PERINATAL JOURNAL

Original Article

Perinatal Journal 2022;30(1):51–56
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The relationship between first trimester screening test and abruptio placentae

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Abstract

Objective: We compared the first-trimester screening test results and perinatal results of pregnant women to determine the diagnosis of abruptio placentae, one of the essential causes of maternal and fetal mortality and morbidity.

Methods: Between 2019 and 2021, 20 pregnant women diagnosed with abruptio placentae in our hospital and 30 pregnant women who did not develop clinical abruptio placentae during their pregnancy in the same period were included in our study. The relationship between the first-trimester screening test results and the perinatal outcomes of the patients was investigated.

Results: No significant differences were found in maternal age, gravida and parity. Significant difference was found in gestational age at birth, being 33±5.1 weeks in the study group and 38.6±1.48 weeks in the control group. No statistical differences were found at PAPP-A or at β-hCG between the groups (p=0.219 and p=0.898, respectively). Nevertheless, a trend of a lower PAPP-A at the study group was noticed (1.03±0.54 MoM vs. 1.28±0.66 MoM). Significant differences were found at fetal birth weight, 1-minute Apgar score and 5-minute Apgar score. When looking at risk factors, no differences between the groups were found at smoking, multiple pregnancy, myoma uteri or diabetes, but preeclampsia and threatened preterm labor were more common at the study group.

Conclusion: When we compared the first-trimester serum biomarkers to predict abruptio placentae, we could not find any significant difference between the two groups. To reach a definite conclusion on this issue, more studies with increasing the number of patients are needed.

Keywords: Abruptio placentae, pregnancy-associated plasma protein A, pregnancy outcome.

Introduction

Abruptio placentae can be explained as the complete or partial separation of the placenta from the place where it was implanted in the uterus before delivery due to bleeding into the decidua basalis. This is one of the most serious causes of third trimester bleeding and it is associated with high mortality and morbidity. It occurs in approximately 0.5–2% of all pregnancies.[1] Its etiology is unknown, but many predisposing risk factors have been described. History of previous abruption of placenta, maternal hypertensive diseases (preeclampsia-chronic hypertension), multiple pregnancies, premature rupture of membranes, chorioamnionitis, trauma, smoking and cocaine use, and maternal age can be listed as risk factors.[1–3]

The usual clinical manifestation of the placenta abruption is severe abdominal pain, often accompanied by uterine contractions, pathological fetal heart rate, and vaginal bleeding.[4,5] Pregnancy-associated plasma protein-A (PAPP-A) and human chorionic gonadotropin (β-hCG) are part of the chromosomal anomaly screening test performed between the 11+0 and 14+0 weeks of gestation, combined with maternal age and nuchal translucency. PAPP-A is secreted from trophoblasts, and β-hCG is synthesized by syncytiotrophoblasts. Many studies are investigating the relationship of these markers with pregnancy complications, apart from chromosomal anomaly screening.[6–9] It has been suggested that PAPP-A may be an important marker in placental pathologies, and low PAPP-A value is associated with preeclampsia,

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e-mail: begumkurt@cumhuriyet.edu.tr **Received:** February 4, 2022; **Accepted:** February 24, 2022

How to cite this article: Kurt B, Alyazıcı Küçükyıldız İ. The relationship between first trimester screening test and abruptio placentae. Perinat J 2022;30(1):51–56. doi:10.2399/prn.22.0301011

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premature birth, pregnancy loss, and low birth weight.[7] Studies conducted in recent years have also tried to examine first-trimester maternal serum biochemical markers of pregnancies with placental pathologies.[8–10]

Our study aimed to investigate the relationship between first-trimester maternal serum PAPP-A and β-hCG values and abruptio placentae.

Methods

The research group of our study consists of 20 pregnant women diagnosed with abruptio placentae in our hospital between October 2019 and March 2021 and the control group was composed of 30 pregnant women who did not develop clinical abruptio placentae during their pregnancy in the same time period. All of the patients in both groups had first-trimester screening test results. All procedures in this study were performed according to the ethical standards of the institutional research committee and the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Human Research Ethics Committee of the Sivas Cumhuriyet University approval was received for this study [registry no: 2021-04/54].

While abruptio placentae is considered a clinical diagnosis, the diagnosis was confirmed by histopathological examination of the placenta. Biochemical markers of the patients from first-trimester screening, demographic data including maternal age, parity, type of delivery, gestational age at delivery, fetal weight, Apgar scores (1- and 5-minute were recorded), and results were also compared between the risk factors in vitro fertilization (IVF) pregnancy, smokers, chronic hypertension, preeclampsia, diabetes, gestational diabetes, preterm premature rupture of membranes (PPROM), threatened preterm labor, intrauterine growth retardation (IUGR), uterine myomas and hypothyroidism.

