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ORIGINAL PAPER / OBSTETRICS

The nightmare of obstetricians — the placenta accreta spectrum in primiparous pregnant women

[Placenta accreta spectrum in primiparous pregnant women]

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ABSTRACT

Objectives: The incidence of PAS is increasing day by day as a life-threatening condition. The purpose of the present study was to determine the factors affecting PAS formation in primiparous pregnant women and to define possible risk factors for the mother and the baby.

Material and methods: Bursa Yüksek İhtisas Training and Research Hospital, department of obstetrics and gynecology, Bursa, Turkey, between June 2016 and December 2020. A total of 58,895 patients were included in the study. After the exclusion criteria, the study was continued with 27 primiparous PAS and 54 non-primiparous PAS patients. The primary purpose is to evaluate PAS risk factors. The secondary aim is to examine maternal and neonatal characteristics.

Result: When the parameters that are significant in terms of PAS risk factors were analyzed by Logistic Regression Analysis, it was found that the increase in age also increased the development of PAS 1.552 times (95% CI: 1.236–1.948) and a history of abortion was 7.928. times (95% CI: 1.408–44.654) and 11,007 times (95% CI: 2.059–58.832) with history of myomectomy; postoperative HB values ($p < 0.001$), an estimated amount of bleeding ($p <$

0.001), need for transfusion ($p = 0.002$), and use of drains (< 0.001) were statistically significant different between two groups. When the neonatal results between patients with and without PAS were examined, birth weight ($p < 0.001$) and gestational week (< 0.001) were statistically significant.
Conclusions: PAS does not occur only in multiparous patients who have a history of previous cesarean section. It may also occur in primiparous patients and is a life-threatening condition.
Key words: spectrum of placenta accreta; high risk pregnancy; primiparous pregnancy

INTRODUCTION

Placenta accreta spectrum (PAS) is defined as the abnormal invasion of the placental tissues into the myometrium [1–3]. The diagnosis of PAS is suspected with ultrasonography and confirmed with pathological diagnosis after surgery [4]. PAS is a maternal life-threatening condition that associated with maternal mortality and morbidity [1–3]. Severe postpartum hemorrhage, need for blood transfusion, Disseminated Intravascular Coagulation (DIC), organ injury, ileus, infection, thromboembolic complications, need for intensive care, renal failure, and increased mortality and morbidity detected in cases with PAS are higher than uncomplicated pregnancies [5–7].

It is stated in the literature that the most important factor for the development of PAS is history of cesarean section before [8, 9]. The incidence of PAS is known to be 2–4.84 per 1000 birth and increasing with cesarean delivery rates throughout the globe [10, 11]. However, when the literature data were reviewed, it was seen that 38% of the patients with PAS were primiparous women [12, 13]. The purpose of the present study was to determine the factors affecting PAS formation in primiparous pregnant women and to define possible risk factors for the mother and the baby.

MATERIAL AND METHODS

The place where the study was conducted

The third-largest education and research hospital in the South Marmara region, where approximately 13.000 births are performed on an annual scale.

Case group

A total of 27 primiparous pregnant women who were diagnosed with PAS between June 2016 and December 2020.

Control group

A total of 54 women (1 case vs 2 controls) who were selected randomLy from among the primiparous women who delivered throughthe elective cesarean section between the same years constituted the Control Group.

Study population

The study was initiated with 58,895 patients. Multiparous patients were excluded from the study. A total of 13.105 of 21.782 primiparous women delivered through cesarean section. Among these, patients with twin pregnancies were excluded from the study. A total of 29 of these patients were diagnosed with PAS Ultrasonographically in the antenatal period. When the postoperative pathology results were evaluated, 27 patients had the diagnosis of PAS. The pathology result of all of these patients was *placenta acreata*, which is the sub-parameter of PAS. The Control Group patients were selected randomLy as 1 case vs 2 controls among the pregnant women who were scheduled to have an elective primiparous cesarean section on the day of surgery of the patients who were diagnosed with PAS. In each of the PAS cases in the study, the placenta completely covers the cervical os. However, the placement of the placenta is anterior or posterior. Similarly, those with anterior or posterior placental location in the non-PAS group were included in the study by random selection. Non-Pass cases where the placenta was fundal located were not included.

