



## PLACENTA ACCRETA – RISK FACTORS, SURGICAL AND CLINICAL OUTCOME

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### ABSTRACT

Placenta accreta is a spectrum of antenatal diagnostic markers, surgical complications and life-threatening diagnoses.

**Objective:** To evaluate the risk factors, the surgical complications and the clinical periparturient outcomes in the placenta accreta spectrum.

**Materials and methods:** The study represents an 11-year prospective follow-up of 58 cases of placenta accreta, sonographically diagnosed, clinically managed and pathohistologically confirmed. The rate of placenta accreta was 34,5%, placenta percreta - 56,9% and partial placenta accreta 8.6%. In The main risk factors were a previous caesarean section and placenta previa. Additional risk factors were advanced maternal age, multiparity, IVF procedures, previous uterine curettage, anterior placenta. The control group consisted of 135 cases with normal placenta.

**Results:** We found an increased rate of caesarean births and a corresponding increase in placenta previa rate. The periparturient hysterectomy rate was 91%. Surgical complications were mostly uterovesical lesions and excessive haemorrhage. Blood loss in the groups with an emergency hysterectomy and laparotomy was in the range of 3510 ml – 6500 ml, compared to 3420 ml in planned delivery with caesarean hysterectomy due to placenta accreta. More resuscitation measures and longer hospital stay was observed in cases with a placenta accreta spectrum. The neonatal clinical outcome was good according to fetal weight and Apgar score at delivery.

**Conclusion:** Our results revealed good clinical confirmation in 90% of cases by expert ultrasonographers, followed by clinical and histopathological confirmation in all cases. This diagnosis and its surgical treatment will continue to be a professional challenge.

**Keywords:** Placenta accreta, placenta previa, Caesarean section, periparturient hysterectomy,

### INTRODUCTION

In recent years, the placenta accreta spectrum has become increasingly common and challenging for prediction diagnosis, even for the most experienced sonographers. This diagnosis is associated with significant morbidity and mortality for both the mother and the fetus. Knowledge of the risk factors and experience in antenatal imaging are crucial for the preliminary diagnosis and subsequent clinical management. Timely diagnosis creates an option for advanced organization and preparedness for foreseeable risk, which aims to avoid the element of surprise. Caesarean hysterectomy in these cases can be challenging for even the most experienced surgeons. The gold standard in diagnosis is pathological confirmation. Due to the risk of periparturient bleeding and possible surgical complications in women with placenta accreta spectrum, the medical centers that care for these patients should have the ability and resources to rapidly organize and deliver blood products, a prepared multidisciplinary team and a department for intraoperative and postoperative intensive care for the mothers and newborns. According to global recommendations [1, 2, 3], it is considered a disease with a spectrum of sonographic markers for diagnosis, standardized and validated by considerable world practice in recent years. It is known that the incidence of placenta accreta is increasing in parallel with the rise in caesarean section rate worldwide, especially over the last decade, and is related to their increase - a major risk factor and cause. In placenta accreta, both placenta adherents and placenta accreta may exist simultaneously, with different degrees of invasion. This explains why ultrasonographic signs for PAS can occur in combinations in one area. The increase of placenta accreta and associated severe complications has given reason for experts in ultrasonography to investigate and update the diagnosis and treatment of this condition, which has the nature of a disease, with a spectrum of risk factors, sonographic markers for diagnosis, clinical presentation and outcome. It was accepted to be named “placenta accreta spectrum” (PAS; often called and known as Placenta accreta) [4]. In order to improve a diagnosis and to avoid errors in the diagnosis of the Placenta accreta spectrum, it is important to know the main risk factors, scan technique, the normal anatomy of the area and the pathophysiology of the disease to recognize the underlying pathology. [5]

The aim of the present study was to present the expe-

rience of University Hospital, Maichin dom, Sofia, Bulgaria, with placenta accreta spectrum in clinical practice. A prospective study was performed about risk factors, perioperative complications and clinical outcome in PAS, using ultrasound diagnostic criteria.

