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First Trimester Bleeding and Pregnancy Outcomes: Case-Control Study

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Abstract

Objectives: The purpose of this study was to determine the perinatal outcome and pregnancy complication (preterm delivery, preterm prelabour rupture of membrane [PPROM], preeclampsia, placental abruption and intrauterine growth restriction [IUGR]) of threatened miscarriage.

Materials and Methods: A total of 963 patients attended the study. Of these, 493 women had threatened miscarriage. The control group included 470 pregnants without first trimester vaginal bleeding. We compared the two groups according to maternal age, gravida, parity, spontaneous or induced abortion history, pregnancy period, livebirth or pregnancy loss, newborn weight and Apgar values after 1 and 5 minutes, newborns' gender for livebirth and preterm deliveries.

Results: Incidence of preterm delivery, abortion, lower gestational fetal weight and preterm rupture of membrane was increased in threatened miscarriage group. Mean pregnancy period in threatened miscarriage group was 243 days; in control group was 263 days. There was adverse influence of maternal age and abortion history on outcomes in pregnancies with threatened miscarriage. However sex of the fetuses and Apgar values after 1 and 5 minutes were similar between two groups.

Conclusion: Threatened miscarriage is an important situation to predict both the maternal and fetal outcomes in late pregnancy. Maternal obstetric history on previous pregnancies should be questioned. It is therefore essential to consider these pregnancies as high risk group and provide careful antenatal care.

Keywords: Abortion, Uterine hemorrhage, Perinatal outcomes, Preterm labor

Introduction

First trimester bleeding is a common symptom of pregnancy, complicating 16%-25% of all pregnancies (1-3). The four major sources of nontraumatic bleeding in early pregnancy are ectopic pregnancy, miscarriage (threatened, inevitable, incomplete or complete), implantation of pregnancy and cervical pathology. Physical and pelvic examination should be done and further with the help of imaging techniques, diagnosis and plan of management is planned.

Abortus imminens is diagnosed as first trimester vaginal bleeding with closed cervix and confirmed with fetal heart rate on ultrasound (3,4). Doppler confirmation of fetal cardiac activity is reassuring as it indicates that bleeding is not related to fetal demise. After determining the diagnosis, management is important. Nearly 50% of pregnancies end in pregnancy loss; if pregnancy continues, poor maternal and fetal outcomes such as preterm delivery (4), preterm prelabour rupture of membrane (PPROM), preeclampsia, placental abruption and intrauterine growth restriction (IUGR) may occur (1,3,5). It is known also that maternal age (5,6), systemic diseases such as diabetes mellitus, hypothyroidism, infertility treatment (1), thrombophilia, maternal weight and uterine structural anomalies increase the risk of abortus imminens.

The purpose of this study was to investigate whether threatened abortion makes pregnancies high risk, what is poor neonatal outcome and which maternal characteristics change these results in our clinic. Answer to these questions can change our antepartum, peripartum and postpartum management. We aimed to investigate threatened abortion and pregnancy outcomes in our patients.

Materials and Methods

In this retrospective study we examined 493 patients with diagnosis of abortus imminens who were admitted to the Department of Gynecology and Obstetric, Medical Faculty, Ankara University between 2007 and 2015. Threatened miscarriage was defined as positive fetal heart rate on ultrasound and a history of vaginal bleeding in the first trimester. We examined 470 singleton pregnant women as control group with no symptoms of threatened miscarriage such as vaginal bleeding, spotting or pelvic pain.

493 women with threatened miscarriage were considered as group A. Control group (group B) included 470 pregnants without first trimester vaginal bleeding. We compared the two groups according to maternal age, gravidity, parity, spontaneous or induced abortion history, pregnan-

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cy period, livebirth or pregnancy loss, newborn weight and Apgar scores after 1 and 5 minutes, newborns' gender for livebirth and preterm deliveries.

Outcome measures included preterm labour, fetal birth weight, Apgar scores after 1 and 5 minutes, livebirth or pregnancy loss, sex of the fetuses, and previous maternal obstetric history (gravidity, parity, spontaneous abortion, induced abortion history). The assessment of all patients included maternal disease; hereditary thrombophilia, chronic hypertension and diabetes mellitus, hypothyroidism, preeclampsia and fetal abnormality. Hereditary thrombophilia included thrombosis, G1691A mutation in the factor 5 gene, G20210A mutation in the prothrombin gene, C677T mutation and A1298C mutation in MTHFR gene, antithrombin 3, protein C and S deficiency.

