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Risk factors for placenta previa among pregnant women of Kyiv, Ukraine: a retrospective cohort study

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Placenta previa is a significant obstetric problem with elevated morbidity and mortality rates for both mother and fetus. The risks associated with placenta previa underscore the necessity for comprehensive treatment and timely intervention to mitigate adverse outcomes.

Purpose — to conduct a retrospective analysis of the impact of obstetric-gynecological factors on the prediction of placenta previa occurrence and its influence on perinatal outcomes.

Materials and methods. A retrospective cohort study was conducted on cases of placenta previa between 2018 and 2022. The study included 22491 deliveries, of which 65 (0.29%) cases were registered as placenta previa. Data from delivery records of 374 patients without placenta previa were used for comparison. The following variables were evaluated for all patients: maternal age, characteristics of the menstrual cycle, gravidity, parity, history of cesarean sections, gestational age at delivery, method of delivery, blood loss during delivery, length of postpartum hospitalization, birth weight, gender of the newborn, Apgar scores at 1 and 5 minutes. Gynecological intervention histories, including curettage/ hysteroscopy, laparoscopy, and cervical treatment, as well as obstetric pathologies, such as cesarean section, ectopic pregnancy, instrumental abortions, missed pregnancies, and assisted reproductive technologies in the last pregnancy, were examined.

Results. Multifactorial analysis revealed four significant risk factors. The risk of placenta previa was found to increase with advanced maternal age (p<0.001), OR=1.14 (95% CI 1.07–1.20), and the presence of previous cesarean sections (p<0.001), OR=5.51 (95% CI 2.73–11.1), while a history of previous deliveries reduced the risk (p<0.001), OR=0.24 (95% CI 0.15–0.40). Instrumental abortions increased the risk of placenta previa (p=0.001), OR=2.14 (95% CI 1.20–3.81). Newborns in the placenta previa group had lower Apgar scores at 1 and 5 minutes and lower birth weight.

Conclusions. The obtained results emphasize the importance of considering risk factors in assessing placenta previa occurrence during antenatal monitoring and can contribute to improving obstetric and perinatal care for women. However, the morphological and functional basis of placenta previa remains unknown and requires further study.

The research was carried out in accordance with the principles of the Helsinki Declaration. The study protocol was approved by the Local Ethics Committee of participating institution. No conflict of interests was declared by the authors.

Keywords: women, placentation, placenta previa, cesarean section, curettage, instrumental abortion, assisted reproductive technologies, obstetric hemorrhage, preterm delivery.

Фактори ризику виникнення передлежання плаценти серед вагітних Києва, Україна: ретроспективне когортне дослідження

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Передлежання плаценти є серйозною акушерською проблемою, що характеризується підвищеними показниками захворюваності та смертності матері та плода. Ризики, пов'язані з передлежанням плаценти, поширюються як на матір, так і на плід, що підкреслює необхідність комплексного лікування та своєчасного втручання для пом'якшення несприятливих наслідків.

Мета — провести ретроспективний аналіз впливу факторів акушерського-гінекологічного анамнезу на прогнозування виникнення передлежання плаценти, а також впливу передлежання плаценти на перинатальні наслідки.

Матеріали та методи. Проведено ретроспективне когортне дослідження випадків передлежання плаценти за 2018–2022 рр. Дослідження охоплює 22 491 пологи, з яких зареєстровано 65 (0,29%) випадків передлежання плаценти. Для порівняння застосовано дані історій пологів 374 пацієнток без передлежання плаценти. В усіх пацієнтів визначено: вік матері, характеристику менструального циклу, гравідитет, паритет, кількість кесаревих розтинів в анамнезі, термін гестації на момент пологів, метод народження, крововтрату при народженні, кількість діб госпіталізації після пологів, вагу, стать новонародженого, оцінку за шкалою Апгар на 1- і 5-й хвилинах. Вивчено анамнези гінекологічних втручань: кюретаж/гістерорезектоскопії, лапароскопії, лікування шийки матки. Досліджено анамнези акушерської патології: наявність кесаревого розтину, позаматкової вагітності, інструментальних абортів, завмерлих вагітностей, допоміжних репродуктивних технологій при останній вагітності.