**MATERIAL AND METHODS**

A prospective study that covers an 11-year period (2012 – 2023) was conducted in the University Hospital “Maichin dom”, Sofia. It included dynamic follow-up of patients from the echographic diagnosis in the third trimester of pregnancy (26 – 34 weeks of gestation) to the clinical outcome during and after labor.

Patients studied included: one or more previous cesarean section – 49 cases; placenta previa or low-lying anterior placenta less than 2 cm from the internal os of the cervical canal – 74 cases, 39 of them in combination with previous SC. The age range of the patients was 18 to 58 years.

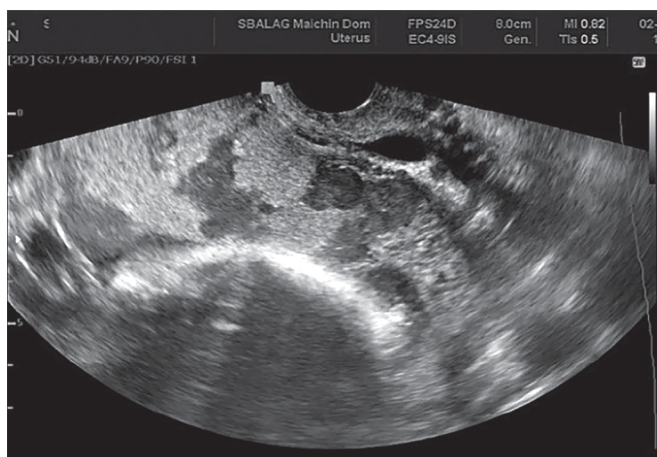
As a high-risk group were 58 cases: placental location – anterior low-lying placenta and placenta previa and previous cesarean section in combination or alone with the presence or absence of additional risk factors – maternal age, uterine curettage, myomectomy, IVF, position of placenta, parity (all included in the risk group were multipara – 54 cases; the remaining 4 cases were 0-para). Control results were compared with 135 cases of various normally attached placentas.

We have accepted the degrees of invasion from a histological point of view to be summarized in two groups: 1. predominantly placenta accreta, and 2. predominantly placenta percreta. Opinions of ACOG and FIGO were taken into account.

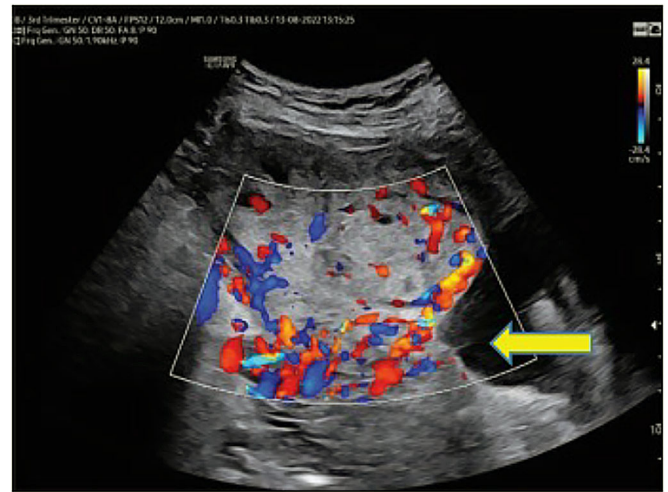
Patients were evaluated with combined transabdominal and transvaginal echographic access: echographic equipment – Medison 320, Samsung WS80A, Phillips Affinity, different frequency: 3 – 5 and 6 – 9 MHz on Gray scale, Colour/Power Doppler. A combination of the two risk factors was found in 39 patients. Peripartur hysterectomy was performed in 53 patients. In 5 cases with partial placenta accreta the uterus was preserved.

