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Evaluation of fetomaternal outcomes and serum analytes in placenta previa and associated placenta accreta spectrum

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ABSTRACT

Aims: Evaluation of fetomaternal outcomes and serum analytes values in patients with placenta previa and associated placenta accreta spectrum (PAS).

Methods: The study comprised 160 patients, of whom 74 (46.3%) had placenta previa, 28 (17.5%) had PAS, and 58 (36.3%) were pregnant women in a healthy condition. The diagnosis was suspected by ultrasound examination and confirmed by the intraoperative findings and the pathology report. Demographic and obstetric characteristics data of the pregnant women, maternal and fetal outcomes, screening tests for the first and second trimester results of serum analysis were obtained retrospectively from the hospital records. The significance threshold was set at $p<0.05$ using the IBM SPSS.25 software.

Results: The mean age was significantly higher in the previa and PAS groups. The groups differed significantly in terms of the history of prior cesarean deliveries and gestational age at delivery. The PAS group had the lowest APGAR score and the lowest newborn weight (p<.001). Compared to the PAS group, the previa group's pregnancy associated plasma protein-A (PAPP-A) Mom value was considerably greater (p=.008). The alpha-fetoprotein (AFP) Mom value was significantly higher in the group of healthy pregnant women than in the group of previa (p=.015). Compared to the previa (p=.008) and PAS (p=.024) groups, the healthy pregnant group's Unconjugated Estriol-3 (UE3) Mom value was much higher.

Conclusion: Although the obstetric, fetal and maternal outcomes in our study were consistent with the literature, the serum analysis results were not.

Keywords: Placenta previa, PAS, PAPP-A, AFP, UE3

INTRODUCTION

Placenta previa refers to complete closure of the cervical os by the placenta.[1,3] The prevalence rate is 5.2/1000.[4] A number of adverse effects for both the mother and the fetus are linked to abnormal placental invasion, such as thrombophlebitis, septicemia, intrauterine growth restriction (intrauterine growth restriction), premature labor, prenatal and postnatal hemorrhage and malpresentation.[1,5] The placenta accreta spectrum (PAS) is used to describe abnormal invasion of the placenta. PAS includes placenta accreta (invasion to myometrium <50%), placenta increate (invasion to myometrium >50%), and placenta percreta (invasion to myometrium, uterine serosa, and neighboring organs).[6] PAS is defined in many guidelines in the literature.[7,9] The main risk factors associated with PAS include previous uterine surgery, curettage, placenta previa, advanced maternal age, multiple births and manual removal of the placenta.[10]

In patients with a history of prior cesarean deliveries, placenta previa is the most significant risk factor for PAS. Patients with placenta previa who have had one cesarean surgery have a 3% chance of developing PAS; however, the risk rises as more cesarean sections are performed.[11] The reported risk of PAS in patients with a history of a single cesarean section without placenta previa was 0.03%.[12] Jauniaux et al.[12] reported that the prevalence rate of PAS was 0.01%–1%. In addition to the demographic and obstetric risk factors, serum analyzes in the

first and second trimester of these patients can now provide information about abnormalities of placental invasion.[13,14]

This study aimed to evaluate serum analytes and fetomaternal outcomes in patients with placenta previa and associated PAS in our hospital.

METHODS

This study was carried on the Perinatology Clinic of Etlik Zübeyde Hanım Women's Health Care Training and Research Hospital between September 2019 and September 2022 by retrospective review of patient records. Approval was obtained from Etlik Zübeyde Hanım Women's Health Care Training and Research Hospital Non-interventional Clinical Researches Ethics Committee for the study (Date: 09.10.2024, Decision No: 2024/09). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. A total of 160 patients, including 74 (46.3%) with placenta previa, 28 (17.5%) with PAS, and 58 (36.3%) healthy pregnant women were included in the study. Upon suspected ultrasonographic signs indicative of the diagnosis, intraoperative results and pathology reports were used for the purposes of confirmation. Demographics (age and body-mass index (BMI)) and obstetric characteristics (gravida, parity, and previous history of cesarean section), maternal and fetal outcomes (hysterectomy, conservative methods, including Bacri balloon introduced after cesarean section, compression sutures, and uterine artery ligation) were used. Neonatal intensive care unit (NICU) and fetal outcomes of pregnant women included in the study were retrieved retrospectively from hospital records (**Table 1**). The diagnosis of PAS was based on the clinical staging system of intraoperative International Federation of Gynecology and Obstetrics (FIGO) and pathologic diagnosis.[7]

The serum analytes of the groups in the first and second trimester screening test are listed in **Table 2**. The values are given as multiples of the median (Mom) and comparison between groups.