Differences between categorical variables were studied by chi-square analysis. In numerical variables, Shapiro-Wilk normality test was applied to decide which test is appropriate to analyze whether there are differences between the groups. As a result of the analysis, compliance with the normal distribution in all dimensions could not be calculated ($p<0.05$). For this reason, numerical variables were analyzed with the Mann-Whitney U test.

Results

Our study was conducted with 50 cases, 20 of them in the study group and 30 in the control group. No significant differences were found in maternal age, gravida, and parity. A significant difference was found in gestational age at birth, 33±5.1 weeks in the study group and 38.6±1.48 weeks in the control group. No statistical differences were found at PAPP-A or at β-hCG between the groups ($p=0.219$ and 0.898, respectively). Nevertheless, a trend of a lower PAPP-A in the study group was noticed (1.03±0.54 MoM vs. 1.28±0.66 MoM) (**Table 1**). Significant differences were found at fetal birth weight, and 1-minute and 5-minute Apgar scores (**Table 2**). When looking at risk factors, no differences between the groups were found at smoking, multiple pregnancy, myoma uteri or diabetes, but preeclampsia and threatened preterm labor (TPL) were more common at the study group (**Table 3**).

Table 1. Comparison of maternal and pregnancy-related variables between the groups.

Variables	Study		Control		Total		p-value
	Mean	Standard deviation	Mean	Standard deviation	Mean	Standard deviation	
Age	30.90	6.03	31.37	6.38	31.18	6.19	0.781
Gravida	3.2	1.47	2.63	1.58	2.86	1.55	0.267
Parity	1.95	1.5	1.33	1.32	1.58	1.41	0.434
Week of gestation	33.00	5.10	38.66	1.48	36.39	4.38	**<0.001**
PAPP-A	1000.57	771.62	1013.68	661.97	1008.44	700.18	0.539
PAPP-A MoM	1.03	0.54	1.28	0.66	1.18	0.62	0.219
β-hCG	103,404.20	46,615.29	100,966.93	37,323.66	101,941.84	40,847.30	0.874
β-hCG MoM	1.10	0.50	1.07	0.38	1.08	0.43	0.898

Table 2. Comparison of birth weight and Apgar scores between the groups.

Variables	Study		Control		Total		p-value
	Mean	Standard deviation	Mean	Standard deviation	Mean	Standard deviation	
Birth weight	2120.00	960.58	3298.63	455.35	2841.61	898.86	**<0.001**
1-minute Apgar	5.10	2.31	7.53	0.86	6.56	1.99	**<0.001**
5-minute Apgar	7.00	3.00	9.00	1.00	7.60	2.17	**0.004**

Discussion

Placental abruption is closely associated with low birth weight, preterm delivery, stillbirth, and early neonatal mortality.[11] The incidence of stillbirth and perinatal mortality rates depend on the degree of separation of the placenta and the week of gestation. Particularly, more than 50% separation of the placenta significantly increases stillbirth rates.[1] It is very important that placental abruption can be predicted and precautions can be taken.

This study is based on the hypothesis that first trimester maternal PAPP-A or β-hCG serum measurements may be associated with poor perinatal outcomes at the end of pregnancy. If pregnant women with a high risk of obstetric complications can be predicted in the first- trimester, taking the necessary precautions for these patients will prevent possible complications. PAPP-A plays a role in the regulation of fetal growth.[12] In addition, it is estimated that they play a key role in the autocrine and paracrine control of trophoblast invasion of the decidua.[13–16] Therefore, it is thought that obstetric pathologies associated with insufficient trophoblastic invasion in the first-trimester may be associated with low PAPP-A.

Although the association between low PAPP-A levels and adverse outcomes is statistically significant, the

Table 3. Comparison of risk factors between the groups.

