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First trimester bleeding and pregnancy outcomes: A case-control study

İlk trimester kanaması ve gebelik sonuçları: Bir vaka-kontrol çalışması

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ABSTRACT

Aim: The objective of this study is to perform a comprehensive assessment of fetal and perinatal results in pregnant women diagnosed with threatened miscarriage during the early trimester, and to evaluate the potential impact of this condition on the progression of pregnancy.

Materials and Methods: In this retrospective study, the study group consisted of 200 patients who were diagnosed with threatened miscarriage and gave birth, while the control group was composed of 200 patients who gave birth without experiencing threatened miscarriage during the same period. The following variables were evaluated: age, gravida, parity, gestational week, and body mass index, as well as fetal and maternal perinatal outcomes.

Results: The analysis of the delivery parameters revealed no statistically significant difference between the groups in terms of mode of delivery (p=1.000). The prevalence of preterm birth and preterm premature rupture of membranes (PPROM) was significantly higher in the case group compared to the control group ($p < 0.001$). No statistically significant difference was observed between the threatened miscarriage group and the control group in terms of the incidence of gestational diabetes, preeclampsia, placenta previa, abruptio placenta, macrosomia and stillbirth (p>0.05).

Conclusions: In pregnant women with threatened miscarriage, the risk of preterm birth and preterm premature rupture of membranes (PPROM) is significantly higher. This finding emphasizes the need for careful monitoring and management of these patients, particularly concerning complications such as preterm birth and PPROM.

Keywords: Threatened miscarriage, perinatal outcomes, preterm labor

ÖZ

Amaç: Bu çalışmanın amacı, erken trimesterde düşük tehdidi tanısı alan gebelerde fetal ve perinatal sonuçların kapsamlı bir değerlendirmesini yapmak ve bu durumun gebeliğin ilerlemesi üzerindeki potansiyel etkisini değerlendirmektir.

Gereç ve Yöntemler: Bu retrospektif çalışmada, çalışma grubu düşük tehdidi tanısı alan ve doğum yapan 200 hastadan oluşurken, kontrol grubu aynı dönemde düşük tehdidi yaşamadan doğum yapan 200 hastadan oluşmuştur. Yaş, gravida, parite, gebelik haftası ve vücut kitle indeksi gibi değişkenlerin yanı sıra fetal ve maternal perinatal sonuçlar da değerlendirilmiştir.

Bulgular: Doğum parametrelerinin analizi, doğum şekli açısından gruplar arasında istatistiksel olarak anlamlı bir fark olmadığını ortaya koymuştur (p=1,000). Erken doğum ve preterm erken membran rüptürü (PPROM) prevalansı vaka grubunda kontrol grubuna kıyasla anlamlı derecede yüksekti (p<0,001). Düşük tehdidi grubu ile kontrol grubu arasında gestasyonel diyabet, preeklampsi, plasenta previa, abruptio plasenta, makrozomi ve ölü doğum insidansı açısından istatistiksel olarak anlamlı bir fark gözlenmemiştir (p>0,05).

Sonuç: Düşük tehdidi olan hamile kadınlarda erken doğum ve preterm erken membran rüptürü (PPROM) riski önemli ölçüde daha yüksektir. Bu bulgu, özellikle erken doğum ve PPROM gibi komplikasyonlar açısından bu hastaların dikkatli bir şekilde izlenmesi ve yönetilmesi gerektiğini vurgulamaktadır.