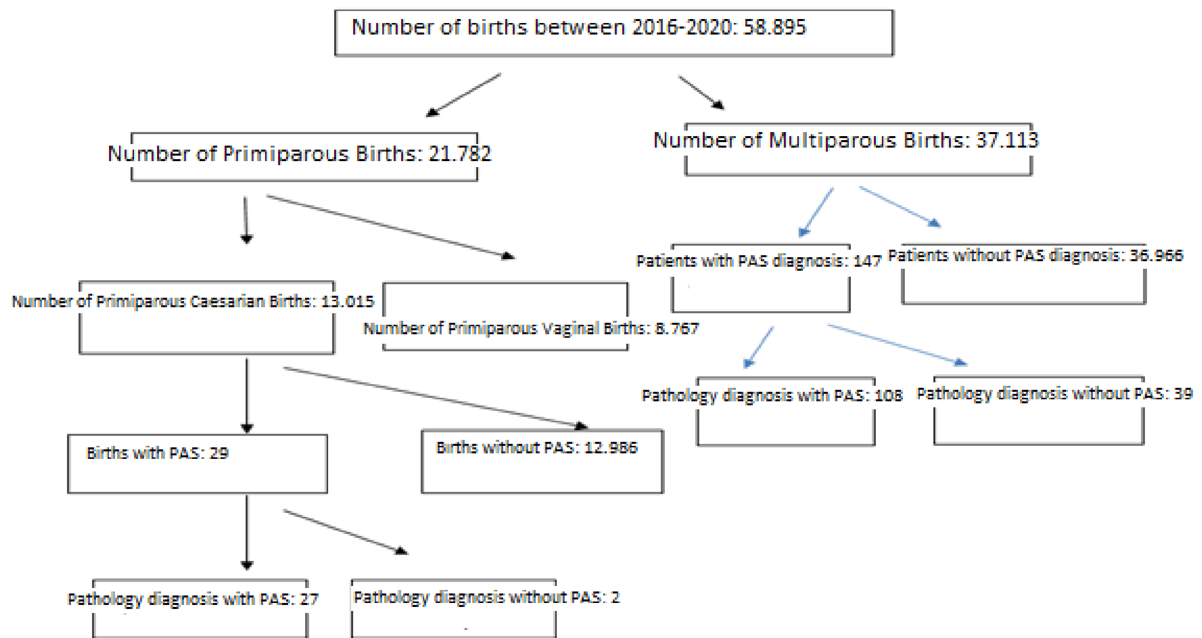

Figure 1. The patients who were includedin the study

Variables: The parameters that were examined in the study are given in the Table 1 of variables and their definitions

Table 1. Variables and their definitions [4]

Variables	**Definition**
PAS diagnosis	The diagnosis was made by experienced obstetricians and gynecologists based on transvaginal and transabdominal ultrasonography findings. Also, the diagnosis was made sure with the pathology materialsthat were taken during the surgery. Diagnostic criteria of PAS in ultrasonography were; decreased hypoechogenicity in the retroplacental area, irregular vascular areas in the placenta, increased vascularity in the myometrium layer between the uterus and bladder [4]
Risk factors for PAS	

	Age [years] (mean)
	BMI [kg/m^2] (mean)
	Curettagehistory (Yes/No)
	Myomectomyhistory (Yes/No)
	Assisted Reproductive Technique (Yes/No)
Intraoperativeandpostoperativecharacteristics	
	Hb: Hemoglobin (preoperative (one day before the operation)and postoperative 6th-hour HB values were recorded)
	Operation type: **Local Resection:** Elective cesarean section was planned for patients with PAS between 34 and 37 weeks according to the degree of invasion. The abdominal cavity was entered with the midline incision. After the peritoneal cavity was entered, exploration was performed to determine the placental invasion margins. The baby was removed from fundal incision, the umbilical cord was tied, and the placenta was left in place. The fundal incision was sutured. After that we ligated internal iliac artery and utero-ovarian ligaman with 1–0 vicryl suture for reducing bloood flow to uterus. we disect the bladder from uterus with advanced bipolar energy source. We excised the placental invasion area with 1 cm invasion free safe margin. After that placenta removed from uterus. Resection was performed with scissors and cautery, and bleeding areas were controlled. One