The inclusion criteria were singleton pregnancies complicated with vaginal bleeding at less than 14 weeks' gestation with positive fetal heart pulsations detected with ultrasound. The gestational age was estimated from last menstrual period and the first trimester ultrasound. If the self reported last menstrual period was >7 days from the calculated ultrasound last menstrual period; then the ultrasound was used to assign the gestational age.

Multiple pregnancies, patient who had gynecological pathologies such as polyps, cervicitis or cervical myomas were excluded. All patients' pregnancy period were recorded and preterm delivery (<37 weeks' gestation) and abortion (<24 weeks' gestation) were accepted.

Data were analysed with SPSS.21.0. The statistical analysis of the differences between the patient and control groups for the parameters showing normal distribution was done with a parametric test "independent-samples Student's *t* test." Used as a non-parametric test, the "Mann-Whitney U" was used to make comparisons among the parameters that did not demonstrate normal distribution. Pearson chi-square tests (non-parametric) were performed to test statistical significance of the differences in proportions. A value of $P < 0.05$ was considered to be statistically significant.

Results

We examined the patients with threatened miscarriage diagnosis who applied to the clinic because of the first trimester vaginal bleeding between 2007 and 2015. A total of 963 patients attended the study. Of these, 493 women had threatened miscarriage (group A). The control group (group B) included 470 pregnants without first trimester vaginal bleeding. Results for the two groups are presented on Table 1.

In group A there were two groups; the first was with livebirth and the second was spontaneous abortion. Both of these groups were compared with each other in regard to maternal age, gravidity, parity, spontaneous or induced abortion history. However there were not statistically significant differences among groups.

In 58 patients (11.7%) from group A, terminated their pregnancies with spontaneous abortion. In 435 patients (88.3%) from group A, pregnancies continued after 24 weeks' of gestation. The relationship between vaginal bleeding and preterm delivery subtypes was also evaluated. In this study population 94 patients (21.6%) of preterm cases delivered between 24-37 weeks' gestation. In preterm deliveries; 60 patients (63.8%) delivered between 34-37 weeks' gestation; 21 patients (22.3%) between 28-34 weeks' gestation and 13 patients (13.8%) between 24-28 weeks' gestation.

In group A; hereditary thrombophilia was found in 20 patients during pre-pregnancy assessment. These patients had used low molecular weight heparin during whole pregnancy period. Twenty-nine patients were hypothyroid, 4 of them complicated with placenta previa and pregnancy induced hypertension occurred in two patients. 11 of them had different diseases such as asthma (one patient), psychosis (3 patients), cervical cancer (1 patient), cardiac surgery (2 patients), chronic hypertension (3 patients), pregestational diabetes mellitus (2 patients), and sarcoidosis (1 patient). Also 29 patients of group A were hypothyroid and 5 of them had spontaneous abortion.

Women in the threatened miscarriage group; 10 of them had complication with placenta previa; 5 of them complicated with preeclampsia. And 13 of these patients had pregnancy induced hypertension during the pregnancy. Only one of them had intrauterine exitus and fetus was terminated after that. Also cholestasis was observed in three patients. In early gestational weeks 5 major fetal abnormalities were determined with ultrasound scan. Three of them were trisomy 21 and all were terminated. The other abnormalities included Walker-Warburg syndrome and cystic hygroma; these pregnancies did not terminate because of absence of parental consent. Only one placental abruption occurred in 33 weeks' gestation. IUGR in 9 pregnancies and gestational diabetes mellitus in 13 patients were diagnosed.

As seen below, in group A with threatened abortion, maternal age was higher than control group and statistically significant. There were no differences in gravidity between two groups. However, there were statistically differences in parity and spontaneous abortion rates. In control group, pregnancy period is more longer than group A expectedly. Gender of fetuses were similar in both groups. Because of the higher rates of preterm delivery in group A; birth weight was lower in this group when compared with control group. However interestingly APGAR scores in first and 5 minutes did not change.

In group A cervical cerclage was performed in only one patient who had history of cervical conization. In eight patients preterm premature rupture of membrane occurred.

In group A, there were two groups; livebirth and spontaneous abortion groups. When we compared these two groups maternal age, gravidity, parity, presence of spontaneous or induced abortion before and livebirth had similar rates. In threatened abortion group, there was no statistically significance between abortion or livebirth during pregnancy (Table 2).