Результати. Багатофакторний аналіз виявив чотири найбільш значущі фактори ризику. Встановлено зростання ризику передлежання плаценти з віком породіллі (p<0,001), ВШ=1,14 (95% ДІ: 1,07–1,20) та за наявності кесаревих розтинів в анамнезі (p<0,001), ВШ=5,51 (95% ДІ: 2,73–11,1), однак наявність пологів в анамнезі знижувала ризик (p<0,001), ВШ=0,24 (95% ВІ 0,15–0,40). Інструментальні аборти збільшували ризик передлежання плаценти (p=0,001), ВШ=2,14 (95% ДІ: 1,20–3,81). Визначено, що новонароджені з групи передлежання плаценти мали нижчі бали за шкалою Апгар на 1-та 5-й хвилинах і мали нижчу вагу при народженні.

Висновки. Отримані результати підкреслюють важливість урахування факторів ризику під час оцінювання ризику виникнення передлежання плаценти під час антенатального спостереження та можуть допомогти поліпшити акушерську і перинатальну допомогу жінкам. Однак на сьогодні залишаються невідомими морфологічна та функціональна основи виникнення передлежання плаценти, які потребують подальшого вивчення.

Дослідження виконано відповідно до принципів Гельсінської декларації. Протокол дослідження ухвалено Локальним етичним комітетом зазначеної в роботі установи. Автори заявляють про відсутність конфлікту інтересів.

Ключові слова: жінки, плацентація, передлежання плаценти, кесарів розтин, вишкрібання, інструментальний аборт, допоміжні репродуктивні технології, акушерські кровотечі, передчасні пологи.

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Introduction

Placenta previa (PP) is a condition characterized by abnormal placental attachment, resulting in partial or complete coverage of the cervical os by the placenta [9]. PP occurs in 0.3–1.5% of pregnancies, potentially leading to severe maternal morbidity and mortality [10]. Most cases of PP are identified through early-term ultrasound examinations (USE), while others may manifest as asymptomatic vaginal bleeding during the second or third trimester of pregnancy [3]. PP also increases the likelihood of «deep» invasion, namely the development of placenta accreta, increta, and percreta [21]. Such conditions escalate maternal risks, as PP precludes vaginal delivery, necessitating cesarean section. Uncontrolled postpartum hemorrhage from placental invasion can result in blood transfusion, hysterectomy, infertility, intensive care unit admission, or even death [4]. Additionally, PP is associated with unfavorable neonatal outcomes, including preterm birth, low birth weight, and perinatal mortality [16]. Understanding the impact of obstetric-gynecological history on the occurrence of PP is crucial for providing appropriate counseling to pregnant women.

The **_purpose_** of the study — to retrospectively examine the influence of obstetric-gynecological history factors on predicting PP occurrence and the impact of PP on perinatal outcomes. The research was carried out in accordance with the principles of the Helsinki Declaration. The study protocol was approved by the Local Ethics Committee of participating institution.

Materials and methods of the research

A retrospective cohort study of PP cases was conducted for 2018–2022. The study was conducted at Maternity Hospital No. 5, which serves as the clinical base of the Department of Obstetrics, Gynecology, and Neonatology of the Postgraduate Education of O.O. Bogomolets National Medical University. The study encompassed 22491 deliveries, with 65 cases of PP registered (PP group).

The analysis involved a retrospective review of electronic medical records, cesarean section protocols, and neonatal records. The diagnosis of PP was confirmed by an expert obstetrician using transabdominal ultrasound scans or Magnetic Resonance Imaging (MRI), and the diagnosis was verified during delivery.

For comparative analysis, data from the delivery histories of 374 patients without PP (non-PP group) were utilized for the same period.

Exclusion criteria included multiple pregnancies, fetal anomalies, absence of records in medical documentation, and PP.