	single layer of continuous suture was used to close the transverse incision in the anterior uterine wall. We insertid bakri postpartum balloon and insuflated with 250 mL saline. We removed balloon after 24 hours of procedure. **Cesarean section:** Primiparous pregnant women who did not have PAS but were planned for elective cesarean section were included in the present study. The cavity was entered with the Pfannenstiel incision. After the peritoneal cavity was entered, exploration was performed to determine the invasion margins. After the disection of bladder, lower uterine segment was incised with a transverse incision, the baby was removed, the umbilical cord was tied, and the placenta was removed. The incision was sutured. One single layer of continuous suture was used to close the uterine incision. We insertid bakri postpartum balloon and insuflated with 250 mL saline. We removed balloon after 24 hours of procedure. **For all patients:** After the fetus and placenta were removed, 20 IU intravenous oxytocin infusion was administered, and 15 IU intravenous oxytocin infusion was continued in the first 24 hours. All

	patients were administered prophylactic 2-gram intravenous Cefazolin half an hour preoperatively. These patients were mobilized at the 6th hour and thromboprophylaxis was administered to the patients.
	The estimated amount of bleeding: It is defined as the bleeding from the beginning of the skin incision to the end of the labor. The amount of bleeding was calculated by taking the sum of the amount of blood that was absorbed by the gauze and the blood in the aspirator chamber.
	Need for transfusion: The obstetrician and anesthesiologist made the decision in this respect. The factors that affected blood transfusion were; preoperative anemia, amount of bleeding during surgery, and hemogram values during surgery.
	Duration of Hospitalization: Given as day(s)
	Wound siteinfection:Yes/No
Neonatal Characteristics	
	Gestational week:Week
	Birth weight: Grams
	APGAR1-5:1 and 5th-minute APGAR Score
	NICU need: Yes/ No

PAS — placenta accreta spectrum; BMI — body mass index; NICU — Neonatal Intensive Care Unit

Purpose of the study

As the primary outcome: The purpose was to evaluate PAS risk factors.

As a secondary outcome:The purpose was to evaluate the estimated amount of bleeding, need for transfusion, length of hospital stay, organ injury, and wound site infection as neonatal outcomes.

Statistical analysis

The SPSS 21.0 was used for all statistical analyses (Statistical Package for the Social Sciences, Chicago, IL). A p-value of ≤ 0.05 was considered statistically significant. The Shapiro-Wilk test was used to evaluate whether or not the mean values fit the normal distribution. The ***t***-test was used for the mean values with normal distribution and the Mann-Whitney U test for those who did not. The Chi-Square test was used for pairwise comparisons. The BackwardLogistic Regression test was usedfor the parameters that were significant among the risk factors.

RESULTS

The study was conducted by examining the data of 58.895 patients between June 2016 and December 2020 in the 3rd Stage Training and Research Hospital, where approximately 13.000 deliveries are recordedon an annual scale. After the exclusion criteria were applied, the study was continued with 27 PAS and 54 Non-PAS primiparous women. PAS rate was 0.2% and the incidence of primiparous PAS was 0.5% in the Study Group.

When PAS risk factors were examined, none of the patients became pregnant with the use of any assisted reproductive technique. None of them had a history of ectopic pregnancy or molar pregnancy. It was the first birth for all patients. Although no statistically significant differenceswere detected between the Body Mass Indicesof both groups (p = 0.740), statistically significant differenceswere found in terms of the history of previous abortion (p < 0.001), myomectomy history (< 0.001), and the mean age of the mothers (< 0.001) (Tab. 2).