Table 1. Comparison of Outcomes of Pregnancies in Control and Case Groups

	Threatened Abortion (n = 493)	Control (n = 470)	*P* Value[a]
Maternal age	33.5±5.4	28.8±5.2	<0.001
Gravida	2.1±1.2	1.9±1.1	0.077
Parity	0.51±0.75	0.68±0.94	0.006
Spontanous abortion	0.51±0.86	0.18±0.5	<0.001
Dilatation curettage	0.14±0.47	0.09±0.42	0.11
Livebirth	0.46±0.71	0.65±0.78	0.002
Pregnancy period	243±59	263±35	<0.0001
Birth weight	3115±665	3239±619	0.005
Gender (f/m)	180/206	188/262	0.147
Apgar 1 min (median ± min-max)	8±(0-9)	8±(0-9)	0.080
Apgar 5 min (median ± min-max)	9±(0-10)	9(0-10)	0.060
Preterm delivery	94/493	40/470	<0.001
Abortus	58/493	20/470	<0.001

[a] $P < 0.05$ is significant.

Table 2. Spontaneous Abortion and Livebirth Groups in Group A

	Livebirth (n = 435)	Abortion (n = 58)	*P* Value
Age	33.3±5.3	34.8±6.1	0.11
Gravida	2.1±1.2	2.1±1.4	0.21
Parity	0.50±0.75	0.55±0.94	0.25
Abortion history	0.51±0.86	0.44±0.78	0.55
Dilatation curettage history	0.13±0.46	0.24±0.51	0.075
Livebirth	0.46±0.70	0,48±0.78	0.61

[a] $P < 0.05$ is significant.

Discussion

This study indicates that women who have vaginal bleeding in the first trimester are at increased risks of later pregnancy complications; especially preterm delivery, shortened mean pregnancy period, lower gestational fetal weight and preterm rupture of membrane (1,2,7). Mean pregnancy period in threatened miscarriage group was 243 days; in control group it was 263 days. There was adverse influence of maternal age and abortion history on outcomes in pregnancies with threatened miscarriage (6,8). However sex of the fetuses and Apgar scores after 1 and 5 minutes were similar between two groups.

Bleeding during first trimester was associated with increased risk of preterm delivery (4). Because of impaired implantation and invasive trophoblasts, spontaneous abortion may occur in early pregnancy while preterm delivery, PPROM, placental ablation and preeclampsia may happen in later period (2,4,9). Our results were similar to those reported before by Hossain et al (4). According to these studies, the first and second trimester bleeding complications are more likely than only the first trimester bleeding. But only risk of preterm delivery in first or second trimester bleeding were similar (4,10).

Preterm delivery and PPROM rates were increased in the threatened miscarriage group (4,7,9,11,12). Because of increased free iron deposits from subchorionic bleeding, hydroxyl radical is catalyzed damaging the membranes (4,7). The other point in PPROM's etiology is the chronic inflammatory reaction within the decidua and placental membranes with weakening and rupture of the membranes. Investigators have speculated that decidual thrombosis, ischemia and necrosis result in vaginal bleeding along with inflammatory response and thrombin formation. Thrombin is a uterotonic agent and may cause preterm labor during late pregnancies and spontaneous abortion during early weeks of gestation (3,9,13,14). Subchorionic hematoma can result in a nidus which may become infected and cause preterm rupture of membranes (13). In Saraswat et al study similar results were demonstrated for PPROM (3).

Both preterm delivery and PPROM are related with low birth weight as predictable factors. Our study demonstrated that the fetal weight was lower in the case than control group. It is related with births at earlier gestations (7,15). Neonatal intensive care unit admission for low birth weight fetuses was increased because of prematurity complications such as respiratory distress (7). The objective parameter of fetal outcome cord blood sample was not detected for fetal pH. But we recorded APGAR scores after one and five minutes. In our study interestingly, we did not find relationship between the control group and threatened miscarriage group for Apgar scores. As an opinion, lower Apgar scores after 1 and 5 minutes were expected in threatened abortion group because of increased rates of preterm delivery.

Additionally in threatened miscarriage group, maternal obstetric history (gravidity, parity and spontaneous or induced abortion, intrauterine exitus) was important for examinations during prenatal care. With previous threatened miscarriages, this pregnancy may be more complicated with preterm delivery, PPROM, lower birth weight (1,2,4,9,13). In literature also this situation was related with pregnancy induced hypertension and preeclampsia and lower Apgar scores with poor previous obstetric history (5).

Bleeding amount and characteristics are related with poor maternal and fetal outcome (7,10,12,14) which was we did not record. Our study was retrospective so that we investigated only patient records. If subchorionic hematoma had occurred, we recorded the size of the hematoma in the ultrasound scanning forms. Our sample size for hematoma wasn't enough so we did not include it. All patients data were obtained from computer database and patients' files so that number of patients are under estimated. In our clinic, very few patients who were complicated with threatened abortion were hospitalized; so very few patients were included in this investigation. We included only those patients that had full data both n computer database and patients files.