The following clinical characteristics were evaluated in all patients: maternal age, characteristics of the menstrual cycle, gravidity, parity, number of previous cesarean sections, gestational age at delivery, method of delivery, blood loss at birth, length of postpartum hospitalization, newborn weight, newborn sex, Apgar score at 1 and 5 minutes. The presence of gynecological interventions (GI) in the history was assessed, including curettage/hysteroscopy, laparoscopy, cervical treatment, and the cumulative number of GI-related factors. The presence of obstetric pathology in the history requiring intervention (OI) was also examined, including previous cesarean section, ectopic pregnancy, instrumental abortions, missed miscarriages, and the use of assisted reproductive technologies (ART) in the last pregnancy, along with the cumulative number of OI-related factors and the combination of OI with ART.

Statistical Analysis. Categorical data were presented as frequencies and percentages (%), while descriptive statistics were reported as mean (M) ± standard deviation (SD). Confidence intervals (CI) of 95% or interquartile range were calculated, odds ratio (OR). Differences in categorical variables were assessed using the chi-square or Fisher's exact test, while differences in continuous variables were evaluated using the Mann–Whitney U test or t-test. Data analysis was performed using R (3.4.1). A two-sided P-value less than 0.05 was considered statistically significant.

Ethical Approval and Informed Consent. The Bioethics Committee of Bogomolets National Medical University, affiliated with the Department of Obstetrics, Gynecology, and Neonatology of the Postgraduate Education, authorized the study, based at Maternity Hospital No. 5 in Kyiv. Patients' data was protected by excluding names, phone numbers, home addresses, and confidential information. Since the study was based on electronic medical records and all information was anonymized, informed consent was waived. The study adhered to the principles of the Helsinki Declaration.

Results of the research

The total number of deliveries during the study period were 22491, with 65 cases of PP, resulting

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Table 1

Comparative characteristics of patients

Indicator	Non-PP group (n=374)	PP group (n=65)	Significance of the difference, P
Age, years	30 (26–34)	34 (30–37)	<0.001
Menarche, years	13 (12–14)	13 (12–14)	0.829
Menstruation, days	5 (5–5)	5 (5–5)	0.906
Menstrual cycle, days	28 (28–28)	28 (28–30)	0.073
Gravidity	2 (1–2)	2 (2–3)	<0.001
Number of cesarean sections (1 or 2)	22 (5.9%)	14 (21.5%)	<0.001
Parity	1 (1–2)	1 (0–1)	<0.001
Blood loss, ml	250 (250–400)	777 (600–912.5)	<0.001
Duration of hospitalization, days	3 (3–4)	5 (3.75–8)	<0.001

Note: The Mann–Whitney U test is used for the comparison.

Table 2

The analysis of gynecological interventions

Indicator		Non-PP group (n=374)	PP group (n=65)	Significance of the difference, P
Hysteroscopy and/or dilation and curettage	0	346 (92.5)	61 (93.8)	0.872
	1	27 (7.2)	4 (6.2)	
	2	1 (0.3)	0 (0)	
Laparoscopy	0	332 (88.8)	54 (83.1)	0.215
	1	42 (11.2)	11 (16.9)	
Cervical treatment	0	319 (85.3)	54 (83.1)	0.707
	1	55 (14.7)	11 (16.9)	
The sum of gynecological interventions	0	269 (71.9)	40 (61.5)	0.105
	1	105 (28.1)	25 (38.5)	

Notes: The chi-square test or Fisher's exact test was used to perform the comparison. The sum of gynecological interventions — If at least one episode of intervention was present, the patient received a mark; however, combinations of factor features were not considered when calculating the sum.

in a prevalence rate of placenta previa among patients in the maternity hospital of 0.29%. In the non-PP group, there were 117 (31.3%) out of 374 deliveries, while in the placenta previa group, all 65 (100%) deliveries were performed by cesarean section, P<0.001. When evaluating background of PP occurrence, it's crucial to consider the interplay between risk factors. Furthermore, making a comprehensive assessment of these factors essential in providing optimal prenatal care and minimizing potential complications associated with PP.

A comparative assessment of age, menstrual history, gravidity, parity, number of previous cesarean sections, blood loss at birth, and duration of hospitalization was conducted among patients in the two groups. The comparative characteristics are presented in Table 1.

Analysis of pregnancy-related interventions among patients in the two groups included a history of cesarean section, ectopic pregnancy, instrumental abortions, pregnancy loss and ART. The analysis of pregnancy-related interventions is presented in Table 3.

