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ORIGINAL RESEARCH

Medicine Science International Medical Journal

Medicine Science 2018;7(3):660-3

Relationship between first trimester vaginal bleeding and the risk of placental abruption

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Received 03 March 2018; Accepted 28 March 2018
Available online .13.04.2018 with doi: 10.5455/medscience.2018.07.8776

Abstract

The aim of this study was to analyze influence of first trimester vaginal bleeding on the risk of placental abruption, as well as to assess the relation of first trimester bleeding and perinatal outcome in this patients with placental abruption. The second objective was to assess the connection of first trimester bleeding with low pregnancy-associated plasma protein-A and maternal serum alpha-fetoprotein with placental abruption. This is the first study that evaluated all relations these analytes in placental abruption with first trimester bleeding. Spontaneous, singleton pregnancies with live fetus ≥26 weeks of gestation with placental abruption were divided into two groups based on their prensence of first-trimester bleeding (Group 1) or without (Group 2). Maternal age, parity, smoking habits, body mass index, history of abortion and abruption, levels of pregnancy-associated plasma protein-A and Alpha-fetoprotein were also analyzed and compared. Main outcome measures were, mean gestational age, gender of baby, APGAR scores, birth length and weight and cesarean section rates. A total of 122 patients were included in the study.There were 44 patients accompanied with first trimester bleeding (group 1) and 78 patients without first trimester bleeding (group 2). The neonatal birthweight was significantly lower in first trimester bleeding group. The rate of smoking mother was significantly higher in first trimester bleeding group. Regarding serum maternal biomarkers, pregnancy-associated plasma protein-A≤0.5 and Alpha-fetoprotein ≥2 MOM was significantly higher in first trimester bleeding group.First trimester bleeding should alert clinicians for the signs of later possible complications in addition to low regnancy-associated plasma protein-A(≤0.5 MOM) and higher Alpha-fetoprotein (≥2 MOM) levels. Presence of vaginal bleeding in first trimester are related with poor maternal and fetal outcome at birth in patient with placental abruption.

Keywords: First trimester vaginal bleeding, Placental abruption, Pregnancy-associated plasma protein-A, serum alpha-feto protein

Introduction

First trimester bleeding (FTB), with an incidence of 16%-25%, is considered when a bloody vaginal discharge or bleeding appears through a closed cervical os during initiation of pregnancy [1]. It is a common risk factor of preterm delivery, perinatal morbidity and mortality. The mechanism of this bleeding is unclear in majority of cases. It is also hypothesized that FTB may indicate an underlying placental dysfunction and manifest adverse perinatal outcome in later pregnancy [2]. Moreover, vaginal bleeding in first trimester (early pregnancy) has been linked to placental abruption (PA) [3,4,5]. It was suggested that bleeding and abruption may use one or more common pathways [1,2,3]. Regarding shared risk factors of FTB and abruption are preterm delivery, placenta previa, pregnancy induced hypertension/ preeclampsia, maternal smoking and heavy jobs involving much standing [4,5].

Eriksen et al. [5] showed that hemorrhage in the first and second trimester was significantly associated with placental abruption. They also thought that earlier bleeding in pregnancy may represent minor episodes of abruption. Although PA is rare, complicating approximately 1% of pregnancies, it is a life threatening obstetrical condition accompanied with serious morbidity and mortality in both mother and infants. However, less has been published on fetal outcome associated with evidence of FTB and PA.

The primary aim of this study was to analyze the influence of FTB on the risk of placental abruption, as well as to assess the relation of FTB and fetal outcome in this patients with PA.

The second objective was to assess the connection of FTB with low pregnancy Pregnancy-associated plasma protein-A (PAPPA) and maternal serum alpha-fetoprotein (AFP) with abruption of placenta. This is the first study that evaluated all relations (PAPP-A and AFP levels) in PA with FTB.

Material and Methods

Study Design

This retrospective cohort study was conducted at Kayseri Research and Training Hospital Department of Obstetrics and Gynecology in Kayseri province of Turkey. Data from 122 patients with placental abruptio (PA) were analyzed between July 2014 and January 2017. The diagnoses and laboratory results were obtained from patient medical records. The study protocol was approved by the institutional review board of the local ethics committee.