Table 2. Comparison of first and second trimester biochemical markers between groups

	Previa (n=74, 46.3%)	PAS (n=28, 17.5%)	Healthy (n=58, 36.3%)	p value
PAPP-A Mom	.98 (.64-1.25)	.58 (.43-.85)	.92 (.57-1.13)	.010*
AFP Mom	.91 (.61-1.24)	1.10 (.57-2.27)	1.13 (.91-1.46)	.016*
FBhcg Mom	.91 (.67-1.51)	1.12 (.68-1.98)	.82 (.59-1.19)	.099
Bhcg Mom	.80 (.51-1.08)	.91 (.68-1.91)	.98 (.65-1.40)	.046*
UE3 Mom	.74 (.43-.99)	.69 (.52-.90)	.88 (.71-1.09)	.003*

Continuous variables median as shown IQR. Abbreviations: PAS: Placenta accreta spectrum, PAPP-A: Pregnancy-associated plasma protein A, AFP: Alfa-fetoprotein, FBhcg: Free beta human chorionic gonadotropin, Bhcg: Beta human chorionic gonadotropin, UE3: Unconjugated estriol-3

Statistical Analysis

Descriptive statistics for continuous variables are reported as median and interquartile range (IQR), whilst categorical variables are represented as frequency (n) and percentage (%). The Kolmogorov–Smirnov test was employed to evaluate the normality of data distribution. The Kruskal–Wallis test was employed to compare continuous variables across groups. Dunn's post-hoc test was utilized for pairwise comparisons when substantial differences were identified. The Chi-square test was employed to investigate the relationships between category variables. All statistical analyses were conducted using IBM SPSS Statistics version 25, with a p-value of <0.05 being statistically significant.

Table 1. Comparison of feto-maternal characteristics between groups

	Placenta previa (n=74, 46.3%)	PAS (n=28, 17.5%)	Healthy (n=58, 36.3%)	p value
Age (years)	32.00 (28.00-37.00)	33.00 (31.25-36.50)	29.00 (24.75-33.00)	.002*
Parity	1.00 (.00-2.00)	2.00 (1.00-3.00)	1.00 (.75-2.00)	.006*
Gravida	3.00 (1.00-4.00)	4.00 (2.25-5.00)	3.00 (2.00-3.00)	.011*
GW at delivery	35.00 (32.00-36.00)	34.00 (31.50-36.00)	38.00 (37.00-39.00)	<.001*
Previous C/S number	.00 (.00-.00)	2.00 (1.00-2.00)	.00 (.00-1.00)	<.001*
BMI (kg/m^{2})	27.00 (25.00-30.00)	28.00 (25.00-30.00)	28.00 (25.00-30.00)	.608
Placental localization				
Anterior	30 (40.5)	16 (57.1)	32 (55.2)	.154
Posterior	44 (59.5)	12 (42.9)	26 (44.8)	
Maternal outcome				<.001*
Histerectomy	0 (0.0)	11 (39.3)	1 (1.7)	
C/S	56 (75.7)	2 (7.1)	52 (89.7)	
Conservative method	18 (24.3)	15 (53.6)	5 (8.6)	
Transfusion				
Yes	22 (29.7)	21 (75.0)	3 (5.2)	<.001*
None	52 (70.3)	7 (25.0)	55 (94.8)	
Fetal outcome				
NICU	28 (37.8)	13 (46.4)	10 (17.2)	.008*
Apgar 5. Dk	9.00 (7.00-9.00)	8.00 (7.00-9.00)	9.00 (9.00-10.00)	<.001*
Newborn weight	2452.50 (1972.50-2816.25)	2322.50 (1920.00-2773.75)	3030.00 (2888.75-3355.00)	<.001*

Continuous variables median (IQR); categorical variables are given as n (%). Abbreviations: PAS: Placenta accreta spectrum, BMI: Body-mass index, GW: Gestational week, C/S: Caesarean section, NICU: Neonatal intensive care unit

RESULTS

Among the 160 pregnant women participating in the study, 74 (46.3%) were diagnosed with placenta previa, 28 (17.5%) with placental accreta spectrum (PAS), and 58 (36.3%) were categorized as the healthy group. Notable disparities were seen across the groups regarding age, parity, and gravida (p=.002, .006, .011, respectively; Kruskal–Wallis test). The Dunn post-hoc test indicated that the mean age of the control group was considerably lower than that of both the previa (p=.025) and PAS groups (p=.004). The parity and gravida values were markedly reduced in the previa group in comparison to the PAS group (p=.004 and p=.008, respectively, **Table 1**).

Anotable disparity existed between groups regarding gestational age (p<.001); the Dunn test indicated that the control group exhibited a significantly greater gestational age than both the previa and PAS groups (p<.001 for each comparison). The quantity of prior cesarean sections varied significantly (p<.001); the PAS group exhibited a markedly greater number of cesarean sections in comparison to both the previa and control groups (p<.001 for each comparison).

The healthy group exhibited a significantly greater birth weight than the previa and PAS groups (p<.001 for both comparisons; Dunn test). The 5-minute Apgar score was considerably elevated in the control group relative to the previa (p<.001) and PAS (p=.002) groups.

Substantial disparities were observed in maternal outcomes (p<.001). The cesarean section rate was minimal in the PAS group (7.1%), much lower than in the previa (75.7%) and control (89.7%) groups. Hysterectomy occurred most frequently in the PAS group (39.3%), although this finding was not statistically significant. Conservative procedures were utilized more often in the PAS group (53.6%) than in the previa (24.3%) and control groups (8.6%), although the difference lacked statistical significance.