Among the newborns in the PP group, 41 (63.1%) were male and 24 (36.9%) were female, while in the non-PP group, 202 (54%) were male and 172 (46%) were female, with a P-value of 0.180. Massive obstetric hemorrhage (>1000 ml) occurred in 3 (0.8%) cases out of 374 cases in the non-PP group, whereas in the PP group, it occurred in 15 (23.1%) cases, with a P-value of <0.001. A comparative analysis of perinatal outcomes between the patients in the two groups was conducted, which included gestational age at

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Table 3

Analysis of pregnancy-related interventions

Indicator		Non-PP group (n=374)	PP group (n=65)	Significance of the difference, P
History of Cesarean section	0	348 (93)	51 (78.5)	<0.001
	1	26 (7)	14 (21.5)	
Ectopic pregnancy	0	365 (97.6)	64 (98.5)	0.768
	1	6 (1.5)	1 (1.5)	
	2	3 (0.9)	0 (0)	
Instrumental abortions	0	331 (88.5)	53 (81.5)	<0.001
	1	38 (10.2)	6 (9.2)	
	2	5 (1.3)	3 (4.6)	
	3	0 (0)	2 (3.1)	
Pregnancy loss	0	310 (82.9)	53 (81.5)	0.839
	1	57 (15.2)	10 (15.4)	
	2	6 (1.6)	2 (3.1)	
	3	1 (0.3)	0 (0)	
Assisted reproductive technologies	0	361 (96.5)	49 (75.4)	<0.001
	1	13 (3.5)	16 (24.6)	
Obstetric sum	0	255 (68.2)	34 (52.3)	0.016
	1	119 (31.8)	31 (47.7)	
Obstetric and Assisted reproductive technologies sum	0	183 (48.9)	19 (29.2)	0.004
	1	191 (51.1)	46 (70.8)	

Notes: Fisher's exact test was used for the comparison. Obstetric sum - If at least one episode of intervention was present, the patient received a mark; however, combinations of factor features were not considered when calculating the sum. Obstetric and assisted reproductive technologies sum — the cumulative assessment of interventions related to pregnancy and assisted reproductive technologies.

Table 4

Analysis of perinatal results of childbirth

Indicator	Non-PP group (n=374)	PP group (n=65)	Significance of the difference, P
Gestational age, weeks	39 (39–40)	37 (36–37)	<0.001
Newborn weight, gram	3460 (3220–3740)	2960 (2577.5–3250)	<0.001
Apgar 1	7 (7–8)	7 (6.75–7)	<0.001
Apgar 5	8 (8–9)	8 (7–8)	<0.001

Note: The Mann–Whitney test was used for comparison.

Table 5

Coefficients of the 4-factor logistic regression model for predicting the risk of placenta previa

Factorial sign	Non-PP group (n=374)	PP group (n=65)	Significance of the difference, p
Age	0.13±0.02	<0.001	1.14 (1.07–1.20)
Number of cesarean sections	1.71±0.36	<0.001	5.51 (2.73–11.1)
Parity	-1.42±0.25	<0.001	0.24 (0.15–0.40)
Instrumental abortion	0.76±0.29	0.001	2.14 (1.20–3.81)

birth, newborn weight, and Apgar scores at 1 and 5 minutes. The respective data are presented in Table 4.

Risk assessment of PP. The logistic regression model construction was employed to analyze the factor features associated with the risk of pathology. The analysis was conducted for 17 risk factors: age, menarche, duration of menstruation, menstrual cycle, number of cesarean sections, parity, hysteroscopy and D&C, laparoscopy, cervical treatment, gynecological sum, ce-

sarean section, ectopic pregnancy, instrumental abortion, pregnancy loss, obstetric sum, obstetric interventions and ART sum, sex of the newborn. The stepwise inclusion/exclusion method (inclusion threshold p<0.05, exclusion threshold p>0.1) was utilized to select significant factor features. During the selection process, four significant risk factors were identified: age, number of cesarean sections, parity, and instrumental abortion. A four-factor logistic regression model for predicting the risk of pathology was constructed based on

the selected features. Table 5 presents the characteristics of the model.