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Placenta abruptio diagnosis was based upon one or more of the following clinical findings: abdominal pain or uterine tenderness with or without abnormal fetal heart rate tracing, hypertonic uterus, observation of retroplacental clot and/or showed seperation of the underlying placental tisue in delivery. If PA was suspected, emergency caesarean section or vaginal birth was performed.

First trimester true vaginal bleeding verified by a physician, in the amount of menstrual bleeding that required hospitalization was considered as 'FTB'. Due to the retrospective character of the research and subjectivity of complaints, the intensity, duration, and number of episodes of vaginal bleeding could not be clearly identified.

Spontaneous, singleton pregnancies with live fetus ≥ 26 weeks of gestation and patients who had first trimester screening test results were included in the study group. Gestational age was based on the date of the last menstrual period (LMP) and confirmed/ verified by ultrasound examination in the frist trimester of pregnancy. The cases were divided into two groups based on their prensence of first-trimester bleeding (Group 1) or without (Group 2). Multiple gestations, evidence of fetal congenital or placental abnormalities, cases with abnormal fetal karyotypes, presence of placenta invasion anomalies, patients with chronic inflammatory diseases, hepatic or renal failure, previous myocardial infarction were stated as the exclusion criteria of the study group. Patient`s obstetric and demographic characteristics, ultrasonography findings, screening test results and birth characteristics were recorded on patient charts for each individual patient. Various risk factors of PA avaliable in medical charts, such as maternal age, parity, smoking habits, body mass index, history of abortion and abruption were also analyzed and compared. Gestational age at delivery, birth weight, birth length, fetal gender and birth characteristics were also recorded.

Multiples of median (MoM) values for PAPP-A and AFP were obtained from first and second trimester screening test results in which maternal serum markers were measured on automated equipment (Clinical Laboratory Improvement Amendments CLIA kit) and, MoM values of markers were adjusted for gestational age, maternal weight, diabetes and smoking habits.

Statistical Analysis

Statistycal analyses were performed using the SPSS for Windows 21.0 (SPSS Inc. IL, USA) software package.With the confidence interval of 95%, $p<0.05$ was considered a statistically significant difference between the groups. The assumption of normality was tested via the Shapiro-Wilk test. Data are presented as means ± SD for continuous variables. To assess the differences of variables between groups, the independent Samples T tests or the chi-square test and Mann-Whitney U test was used.

Results

A total of 122 patients were included in the study. Patients were divided into two groups regarding presence or absence of first trimester bleeding (FTB). There were 44 patients accompanied with FTB (group 1) and 78 patients without FTB (group 2). Almost half of patients 21(47.7%) presented with spotting. 17 cases had moderate bleeding while 6 patient had heavy bleeding. The gestational age at the time of FTB were from 6 to 14 weeks. There were no statistically significant differences in obstetric and demographic characteristics between the groups. (Table 1) The average gestational age at birth was 35.2±4.1 (26-41 min-max) weeks.

Table 1. Obstetric and demographical characteristics of groups

(mean±SD)*	Abruptio Placenta With FTB n=44	Abruptio Placenta Without FTB n=78	P
Age (year)	28.7±6.1	29.1±6.1	0.68
Gravida	2.41±1.3	3.0±2.1	0.24
Parity	1.27±1.2	1.8±2.0	0.26
Gestational age at birth (week)	35.1±4.4	35.2±4.2	0.91
BMI	27.3±4.3	27.4±4.6	0.93
History of abortion	0.13±0.46 (0-2 min-max)	0.17±0.41 (0-2) min-max	0.61

* Mann-Whitney U test FTB: first trimester bleeding BMI: Body mass index

There were no statistically significant differences in terms of maternal and gestational age at delivery, maternal number of gravida and parity, maternal body mass index value at delivery, gender of baby, 1 th and 5 th APGAR scores, mode of delivery, Neonatal Intensive Care Unit (NICU) admission status, stillborn to liveborn ratio between the groups. The statistically significant differences were birthweight of infants, maternal smoking habits, maternal serum PAPPA and AFP MOM values between the groups. ($p=0.043$, $p=0.024$, $p<0.0001$ and $p<0.0001$, respectively). The neonatal birthweight was significantly lower in FTB group. 23 pregnancies (23/44) of group 1 and 45 pregnancies (45/78) of group 2 were preterm deliveries ($p=0.57$). (Table 2)