Variables	Category	Study		Control		Total		p-value
		n	%	n	%	n	%	
IVF	No	19	95.00	30	100.00	49	98.00	0.216
	Yes	1	5.00	0	0.00	1	2.00	
Smoker	No	18	90.00	29	96.70	47	94.00	0.331
	Yes	2	10.00	1	3.30	3	6.00	
Chronic hypertension	No	19	95.00	29	96.70	48	96.00	0.768
	Yes	1	5.00	1	3.30	2	4.00	
Preeclampsia	No	17	85.00	30	100.00	47	94.00	0.029
	Yes	3	15.00	0	0.00	3	6.00	
Diabetes	No	19	95.00	30	100.00	49	98.00	0.216
	Yes	1	5.00	0	0.00	1	2.00	
Gestational diabetes	No	20	100.00	27	90.00	47	94.00	0.145
	Yes	0	0.00	3	10.00	3	6.00	
PPROM	No	17	85.00	29	96.70	46	92.00	0.136
	Yes	3	15.00	1	3.30	4	8.00	
Threatened preterm labor	No	12	60.00	27	90.00	39	78.00	0.012
	Yes	8	40.00	3	10.00	11	22.00	
IUGR	No	18	90.00	30	100.00	48	96.00	0.077
	Yes	2	10.00	0	0.00	2	4.00	
Uterine myomas	No	19	95.00	29	96.70	48	96.00	0.768
	Yes	1	5.00	1	3.30	2	4.00	
Hypothyroidism	No	16	80.00	28	93.30	44	88.00	0.155

sensitivity to individual outcomes is relatively low. Therefore, a low PAPP-A level alone, although strongly associated with a range of adverse obstetric outcomes, is not sufficient for prediction.[7] In some studies in the literature, an inconsistent relationship was detected between first trimester PAPP-A and β-hCG levels and perinatal outcomes.[17–22]

In the study of 137,915 women in California, Blumenfeld et al. reported that PAPP-A ≤5 percentile value was associated with 1.6 times increased risk of abruption.[23] First trimester low PAPP-A, second trimester high AFP, low uE3 and high dimeric inhibin-A levels were found to be associated with placental abruption. PAPP-A has also been shown to be associated with an increased risk of other placental dysfunction disorders, including stillbirth.[23–25]

Smith et al. determined that PAPP-A level, which is ≤5th percentile in the first trimester, increases the risk of stillbirth 60 times due to abruptio placentae.[26] In a similar study, it was reported that the probability of abruptio placentae was 1.8 times higher in women with low PAPP-A (≤5th percentile), but no relationship was found for free β-hCG.[7] In a retrospective study conducted by Kececioglu et al. in 2016, including 120 term pregnant women who gave birth by cesarean section, first- and second-trimester serum biomarker levels were compared. There was no significant difference between the biomarkers examined in the first and second trimesters in predicting cases with abruptio placentae at term without known risk factors.[27] A hospital-based study[28] in Finland reported no association between low PAPP-A (<1.0 MoM) and abruptio placentae. Another study by Pilalis et al. in Greece[29] reported that the prevalence and risks of abruptio placentae were similar among women with and without low first trimester PAPP-A. A study from Israel also found no association between low PAPP-A MoM values and abruptio placentae.[18]

Our study showed a significant difference between the abruptio placentae and control groups in terms of the weeks of gestation, birth weights, and Apgar scores, consistent with the literature. When we compared the risk factors, there was a significant difference between the abruptio placentae and control groups in preeclampsia and preterm birth threat. However, when we compared the first-trimester serum biomarkers to predict abruptio placentae, we could not find a significant difference between the two groups.

The limitation of our study is the number of patients. But placental abruption is a relatively rare condition. Our hospital's annual number of births and abruptio placentae rate is 0.85%, compatible with the world literature. As reported in FASTER TRIAL (one of the studies with the largest case series on first trimester maternal serum PAPP-A level and obstetric complications), first trimester low PAPP-A level is associated with significantly spontaneous fetal loss at ≤24 weeks of gestation, preterm birth, gestational, preeclampsia, and low birth weight.[7] However, researchers found some evidence that low PAPP-A levels are also associated with intrauterine fetal death at >24 weeks of gestation, PPROM, and abruption, although this did not meet our strict significance criteria reported. The fact that no decision has been made on this issue has encouraged us to carry out this study. Therefore, we anticipate that any research that will contribute to the literature on this subject can be valuable.

Conclusion

Placental abruption still remains an obstetric challenge in terms of prediction and prevention. There is a need for more comprehensive studies on this subject by increasing the number of patients. Future studies aiming to develop predictive models based on Doppler profiling of uterine and umbilical arteries, and maternal early pregnancy serum biomarkers combined with demographic factors may provide clinically relevant information.

Funding: This work did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Compliance with Ethical Standards: The authors stated that the standards regarding research and publication ethics, the Personal Data Protection Law and the copyright regulations applicable to intellectual and artistic works are complied with and there is no conflict of interest.

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