Ultrasound methodology: The criteria of the European Working Group on Spectrum of Placenta Accreta, 2016. [6]

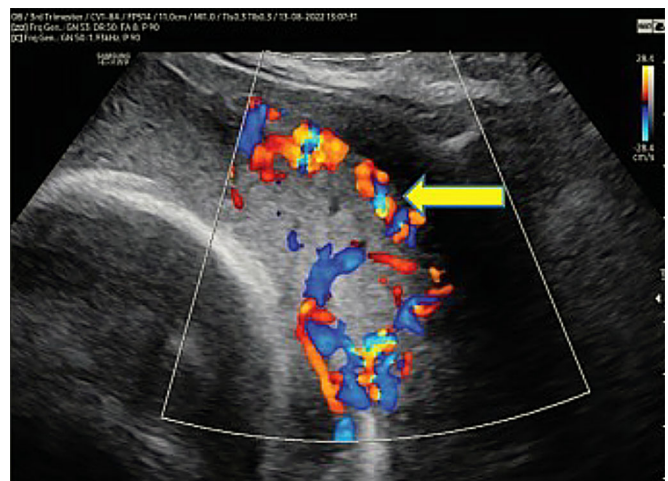
**Fig. 1.** Sagittal view of the lower uterine segment and placenta with lacunae, Gray scale



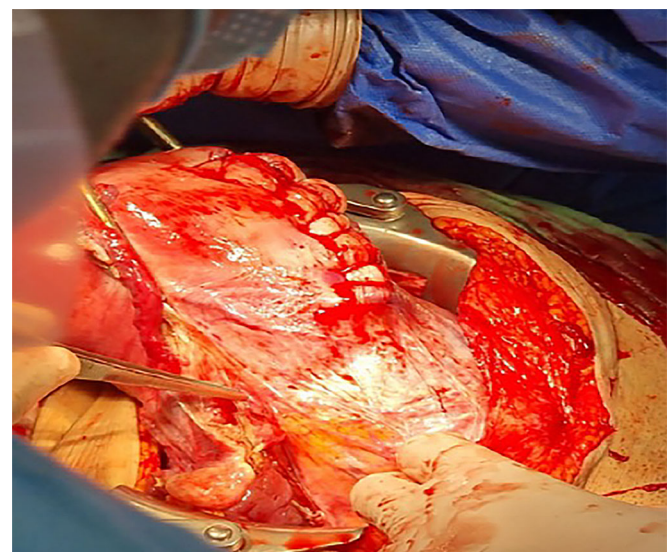
**Fig. 2.** Transverse view of the isthmic part of the uterus



**Fig. 3.** Transabdominal sagittal view of uterine serosa – bladder wall space on color doppler



**Fig. 4.** Intraoperative bulging and neovascularisation



Images 1-4: Bridging vessels, turbulent blood flow in the lacunae, compromised uterine serosa – bladder wall interface, subvesical hypervascularity on transvaginal section images 1, 2, and on a transabdominal section - image 3. Large lacunae are observed in the 3rd stage with the presence of turbulence and a feeding vessel in the lacuna. Clear space is absent in all three images (in fact, these are three separate cases), and the phenomenon of multidirectional blood flow with alienation is present, feeding a vessel in the lacunae. Image 4: intraoperative uterine hypervascularity.

**Statistical processing of the results**

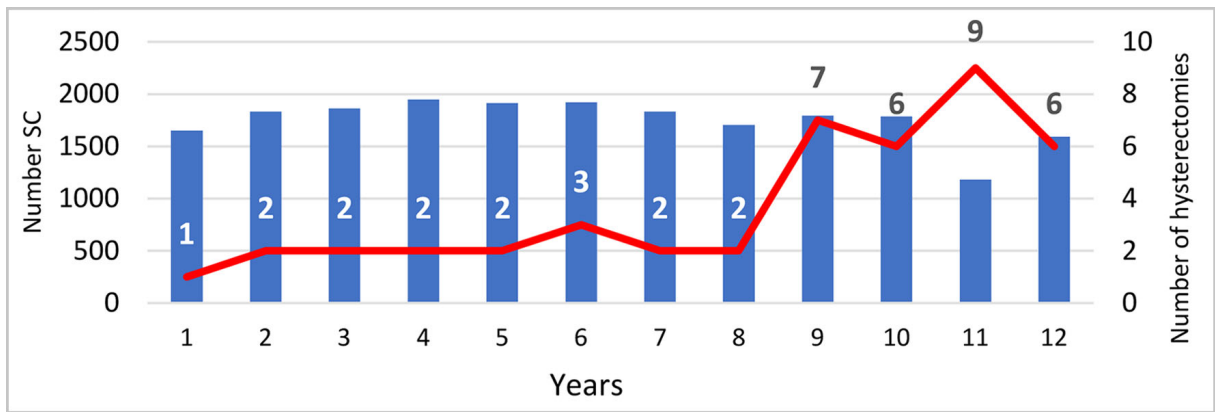
The data is organized into one-dimensional and multi-dimensional tables, with quantitative parameters represented by mean values and standard deviations and qualitative parameters by relative shares by categories.