Table 2. Peripartum features and pregnancy outcomes of the groups

	Abruptio Placenta With FTB n=44	Abruptio Placenta Without FTB n=78	p value
BirthWeight(g) (mean±SD)*	2302±849	2636±884	0.043
BirthLength(cm) (mean±SD)*	45.8±5.6	46.6±5.2	0.41
APGAR 1.min≤5 **	25/19 (%56.8/43.2)	39/39 (%50/50)	0.47
APGAR 5.min≤5 **	19/25 (%43.2/56.8)	23/55 (%29.5/70.5)	0.12
Mode of delivery vaginal/cesarean**	9/35 (%20.5/79.5)	10/68 (%12.8/87.2)	0.26
Gender of the baby male/female**	22/22 (%50/50)	33/29 (%59/41)	0.33
Stillborn/liveborn **	8/36 (%18.2/81.8)	17/61 (%21.8/78.2)	0.63
NICU **	22/22 (%50/50)	32/46 (%41/59)	0.34
Delayed discharge NICU≥ 10days **	7/37 (%15.9/84.1)	10/68 (%12.8/%87.2)	0.63
LOS NICU *	3.23±4.3	4.04±7.8	0.46
Smoking **	22/22 (%50/50)	23/55 (%29.5/70.5)	0.024
PAPPA* MOM	0.75±0.72	1.26±0.75	<0.0001
PAPPA≤ 0.5 MOM**	29/15 (%65.9/34.1)	16/62 (%20.5/79.5)	<0.0001
AFP* MOM	1.98±0.93	1.36±0.89	0.001
AFP≥2 MOM**	19/25 (%43.2/56.8)	11/67 (%14.1/85.9)	<0.0001

* Mann-Whitney U test ** Pearson Chi Square test LOS: Lenght of Stay NICU :Neonatal Intensive Care Unit, PAPPA: Pregnancy-associated plasma protein-A FTB: First trimester bleeding

The rate of smoking mother was significantly higher in FTB group. Regarding serum maternal biomarkers, PAPPA≤0.5 and AFP≥2 MOM was significantly higher in FTB group.

Discussion

In this study, we retrospectively investigated whether there was a relationship between first trimester bleeding, maternal serum biomarkers (PAPPA, AFP) and perinatal outcome in women who had abruptio placenta. The neonatal birthweight was significantly lower in FTB group. Maternal serum PAPPA was significantly lower and AFP MOM values were significantly higher in FTB group.

Some studies revealed that decidual thrombosis, ischemia, and necrosis may lead to vaginal bleeding, which in turn leads a chronic inflammatory reaction in decidua and thrombin formation [3,6]. Thrombin itself was known to be an uterotonic agent promoting spontaneous uterine contractions [3,7]. Weiss et al. [2] also hypothesized that the disruption of chorionic-amniotic plane by hemorrhage might make the membranes more fragile – the heavier the bleeding, the greater the susceptibility to rupture prematurely. Therefore, vaginal bleeding in first trimester may trigger these mentioned mechanisms and may cause placental hemorrhage, abruption, preterm ruptur of membranes and preterm delivery. Moreover, these defective placentation, reduced cytotrophoblast invasion, thrombosis and inflammation in first trimester increased the risk of maternal and perinatal outcome [8].

Smoking also plays role in necrosis and ischemia to the decidua. In our study, the rate of smoker mother was significantly higher in FTB group (p=0.024). Although there was not a statistically significancy between preterm delivery rates of groups, infant birthweight was significantly lower in FTB group. Higher smoking rates and prematurity (the average gestational age at delivery was 35.2±4.1 weeks) may be an answer to this result. On the other hand, impaired placentation was related to small for gestational babies in the literature [8].

In another point of view, current evidence does suggest an association between low PAPP-A levels and abnormal placentation [9]. Low PAPP-A levels were related with small size for gestational age, preterm delivery, hypertensive disorders of pregnancy, and stillbirth [11]. In this study, mean PAPP-A levels were 0.75±0.72 MOM, 1.26±0.75 MOM in group 1 and 2, respectively (p<0.0001). We showed lower PAPP-A levels (of these 65% ≤0.5 MOM) and neonatal birthweight in patients with placental abruption accompanying FTB history. Low levels of maternal serum PAPP-A were thought to be proclivity of decreased local levels of PAPP-A and this resulted to low levels of active insulin-like growth factor (IGF) [10]. Thus, impaired level of free IGF affecting the fetal growth may reflect other adverse pregnancy complications, such as stillbirth, intrauterine growth restriction (IUGR), preeclampsia and preterm labour [11].

