Smoking	1.73	1.12–2.67	0.14
Recurrent abortions	1.23	0.97–1.57	0.09
Maternal age (years)	1.08	1.07–1.09	<0.001

section, and infertility treatments. Using a multivariable logistic regression analysis, our data demonstrate that, these are independent risk factors for placenta previa. Interestingly, after controlling for confounders, smoking and habitual abortions were not found to be independent risk factors for placenta previa.

As the number of women undergoing fertility treatments increases worldwide [21, 22], as well as the maternal age during first childbirth [17–20], and the rate of cesarean deliveries increases steadily [12–16], our results are expected and noteworthy. Pregnancies complicated with placenta previa have been shown to be prone to adverse outcomes, such as neonatal mortality, postpartum hemorrhage, maternal sepsis, maternal blood transfusion, and hysterectomy [3, 4, 8, 9]. The large number of patients with placenta previa in our study ($n = 771$) gave us statistical power to detect rare associations, such as vasa previa, maternal sepsis, maternal blood transfusion, and hysterectomy following uncontrolled bleeding. Indeed, these outcomes have been found to be significantly higher in the placenta previa group, with rates higher than previously reported [3].

While controlling for confounders, placenta previa was not found to be an independent risk factor for perinatal mortality. It is, therefore, not the direct result of abnormal implantation, but rather its association with other risk factors for adverse perinatal outcome, such as congenital malformations and early gestational age at delivery, that contribute to this increased risk of perinatal mortality.

In conclusion, our study shows that independent risk factors for placenta previa are infertility treatments, previous cesarean section, and advanced maternal age. An increase in the incidence of these risk factors probably contributes to the small, yet appreciable increase in the incidence of placenta previa in our institution. As these risk factors are becoming more common worldwide, our findings should serve as a reminder to the serious adverse affects women with placenta previa are prone to. A careful surveillance for these risk factors, along with careful monitoring during pregnancy, and a timely delivery may help minimize the occurrence of maternal and perinatal complications associated with placenta previa.

Conflict of interest None.

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