Large, statistically comparable samples have been studied. Nominal variables are recorded as numbers and frequencies, and continuous variables as median and range. Differences are considered statistically significant at a confidence probability (the degree of certainty of the statistical conclusion, at which p. 95%, i.e., a 5% chance of error)  $P < 0.05$ . Standard deviations have been calculated. A measure of the dispersion of multiplicity around the mean value and Fisher Exact test, T-test and Mc Namara test.

**RESULTS**

We graphically plot the incidence of CS in the University hospital “Maichin Dom” for an approximately 11-year period from 2011 to 2022 relative to the total number of normal births (Graph 1).

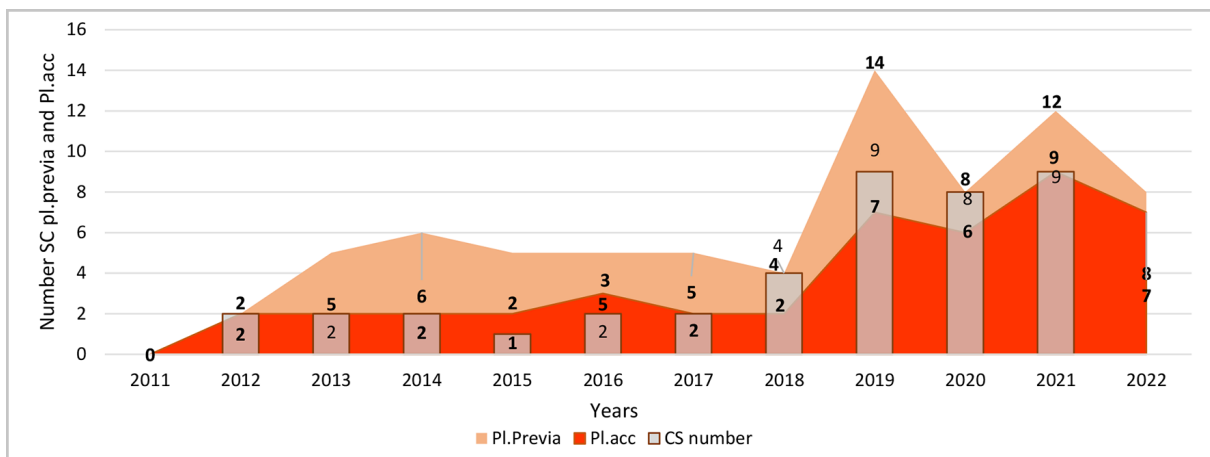
**Graph 1.** Cesarean hysterectomies /red line/ compared to the growth of cesarean section rate /blue/



Parallel to the increase in cesarean section rate, a similar curve of cesarean/peripartal hysterectomies was observed with the same rate from 2012 to 2018, i.e. a 7-year steady run followed by a sharp jump for the next 4 years with a 3 to 4 times increase.

The graphic representation of the two main risk factors – previous caesarean section and placenta previa in correlation with placenta accreta are presented graphically (Graph 2).