Higher AFP levels (%43 ≥2 MOM) were presented in this study in patients with placental abruption with FTB. In a recent study, they were also showed that maternal serum AFP 95th percentile or greater was more common among abruption (9.6%) than non abruption (5.1%) pregnancies (RR 1.9, 95% CI 1.3–3.0) [12]. They concluded that origins of placental abruption may extend to the early stages of pregnancy [12]. The suggested mechanisms for elevated maternal serum AFP with a structurally normal fetus included placental vascular damage from early subclinical abruption, disruption of the fetal–maternal–placental barrier or fetal–placental ischemia [13]. FTB may be the clinical aspect of early subclinical abruption of vascular placental damage in these patients.

One of the limitations of presented study was its retrospective design. On the other hand it was impossible to assess which patient would have placental abruption. So, the major strength of the study included patients diagnosed abruption.

Conclusion

In conclusion, first trimester bleeding may be a predicting component for late trimester pregnancy outcome; both pregnant women and offspring outcomes. The origins of placental abruption may extend to the early stages of pregnancy. Therefore, it is need to consider these pregnancies as a high risk group for which antenatal care should be performed carefully. FTB should alert clinicians for the signs of later possible complications in addition to low PAPP-A (≤0.5 MOM) and higher AFP (≥2 MOM) levels. Presence of vaginal bleeding in first trimester are related with poor maternal and fetal outcome at birth in patient with PA.

Competing interests
The authors declare that they have no competing interest.

Ethical approval
There are no financial supports

Funding
This study did not receive any specific grant from any funding agency in the public, commercial, or not-for-profit sector

References

1. Hossain R, Harris T, Lohsoonthorn V, et al. Risk of preterm delivery in relation to vaginal bleeding in early pregnancy. Eur J Obstet Gynecol Reprod Biol. 2007;135:158-63.

2. Weiss JL, Malone FD, Vidaver J, et al.; FASTER Consortium. Threatened abortion: a risk factor for poor pregnancy outcome, a population-based screening study. Am J Obstet Gynecol. 2004;190:745-50.

3. Ananth CV, Oyelese Y, Prasad V, et al. Evidence of placental abruption as a chronic process: associations with vaginal bleeding early in pregnancy and placental lesions. Eur J Obstet Gynecol Reprod Biol. 2006;128:15-21.

4. Petriglia G, Palaia I, Musella A, et al. Threatened abortion and late-pregnancy complications: a case-control study and review of literature. Minerva Ginecol. 2015;67:491-7.

5. Eriksen G, Wohlert M, Ersbak V, et al. Placental abruption. A case-control investigation. Br J Obstet Gynaecol. 1991;98:448-52.

6. Esmon CT. Does inflammation contribute to thrombotic events? Haemostasis. 2000;30:34-40.

7. Elovitz MA, Baron J, Phillippe M. The role of thrombin in preterm parturition. Am J Obstet Gynecol. 2001;185:1059-63.

8. Saraswat L, Bhattacharya S, Maheshwari A, et al. Maternal and perinatal outcome in women with threatened miscarriage in the first trimester: a systematic review. BJOG. 2010;117:245-57.

9. Huynh L, Kingdom J, Akhtar S. Low pregnancy-associated plasma protein A level in the first trimester. Can Fam Physician. 2014;60:899-903.

10. Gupta S, Goyal M, Verma D, et al. Adverse pregnancy outcome in patients with low pregnancy-associated plasma protein-A: The Indian Experience. J Obstet Gynaecol Res. 2015;41:1003-8.

11. Conover CA, Bale LK, Overgaard MT et al. Metalloproteinases pregnancy associated plasma protein A is a critical growth factor during fetal development. Development. 2004;131:1187–94.

12. Ananth CV, Wapner RJ, Ananth S, et al. First-Trimester and Second-Trimester Maternal Serum Biomarkers as Predictors of Placental Abruption. Obstet Gynecol. 2017;129:465-72.

13. Spong CY, Ghidini A, Walker CN, et al. Elevated maternal serum midtrimester alpha-fetoprotein levels are associated with fetoplacental ischemia. Am J Obstet Gynecol. 1997;177:1085–7.