Table 2. The distribution of the variables according to case-control groups

Variables		Control (n = 54)	Case (n = 27)	P
		Number (%)	Number (%)	
Curettage history	2 +	10 (18.5)	17 (63.0)	< 0,001*
	1	44 (81,5)	10 (37.0)	
Myomectomy	No	47 (87.0)	10 (37.0)	< 0,001*
	Yes	7 (13.0)	17 (63.0)	
BMI	Mean ± (SD)	25.62 ± 2.79	25.85 ± 3.32	0.740**
Age	Mean ± (SD)	22.85 ± 3.92	30.52 ± 4.57	< 0.001***

*Chi-Square Test, **t-test, ***Mann-Whitney U test; BMI — body mass index; SD — standard deviation

When the parameters that were significant regarding the PAS risk factors were analyzed with the logistic regression analysis, the increase in age increased PAS development 1.552-fold (95% CI: 1.236–1.948), a history of curettage 7.928-fold (95% CI: 1.408–44.654), and history of myomectomy 11.007-fold (95% CI: 2.059–58.832) (Tab. 3).

Table 3. Placenta accreta spectrum risk factors logistic regression analyses results

Independent variables	**Odds ratio**	**95% CI (Min–Max value)**
Age	1.552	1.236–1.948
Curettage	7.928	1.408–44.654
Myomectomy	11.007	2.059–58.832

CI — confidence interval

All patients with PAS underwent local resection and Cesarean Section was performed for all cases without PAS.

Although no statistically significant differences were detected between preoperative HB values ($p = 0.104$), wound infection development ($p = 0.895$), and hospitalization durations ($p = 0.463$) between the patients with and without PAS, statistically significant differences were found in the postoperative HB values ($p < 0.001$), estimated bleeding amount ($p < 0.001$), the need for transfusion ($p = 0.002$), and the use of drains (< 0.001). Also, bladder or bowel damage wasnot detected in any patient (Tab. 4).

Table 4. Evaluation of the preoperative and postoperative characteristics of the patients

Variables		Control (n = 54)	Case (n = 27)	P
		Number (%)	Number (%)	
Preoperative HB	Mean ± SD	11.2985 ± 1.019	10.829 ± 1.083	0.104**
Postop HB	Mean ± SD	11.2204 ± 0.820	9.451 ± 1.403	< 0.001**
Estimated Bleeding	Mean ± SD	302.037 ± 191.512	523.333 ± 279.642	< 0.001**
Hospitalization	Mean ± SD	3.259 ± 0.442	3.777 ± 2.189	0.463**
Tx necessary	Yes	1 (1.9)	7 (25.9)	0.002*
	No	53 (98.1)	20 (74.1)	

Drain	Yes	5 (9.3)	24 (88.9)	< 0.001*
	No	49 (90.7)	3 (11.1)	
Type surgery	Cs	54 (100.0)	17(63.0)	< 0.001*
	Local resection	0 (0.0)	10 (37.0)	
Surgery side infection	Yes	6 (11.1)	2 (7.4)	0.895*
	No	48 (88.9)	25 (92.6)	

*Chi-Square Test; **Mann-Whitney U; SD — standard deviation; HB — Hemoglobin; Tx — transfusion; Cs — cesarean section

When the neonatal outcomes of the patients with and without PAS were examined,although 1st-minute APGAR score (p = 0.532), 5th-minute APGAR score (p = 0.70) values , and NICU need (p = 0.204) were statistically insignificant, birth weight (p < 0.001) and gestational week (< 0.001) were found to be statistically significant (Tab. 5).

Table 5. Neonatal results

Variables		Control (n = 54) Number (%):	Case (n = 27) Number (%):	P
NICU	No	53 (98.1)	24 (88.9)	*0.204
	Yes	1 (1.9)	3 (11.1)	
Birth weight	Mean ± SD	3261.06 ± 432.96	2707.96 ± 510.38	** < 0.001
Gestational week	Mean ± SD	38.70 ± 1.34	35.60 ± 2.14	*** < 0.001
APGAR1	Mean ± SD	8.96 ± 0.19	8.59 ± 1.29	***0.532
APGAR5	Mean ± SD	9.96 ± 0.19	9.78 ± 0.64	***0.070

* Chi-Square Test; **t-test, ***Mann-Whitney U; NICU — Neonatal Intensive Care Unit; SD — standard deviation

DISCUSSION

Consistent with the literature data, the PAS rate was found to be 0.2% in the Study Group, and the incidence of primiparous PAS was 00.5%. When the literature data were reviewed, it was found that the worldwide PAS rate was reported to be 0.01–4.84%, the primiparous PAS rate was approximately 1 in 3 of all PAS cases, and in another study, this rate was reported as 2.4 per 1000 among all pregnancies [10–14]. When the previous publications on the subject were examined and in our study, although it is reported that the history of previous cesarean section is the most important factor in the development of PAS, it is seen that it can also occur in women who have not given birth before [13].