An increase in the risk of pathology with maternal age was established (p<0.001), OR=1.14 (95% CI 1.07–1.20) per year (considering the influence of other risk factors). The risk of pathology increases (p<0.001) with a history of cesarean sections, OR=5.51 (95% CI 2.73–11.1) per operation (accounting for the influence of other risk factors). A decrease in the risk of pathology was found with a history of previous deliveries (p<0.001), OR=0.24 (95% CI 0.15–0.40) per delivery (considering the influence of other risk factors). In the presence of instrumental abortions in the medical history, the risk of pathology increases (p=0.001), OR=2.14 (95% CI 1.20–3.81) per instrumental abortion (accounting for the influence of other risk factors). Figure 1 presents the receiver operating characteristic curve of the model.

The area under the curve (AUC) of the model's receiver operating characteristic is 0.79 (95% CI 0.75–0.83), indicating a good fit of the model and a moderate level of association between the risk of PP and age, number of cesarean sections, parity, instrumental abortions. When selecting the optimal decision threshold based on the Youden Index, the model demonstrated a sensitivity of 75% (95% CI 65.1–85.2%) and a specificity of 77.8% (95% CI 73.3–81.9%). The positive predictive value was 36.3% (95% CI 31.1–41.8%), while the negative predictive value was 94.7% (95% CI 92.1–96.5%).

Discussion

Placenta previa is a common and severe complication of pregnancy that can lead to complications such as postpartum hemorrhage and amniotic fluid embolism [25]. Furthermore, studies have shown that the frequency of preterm delivery and low birth weight infants is significantly higher in women with PP than those with a normal placental position [2,5], indicating an increased risk of adverse neonatal outcomes. Therefore, investigating the risk factors associated with PP is crucial for reducing the likelihood of unfavorable consequences for both the mother and the child. In order to elucidate the etiology of PP in pregnant women, we conducted a retrospective analysis of 65 records of obstetric histories of women with PP.

The study found that advanced maternal age, defined as ≥34 years, is a significant risk factor for PP with a six-fold increased risk. This finding
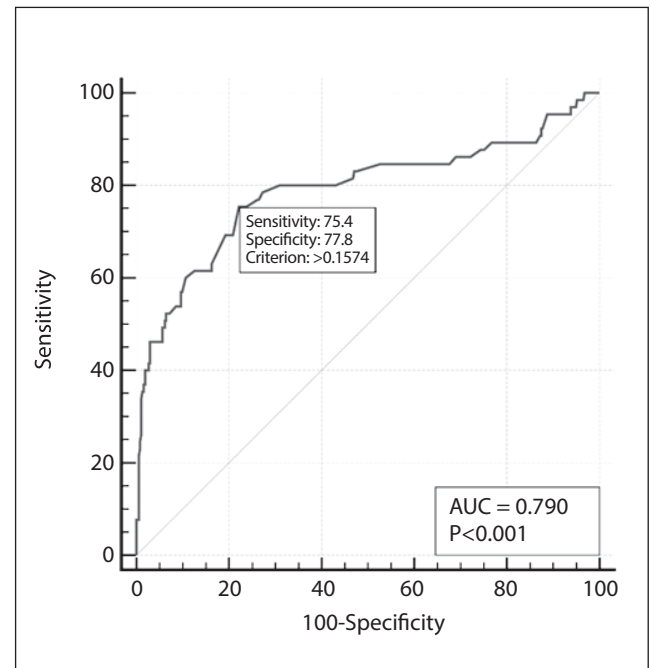

Fig. ROC-curve of the 4-factor logistic regression model for predicting the risk of pathologya

is consistent with the studies conducted by L. Tuzovic et al., as well as M. Kollmann et al., who reported an increased risk of PP with higher parity, possibly due to endometrial scarring and reduced uteroplacental blood flow due to atherosclerotic changes in blood vessels [11,22]. However, our study revealed a reduced risk of PP in patients with a history of previous deliveries, OR=0.24 (95% CI 0.15–0.40), which the distribution of patients can explain according to risk factors affecting the occurrence of PP.