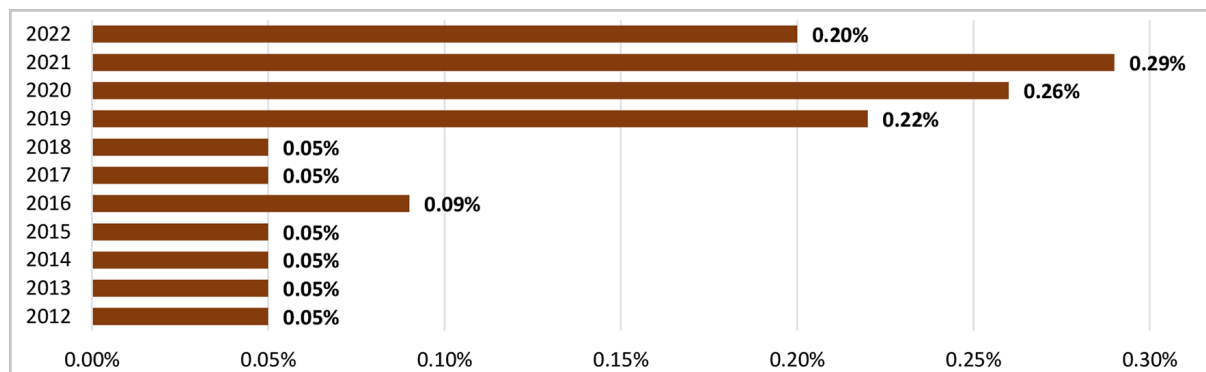
**Graph 2.** Correlation of placenta previa, Cesarean section rate and placenta accreta



It can be summarized that with the increase in caesarean section rate, the number of cases with placenta previa and placenta accreta increases. According to the literature, this is a well-recognizable fact. The frequency of placenta previa in the study was 5.2%, but it does not exceed 4-5% (about 1: 200 births).

The trend, as graphically illustrated below, showed a permanent increase in frequency, and in terms of percentage, it should be noted that for an approximately 7-year period, 0.05% per thousand births were observed, i.e. 0.05%, the lowest recorded incidence of placenta accreta worldwide, after which the rate increased from 0.20% to 0.29% with the highest incidence in 2021 (Graph 3).

**Graph 3.** Placenta accreta versus total number of births



Patient characteristics and risk factors for PAS were analyzed as follows (Table 1):

**Table 1.** Patients characteristics and risk factors for PAS

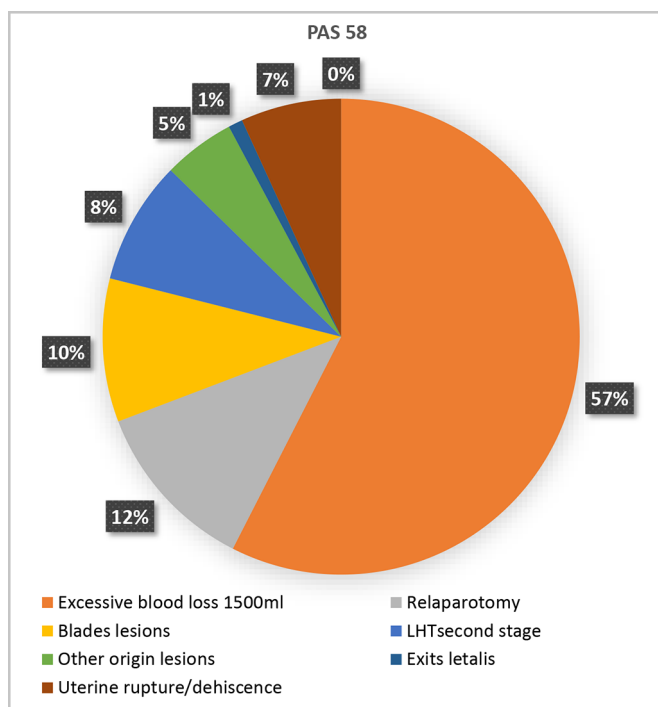
Characteristics and risk factors	Pl normal	%	Pl acc p	%	P
Patients number	135		54		
Mean age	31.5		34.6		0.0212
SD	3.4		4.6		
Over 35	25	18.5	24	44.4	0.000102
SD	3.9		6.8		
Parity					
Primi –para	36	26.60%	4	7.40%	0.00166233
Multi –para	99	73.30%	50	99.50%	0
Previous Sc 1	70	51.90%	42	77.80%	0.0005
Previous 2 Sc	0	0.00%	7	12.9%	Na
Pl previa / low-lying Pl	7	5.20%	35	64.80%	0
Uterine curettages	28	20.70%	18	33.30%	0.0345
IVF	4	3.00%	7	13.00%	0.0039
Myomectomy	0	0.00%	2	3.70%	Na
Anterior previa/low	5	4%	47	87%	0
Mostly posterior	42	31%	2	4%	0.00002823
Anterior/Normal	85	63%	2	4%	0
Additional pl. and vasa previa	1	0.7%	3	6%	0.028

An ultrasound scan was done first at 26.6. w.g (24.5 – 27.4 ) and secondly – in 32. w.g. (31.5 – 33.2). The results showed a significant dependence of PAS on the position of the placenta (p – 0.00). In 87%, anterior placenta praevia or low attached placenta were the second risk factors for PAS.