A total of 810 women die every day in the world because of complications related to childbirth [15]. PAS is among the most important causes of maternal mortality and morbidity in primiparous patients and should be examined in detail. However, when the literature data were reviewed, it is not specified in which primiparous pregnant women the clinician should be especially alert. When the results of the present study are examined, the history of myomectomy, previous abortion, and increased maternal age were found to be risk factors. In the meta-analysis that was conducted by Iacovelli et al. [16], although increasing maternal age and myomectomy history were found to be effective in terms of PAS development in line with the current study, uterine curettage history was found to be insignificant in terms of PAS development. However, we think that this was because both multiparous and primiparous women were examined in the meta-analysis, but only the data of primiparous women were examined in the current study [16]. However, in studies that included fewer cases, it was reported that a history of curettage is a risk factor for the development of PAS as it caused endometrial damage. However, when the data of these studies were reviewed, it was found that they included both multiparous and primiparous patients [13, 17–20]. Increasing maternal age was identified as an independent risk factor in a previoıus study that was conducted to determine the incidence of PAS in primiparous women [14]. Also, in a study that examined the 7-year PAS data in a tertiary health institution, although multiparous patients were included, increasing maternal age was found to be an independent risk factor in the development of PAS, which is in line with the results of the present study [21].

Baldwin et al. [14] reported that previous gynecological surgery increased the risk in women diagnosed with primiparous PAS. However, in their study, unlike the present study, gynecological operations were not examined separately, but regardless of the type, it was examined whether there were gynecological operations in the anamnesis. For this reason, a separate risk assessment was not performed for each gynecological operation [14].

In the study conducted by Khander et al. which included 46 PAS cases, the history of cesarean section and myomectomy were compared and it was found that myomectomy was more effective in PAS formation than previous cesarean section [22]. However, the patients who were included in this study were multiparous. In the present study, it was found that previous myomectomy increased PAS formation 11.007-fold.

When the literature data were examined, although few studies report the incidence of primiparous PAS and examine some risk factors, there are not enough data on maternal and neonatal outcomes [14].

In the present study, statistically significant differences were detected in terms of the estimated amount of bleeding, postoperative HB values, need for transfusion, and drain, which is in line with the literature data. The reason for this is serious maternal bleeding during the separation of the placenta in cases complicated with PAS. Although multiparous PAS cases were evaluated in previous studies, it was reported that bleeding during the operation is more common in cases complicated by PAS [5–7].

When the pregnancy results of primiparous PAS cases were examined in the literature, it was found that only the gestational weeks were lower at birth, which is consistent with the results of the present study [14]. The cause of this is that PAS cases undergo cesarean section at the 34–37th gestational weeks [23]. For this reason, the newborn birth weights are statistically less and the gestational weeks at birth are lower.

Limitations

The limitation of the study is that none of the patients who were included in it became pregnant through assisted reproduction method. In addition, PAS cases included in the study do not have long-term results.

Strengths of the study

The strengths of the study are that it was conducted in the largest hospital in the South Marmara region and that all the patients who were included in the study had antenatal follow-up and were elective cases. Also, although there are few studies in the literature investigating the risk factors for PAS in primiparous women, to the best of our knowledge, the present study is the first to evaluate maternal and neonatal outcomes in these women simultaneously.

CONCLUSIONS

PAS is also present in primiparous pregnant women at a considerable rate, and it must be known which patients should be examined in more detail especially in terms of PAS because it is a life-threatening condition in women.

Ethical approval

The approval for the study was obtained from the local ethics committee of a tertiary education and research hospital with the ethics committee number 2011-KAEK-25 2019/08-06. Also, the study was conducted in line with the Declaration of Helsinki principles.

Conflict of interest

There is no conflict of interest betwee

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