The necessity for transfusion exhibited considerable variation among groups (p<.001). The transfusion rate in the control group (5.2%) was statistically significantly lower compared to the previa (29.7%) and PAS (75.0%) groups. The rate of neonatal admissions to the intensive care unit (ICU) was greater in the PAS group (46.4%) than in the control group (17.2%), with this difference being statistically significant (p=.008, **Table 1**).

Serum tests revealed significant variations in PAPP-A MoM values between groups (p=.010); Dunn's test indicated that the previa group exhibited considerably greater values than the PAS group (p=.008, **Table 2**).

AFP MoMreadings exhibited notable variations (p=.016); the control group demonstrated significantly elevated values compared to the previa group (p=.015). BhCG MoM values exhibited borderline significance between groups (p=.046); however, the Dunn test could not identify any significant differences in pairwise comparisons. UE3 MoMlevels exhibited significant differences (p=.003); the Dunn test revealed that the control group had markedly higher values than both the previa (p=.008) and PAS (p=.024) groups (**Table 2**).

DISCUSSION

This study compared risk factors associated with placenta previa, PAS and maternal-fetal outcomes. A number of risk factors for placenta previa were suggested by previous studies, including advanced maternal age (>35 years), multipartite, previous history of uterine surgery, history of placenta previa, assisted reproductive technology, and dilatation curettage.[14,17] In this study, the mean age was relevantly higher in the previa and PAS groups. With increasing age, damage to the vascular endothelia can occur, leading to insufficient development of the decidua and implantation of the placenta, which in turn leads to the development of PAS.[18] The number of previous cesarean section was higher in the PAS group. Previous studies have suggested that the main risk factors for PAS are placenta previa previous uterine surgery.[19] Cesarean section scars, curettage or previous uterine surgery damage the endometrial tissue and trophoblasts can grow abnormally in these areas.[20] Patients included in the previa and PAS groups delivered earlier than healthy pregnant women. Relevant guidelines currently recommend delivery between 36 0/7 and 37 0/7 weeks of gestation in cases of placenta previa.[21] The gestational age at delivery was earlier than the recommended gestational age due to emergency hemorrhagic presentation in certain patients included in the study. The recommended gestational age for planned cesarean section or hysterectomy in stable PAS cases was week 34 0/7-35 0/7; where an earlier gestational week may be recommended in cases such as persistent bleeding, premature rupture of membranes, and preeclampsia.[22] The PAS cases in this study were scheduled to deliver at the recommended week upon completion of antenatal steroid doses. Compared to the group of healthy pregnant women, the previa group had greater rates of hysterectomy and transfusion. The high rate of hysterectomies and blood transfusions in PAS cases was also shown in the study by Ogawa et al.[23] This suggests that the gynecologist may be less hesitant to perform a hysterectomy in cases of advanced age, multiparity and a history of cesarean sections. There was no significant difference between the anteriorly and posteriorly placenta. In the study by Fındık et al.,[24] hysterectomies and blood transfusions were observed more frequently in cases with an anterior placenta. In our study, there was no significant difference between anteriorly and posteriorly placenta. None of the patients with PAS were admitted to the adult intensive care unit. This may be attributed to planned delivery and the preparation of blood in advance. Newborn weight was lower in the previa and PAS groups because of the earlier delivery week. The results found in the comparison of serum analyzes did not correspond to the literature. Many studies in the literature have shown that the PAPP-A value in the first trimester and the screening test of serum analytes performed in the second trimester can predict abnormalities of the placenta.[25,26] Maternal serum analytes in first and second trimester screening tests can provide insights into various fetal or maternal disorders during other trimesters of pregnancy. Unexplained AFP values exceeding 2.5 Mom in the second trimester indicate conditions such as intrauterine death, intrauterine growth restriction, spontaneous abortion, oligohydramnios, gestational hypertension, and placental abruption; elevated human chorionic gonadotropin (HCG) levels (>2.0 Mom) may result in adverse pregnancy outcomes, including gestational hypertension and preterm birth.[28,29] Low UE3 levels have

been correlated with worse pregnancy outcomes.[28,29] Awareness of these concerns, including placental anomalies, is crucial to ensure that the clinical management and delivery of these pregnancies are managed by skilled teams in tertiary hospitals, therefore reducing maternal and fetal morbidity and mortality. Our study showed that the PAPP-A value was higher in the previa group. AFP and HCG levels measured in the second trimester were not elevated in the previa and placental invasion abnormalities groups.

Limitations

This study is limited by its nature as a single-center retrospective analysis. This situation restricts the establishment of a causal relationship. The other reason was the limited number of patients and the unavailability of serum analyses for certain individuals.

CONCLUSION

Early detecting of placenta previa instances facilitates the anticipation of potential hemorrhaging and the execution of requisite interventions; it guarantees that cases are referred to hospitals with the appropriate equipment.

ETHICAL DECLARATIONS

Ethics Committee Approval

Approval was obtained from Etlik Zübeyde Hanım Women's Health Care Training and Research Hospital Non-interventional Clinical Researches Ethics Committee for the study (Date: 09.10.2024, Decision No: 2024/09).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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