Assuming a minimal margin of error, variations in the shape of the placenta – placenta succentoriata and vasa praevia can be accepted as a significant risk factor for PAS, p< 0.02.

Operative complications and outcome are presented in percentages below (Graph 4)

**Graph 4.** Clinical complications for the study period



Haemorrhage was significant, although the uterine incision avoided the placenta in order to minimize bleeding, but overall, the nature of the procedure and the increased neovascularization were decisive for the volume of bleeding. There were 7 cases with relaparotomy for the entire period of observation due to intra-abdominal bleeding, one of them with two subsequent relaparotomies, achieving 12% relaparotomy rate. Second-stage hysterectomy also due to postoperative hemorrhage was observed in 8.6% of cases. In the last four years of our work, when the number of cases increased three times, with more experience and organization (preliminary team preparation), organ lesions were absent, second-stage laparohysterectomy was observed in 2 cases, in one of which definitely due to an element of unexpectedness in the diagnosis required hemostatic ligature of a. iliaca interna – 3.4%. We had one exitus letalis due to postoperative hemorrhage, shock, DIC and multiple organ failure. Uterine rupture/dehiscence of cicatrix was observed in 5 cases (8.6%), three of which were in 2023.

In table 2, operative complications were compared between two different groups of patients: 54 patients with placenta accreta and 39 with placenta praevia with significant difference in haemorrhage volume, relaparotomy and second-stage hysterectomy. These operative complications showed no significant difference depending on the depth of invasion of the placenta comparing the same two groups.

**Table 2.** Comparison of operative complications between placenta praevia and placenta accreta

	PI accrete	PI praevia	P-value
Exc. hem. over 1500 ml	59%	33%	0.0065
Relaparotomy	13%	3%	0.0475
Bladder lesion	11%	3%	0.0776
LHT second stage	22%	3%	0.0044
A lesion of the ureter	3%	0%	Na
Vaginal hematoma	2%	0%	Na
Ligatures of a. Iliaca	2%	0%	Na
Exitus letalis	2%	0%	Na
Total	54	39	

**Table 3.** Blood loss - mean and median between 3 groups.

Hysterectomy n- 53	%	blood loss	p-value
Planned n – 44 3400+–1800 ml/2SD median 3500 ml	83%	3420	
Urgent n –9 3500+–1100 ml/2SD median 4000 ml	16.90%	3510	0.394011841
Relaparotomies n –7 4500+–2500/2SD median 5000 ml	13.20%	6500	0.000097661

Summarized by the tabular and graphical representation of the results, the frequency of hemorrhages for the studied period was 60.3%, and in the first period of our study, with 2-3 cases per year, it was 13.8%, and in the second period after 2019, when cases increased approximately threefold, hemorrhage was also observed in three times more cases - 46.5%, which necessitates the conclusion that excessive hemorrhage in placenta accreta is an invariable quantity despite preoperative readiness, depends on intraoperative findings and is only influenced by the degree of invasion of the placenta in depth and to adjacent organs and tissues.

Statistical dependence showed the degree of hemorrhage over 1500 ml, with the average value of excessive hemorrhage being 3420 ml, with a median of 3500 ml, which correlates with the median blood loss accepted by world experience – 3500 ml. According to the American College, blood loss in the placenta accreta averages 3,000-5,000 ml, with an estimated total blood volume in the human body of 5,000 ml. Another significant factor related to the severity of operative complications was second-stage relaparotomy and hysterectomy, where operative

procedures were performed at a later stage of several hours after cesarean section due to acute hemorrhage due to attempts to preserve the uterus and despite the preliminary diagnosis of placenta accreta spectrum. It can be said that the hemorrhage in these cases is double, and, as is known, it is difficult to calculate the intermediate one, i.e. between the two surgeries.