Previous cesarean deliveries are a well-known risk factor for PP, as demonstrated in this study and confirmed by a meta-analysis of 170,640 pregnant women [20]. A cohort study conducted at the National Health Service Hospital in the United Kingdom also found that PP occurred in 32.9‰ out of 1000 women with a planned cesarean section [13]. Thus, H.S. Abduljabbar et al. concluded in their meta-analysis that 359 cesarean sections are needed during first deliveries to obtain one additional case of PP in subsequent pregnancies [1]. The increased risk may be a result of prolonged damage to the myometrium and endometrium due to surgical disruption of the uterine cavity, leading to hypoxia, incomplete decidualization, and abnormal trophoblast invasion, which can cause placental adhesion [24]. The data above are consistent with our study, as patients with a history of cesarean section had a 5-fold higher risk of developing PP, OR=5.51 (95% CI 2.73–11.1).

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Another well-known fact is a history of instrumental abortions, a risk factor for PP. In the study by L. Tuzovic et al., abortions increased the risk of PP by 2.75 times. The mechanism of this association may be attributed to the damage to the endometrium during repeated abortions, leading to impaired successful placental implantation [22]. The data obtained in this study also confirm the significant impact of instrumental abortions on the risk of developing PP, specifically an OR of 2.14 (95% CI 1.20–3.81).

ART has drawn attention due to its wide application in clinical practice, particularly among older patients with a history of endometriosis and chronic salpingitis [14]. Furthermore, ART often involves the use of ovulation-stimulating drugs, which can disrupt the regulation or uncontrolled expression of genes associated with endometrial growth, leading to asynchrony between endometrial and embryonic development and ultimately resulting in PP formation [12,17]. Additionally, the mechanical implantation of embryos using a transfer catheter can cause the release of prostaglandins during passage through the cervical canal, leading to uterine contractions and an increased likelihood of placental implantation in the lower uterine segment [15]. The findings of this study demonstrate a difference in the number of patients who conceived through ART, although the sample size is not representative for analysis.

Placenta previa also has a significant impact on neonates. A cohort study of 3,550,842 deliveries revealed that PP after 37 weeks of gestation is an independent risk factor for adverse neonatal outcomes [18]. The risk of preterm birth is 14 times higher in women with PP [22]. A systematic review [23] identified that 57.7% of deliveries in women with PP occur prematurely, whereas, in another study, this rate was 52% compared to 8% for preterm births in women without PP [6]. C. Zhou et al., in a study on the impact of PP on neonatal outcomes, found that the PP group had lower birth weight and lower Apgar scores at 1 and 5 minutes, leading to an increased risk of delivery complications, respiratory distress syndrome in newborns, and increased neonatal mortality [25]. This conclusion aligns with a study conducted by J.M. Crane et al., where newborns delivered by women with PP had a fivefold increased risk of developing respiratory distress syndrome [7]. Similar results were obtained in our study. It was determined that newborns in the PP group had lower Apgar scores at 1 and 5 minutes and lower birth weight.

Maternal mortality and antenatal hemorrhage are among the most severe complications during pregnancy. In patients with PP, the risk of antepartum hemorrhage is nine times higher than in patients with customarily located placenta [19]. It has been reported that the frequency of antepartum hemorrhage in women with PP is approximately 51.6% [8], underscoring the critical nature of this condition and the necessity for careful monitoring and treatment during pregnancy. Similar to the findings of C. Zhou et al. [25], the results obtained from the study indicate that the frequency of postpartum hemorrhage and the duration of hospital stay was significantly higher in the PP group compared to the non-PP group.

Conclusions

This study has identified an association between the risk of PP and maternal age, parity, previous cesarean section, and history of instrumental abortions. The risk of developing the pathology increased with advancing maternal age and the presence of a history of cesarean section or instrumental abortions, while the risk decreased with prior deliveries. PP increases the risk of giving birth to newborns with lower Apgar scores than pregnant women without PP. These findings emphasize the importance of considering these factors when assessing the risk of PP during antenatal surveillance, which can help improve obstetric care for women. However, the morphological and functional basis for the occurrence of PP remains unknown and requires further investigation.

No conflict of interests was declared by the authors.

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