Conclusion

In conclusion threatened miscarriage is an important situation to predict late pregnancy results; both maternal and fetal outcomes. Maternal obstetric history about previous pregnancies should be questioned. It is therefore acceptable to consider these pregnancies as high risk group for which antenatal care should be performed carefully.

Ethical issues

An inquiry was made and sent to Ankara University Ethics Commission. Due to nature of non-confidential data required for study, retrospective nature of data collection, ethics approval and patient consent was deemed unnecessary.

Conflict of interests

None to be declared.

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References

1. Evrenos A, Güngör A, Gülerman C, Cosar E. Obstetric outcomes of patients with abortus imminens in the first trimester. Arch Gynecol Obstet. 2014;289(3):499-504. doi:10.1007/s00404-013-2979-5.
2. Lykke JA, Dideriksen KL, Lidegaard O, Langhoff-Roos J. First trimester vaginal bleeding and complications later in pregnancy. Obstet Gynecol. 2010;115(5):935-944. doi: 10.1097/AOG.0b013e3181da8d38.
3. Saraswat L, Bhattacharya S, Maheshwari A, Bhattacharya S. Maternal and perinatal outcome in women with threatened miscarriage in the first trimester: a systematic review. BJOG. 2010;117:245-257. doi:10.1111/j.1471-0528.2009.02427.x.
4. Hossain R, Harris T, Lohsoonthorn V, Williams M. Risk of preterm delivery in relation to vaginal bleeding in early pregnancy. Eur J Obstet Gynecol Reprod Bio. 2007;135(2):158-163. doi.org/10.1016/j.ejogrb.2006.12.003.
5. Dadkhah F, Kashanian M, Eliasi GA. Comparison between the pregnancy outcome in women both with or without threatened abortion. Early Hum Dev. 2010;86(3):193-196. doi:10.1016/j.earlhumdev.2010.02.005.
6. Gitau G, Liversedge H, Goffey D, Hawton A, Liversedge N, Taylor M. The influence of maternal age on the outcomes of pregancies complicated by bleeding at less then 12 weeks. Acta Obstetricia et Gynecologica 2009;88(1):116-118. doi:10.1080/00016340802621005.
7. Johns J, Jauniaux E. Threatened miscarriage as a predictor of obstetric outcome. Obstet Gynecol. 2006;107:845-850. doi:10.1097/01.AOG.0000206186.91335.9a.
8. Yang J, Savitz DA, Dole N, et al. Predictors of vaginal bleeding during the first two trimesters of pregnancy. Paediatric Perinatal Epidemiol. 2005;19(4):276-283. doi: 10.1111/j.1365-3016.2005.00655.x.
9. Hackney DN, Glantz JC. Vaginal bleeding in early pregnancy and preterm birth: systematic review and analysis of heterogeneity. J Maternal-Fetal Neonatal Med. 2011;24(6):778-86. doi:10.3109/14767058.2010.530707.
10. Velez Edwards DR, Baird DD, Hasan R, Savitz DA, Hartmann KE. First trimester bleeding characteristics associate with increased risk of preterm birth: data from a prospective pregnancy cohort. Hum Reprod. 2012;27(1):54-60. doi:10.1093/humrep/der354.
11. Yang J, Savitz DA. The effect of vaginal bleeding during pregnancy on preterm and small for gestational age births: US national Maternal and Infant Health Survey, 1988. Paediatric Perinatal Epidemiol. 2001;15(1):35-39. doi:10.1046/j.1365-3016.2001.00318.x.
12. Mulik V, Bethel J, Bhal K. A retrospective population based of primigravid women on the potential effect of threatened miscarriage on obstetric outcome. J Obstet Gynecol. 2004;24(3):249-253. doi:10.1080/01443610410001660724.
13. Rosen T, Kuczynski E, O'Neill LM, Funai EF, Lackwood CJ. Plasma levels of thrombin-antithrombin complexes predict preterm premature rupture of the fetal membranes. J Maternal- Fetal Med. 2001;10(5):297-300. doi:10.1080/jmf.10.5.297.300.
14. Yang J, Hartmann KE, Savitz DA, et al. Vaginal bleeding during pregnancy and preterm birth. Am J Epidemiol. 2004;160(2):118-125. doi:10.1093/aje/kwh180.
15. Sun L, Tao F, Hao J, Su P, Liu F, Xu R. First trimester bleeding and adverse pregnancy outcomes among Chinese women: from a large cohort study in China. J Maternal-Fetal Neonatal Med. 2012;25(8):1297-1301. doi:10.3109/14767058.2011.632034.