### Perinatal outcome

The postoperative indicators, according to which the risk and quality of our medical activity were calculated, are presented in the table below (Table 4). It compares the group of normally positioned placentas (135 cases) with that of PAS-proven cases (54).

**Table 4.** Surgical outcome - resuscitation measures, blood loss and hospital stay

Exit	Pl normal, n135	%	Pl acc, n54	%	P
Resuscitation measures	5	3.70%	49	90.70%	0
Blood loss average	650		3420		0
Hospital stay	5.5		9.5		0.0002

The three indicators showed a strong statistical relationship when comparing the two main groups. According to the resuscitation measures carried out, the volume of hemo-plasma transfusions was required in 3% of the usual operative interventions in the control group of normally attached placentas, which proceeded without com-

plications. Respectively, significant resuscitation measures of different caliber and type in PAS were proven in 90.7% with established statistical significance.

The neonatal outcome was assessed by three indicators presented in Table 5.

**Table 5.** Neonatal outcome

Exit	Pl normal, n135	%	Pl acc, n54	%	P
Gestational age at birth	36.6		34.4		0.0199
Average newborn weight	2230		2040		0.1992
Apar score	9		7		0.0017

The mean weight of the newborns was 2230 g. per year in the group with normally placed placenta and 2040 g. per year in the PAS group, with no statistical significance. Apgar score showed a statistically significant difference ( $p < 0.001$ ) between the two groups. Apgar score of the newborn at the fifth minute was  $9 \pm 1$  SD in the placenta previa group and  $7 \pm 2$  SD in the PAS group, which correlates with the risk of prematurity and bleeding described in the literature in these patients.

The gold standard in the treatment of placenta accreta is cesarean hysterectomy. It was performed in 91% of all cases in our study, with 10% delayed interval hysterectomy. We had 56,9% placenta percreta, 34,5% placenta accreta and partial placenta accreta 8.6%.

### DISCUSSION

Our research was prospective and presented own factology and ultrasound finding. The rate of PAS showed a chronological increase from 0.05% for the period 2012 – 2018 to a sharp jump of 0.20 – 0.29% for the last four years (2019 – 2022). Our rate of placenta accreta correlated with the reported literature data of 0.5 - 3/1000. Our study proved that a preceding cesarean section is the primary risk factor for PAS. The progressive increase in the

rate of cesarean section leads to an increased frequency of both PAS and placenta previa.

According to WHO, the caesarean section has become an epidemic, exceeding more than 50% of middle-income countries, among which is Bulgaria, reaching 85% of countries like Brazil [7].

Advanced maternal age over 35 years is a risk factor, with the average age showing statistically high significance with  $p < 0.02$  significant values as a risk factor for placenta accreta. Multiparity is also an additional risk factor [8, 4].

A preceding CS is a major risk factor for the placenta accreta spectrum, and the combination with placenta previa increases the risk, as per literature data. In our study, we found a 64.8% calculated risk.

The largest multicenter studies have shown the rate of PAS in cases with previous cesarean section and placenta previa to be about 3%, 11%, 40%, 63% and 70% when there were 2 to 5 previous cesarean sections, respectively.

The percentage of PAS has increased over the years. In the USA, it was 1:2510 deliveries in the period 1970-1980, 1:533 by 2002 and in 2016 it has reached 1:272 [9, 10, 11, 12, 13, 14].

IVF is also an independent risk factor. Women subjected to ART usually have primary infertility and a low likelihood of preceding pregnancies, in this sense, the in vitro procedure itself is an independent risk factor, confirmed by our study with a significant difference between the low-risk and high-risk group [15, 16].

Myomectomy is reported as a risk factor for placenta accreta, especially in cases where the integrity of the uterine cavity has been affected, or the myoma was in the area of the anterior uterine wall and lower uterine segment. However, the rate is low and carries a low risk for placenta accreta, according to the summarized data of FIGO. According to our data, the increase of PAS in cases with myomectomy was not significant [1].

Our results showed a significant increase of PAS when there was an anteriorly located placenta or low attached placenta previa.

In our study, the progressive increase in the rate of cesarean section has led to an increased incidence of both PAS and Placenta praevia, starting with a rate of 47 – 48% SC in the first five years and reaching 52 – 53% in the last four years of the study. The rate of placenta previa started from 0.5% - 0.7% in the beginning and rose to 5,2% in recent years, correlating with the global trend. We have registered an increase in the incidence of PAS from approximately 0.5 per 1000 births to almost 3 per 1000 births. The results obtained correlate with the frequency of PAS reported in scientific studies [17].

Blood loss remains a variable quantity, persistently high over the years. It derives mainly from the severity of the placenta invasion and during relaparotomy. The mean and median correspond to global scores. The new surgical techniques are presented in the literature to minimize blood loss [18, 19]. The average blood loss was calculated to be 3400 ml, and the median blood loss was 3500 ml, corresponding to the results reported by other authors. Statistical significance has been shown by the results of blood loss during relaparotomy and second stage hysterectomy when comparing the group of placenta previa and placenta accreta.

The most significant indicators for the severity, therapeutic and operative risk of our work and the outcome for the patient throughout the entire treatment process were the volume of blood loss, the volume of resuscitation efforts and the duration of the hospital stay.

A good neonatal outcome was shown in terms of mean gestational age at birth and Apgar score. Our average gestational age for delivery was 34.4 g.w. and correlates with global recommendations - not to exceed 35-36 g.w., while in the group with normally positioned and attached placentas, the factors determining the mode and timing of delivery are of a different nature.

The type and rate of operative complications were comparable to other authors' results. They were more severe in more deeply invasive placenta with statistically significant higher mean and median blood loss. Organ

damage and relaparotomy were mainly observed in the more severe degree of invasion of the placenta, especially in the first 4-5 years of observation. The accumulation of operative experience and organization has reduced all type of complications. The incidence of placenta percreta was higher than placenta accreta.

Given the above-presented trend for a sharp increase in the frequency of the studied nosological unit and considering the accumulated experience and capabilities for orientation and reaction in such situations, including emergencies, the results regarding the minimization of organ lesions have improved for the period 2019 – 2022. The pre-prepared team of specialists also contributed to the results. In a cohort study, Morlando and Collins, 2020, reported the frequency of placenta accreta haemorrhage to be around 40-50%, maternal mortality to be 7%, median blood loss to be 3500 ml, urinary tract lesions 29%, of which 76% were lesions of the urinary bladder, 17% ureteral lesions, 5% genito-urinary fistulas. A second stage hysterectomy usually occurs between 3-12 weeks after a cesarean hysterectomy [12]. Our organ complications, both in percentage and by type, correspond to global experience. Urgency and uterine rupture, as a surprising element, cannot be predicted and controlled. Perioperative hemorrhage didn't show significant differences over the years in quantity – from 1500 ml to 6000 ml. In cases of postoperative hemorrhage and second-stage hysterectomy, it is categorically larger, almost double.

The gold standard in treatment is hysterectomy, with pathohistological evidence in diagnosis. There are difficulties in the pathohistological diagnosis with retained placenta peripartum hemorrhage and second-stage hysterectomy – the organ provided for diagnosis has structural tissue changes. Definitive diagnosis is the intraoperative finding before the uterotomy. All cases have a clinical and histological conformation.

On the basis of all normal and abnormal placental findings and the fact that the placenta is the most vascular organ in the human body, its formation and attachment to the uterine wall are complex, demonstrably self-regulating processes of decidua. This pathological condition of the placenta is unique in its nature, and throughout the living world, it occurs only in humans. Dannheim K et al. reported a difficulty in the pathohistological diagnosis of placenta accreta in a case of surgical emergency haemorrhage, where the pathohistological diagnosis was modified and difficult due to tissue, infiltrative and inflammatory changes due to prolonged haemorrhage [20].

## CONCLUSIONS

This is a prospective follow-up, which avoids the scientific limitations of retrospective studies –clinical and histopathological evidence. The gold standard for diagnosing PAS is ultrasound; the histological specimen after hysterectomy makes the final diagnosis.

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