Anahtar Kelimeler: Düşük tehdidi, perinatal sonuçlar, erken doğum

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INTRODUCTION

In the first trimester of pregnancy, approximately 16-25 out of every 100 pregnant women may experience vaginal bleeding (1, 2). The four principal categories of non-traumatic bleeding in the early stages of pregnancy are ectopic pregnancy, miscarriage, fertilisation of the pregnancy and cervical pathology. These conditions vary in severity and require careful assessment to determine appropriate management. Physical and pelvic assessments should be conducted, and the use of imaging techniques should guide the diagnosis and treatment plan. These assessments are crucial for determining the underlying cause of bleeding and ensuring appropriate management for the patient. The diagnosis of imminent abortion is based on the observation of a closed cervix in conjunction with the presence of vaginal spotting in the early stage of pregnancy. This diagnosis is subsequently confirmed through the detection of fetal heart rate on ultrasound imaging (2,3). Approximately 50% of pregnancies diagnosed as abortus imminens result in pregnancy loss (4). Should the pregnancy persist, the probability of unfavourable maternal and foetal outcomes, including preterm labour, premature rupture of the membranes (PPROM), preeclampsia, placental abruption and intrauterine growth restriction (IUGR), is heightened (5-8). It has been demonstrated that maternal age (9,10), the presence of systemic diseases including diabetes mellitus and hypothyroidism, the necessity for infertility treatment (11), thrombophilia, maternal weight and uterine structural anomalies are factors that elevate the risk of threatened miscarriage. This study sought to investigate whether the threat of miscarriage increases the likelihood of pregnancies being classified as high risk in our clinic, to identify poor neonatal outcomes, and to determine which maternal characteristics influence these outcomes. The answer to these questions may influence our approach to prenatal and postnatal management.

MATERIAL AND METHOD

The study was conducted as a retrospective cross-sectional case-control investigation. The study was approved by the Non-Interventional Ethics Committee of the University of Niğde Ömer Halisdemir University Faculty of Medicine, with decision number 2022/109. The study included a total of 400 pregnant women with gestational ages ranging from 5 weeks to 14 weeks, who had applied to the obstetrics and gynaecology clinic of our hospital between January 2021 and January 2023.

Study Population

The study includes a total of 400 women who have given birth, with 200 of them diagnosed with threatened miscarriage, while the other 200 are women who have given birth without a threatened miscarriage diagnosis. Data on age, gravidity, parity, fetal birth weight, body mass index (BMI), placental pathologies (placenta previa, abruptio placenta), preeclampsia, gestational diabetes mellitus (GDM), macrosomic fetus, preterm birth, PPROM, stillbirth, and the need for neonatal intensive care after birth were collected for both groups.

Exclusion Criteria

During follow-up, patients who experienced either a complete miscarriage (where all pregnancy tissue is expelled from the uterus) or an incomplete miscarriage (where some pregnancy tissue remains in the uterus) were evaluated, along with those who had no fetal heartbeat detected on ultrasound (USG), systemic disease or multiple pregnancies were excluded. Patients who were initially included in the study but whose vaginal bleeding examination revealed cervical erosion and cervical polypoid formation were subsequently excluded. After excluding other causes of vaginal bleeding, pregnant women with vaginal bleeding and pelvic pain, no cervical dilatation, and ultrasonographic evidence of gestational sac or fetal heartbeat were included in the study. The clinical conditions experienced by the patients during and after the delivery, as well as the care needs of the newborns, were obtained from patient records. In our clinic, pregnancies resulting in delivery before 37th gestational week were defined as preterm delivery and babies born over 4 kg were defined as macrosomia. After 20 weeks of gestation, babies born without a heartbeat were considered stillbirth.

Statistical Analysis

Categorical variables were presented as frequency and percentage, while numerical variables were expressed as mean and standard deviation. Groups were compared using Student's t-test, Mann-Whitney U test, and chi-square test. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The study encompassed a total of 400 cases, with 200 patients constituting the abortus imminens group and 200 patients forming the control group. In the abortus imminens group, mean age was 28.5±4.5 years, median gestational age at birth was 36 (32-41) weeks, and BMI was 28± 3.8 (Table.1).

154 (77%) patients were delivered vajinal and 46 (23%) patients were delivered by caesarean section (Table 2). A comparison of the groups revealed no statistically significant differences in terms of age, gravida, parity or BMI (p=0.213, p=0.168, p=0.512, p=0.112 respectively) (Table 1). The gestational week at termination of

Table 1. Distribution of patients' demographic data by group

	Threatened Abortion (n=200)	Control (n=200)	p-value
Maternal age (years, mean ± SD)	28,5±4,5	29,2±3,8	0,213
Gravida (mean ± SD)	2(1-3)	3(1-4)	0,168
Parity (mean ± SD)	2(0-3)	2(0-3)	0,512
Gestational age at birth (weeks median, min–max)	36(32-41)	39(32-41)	**0,001**
BMI (kg/m², mean ± SD)	28± 3,8	27,3±3,4	0,112
Birth weight (kg, median, min–max)	2867 (2000–4500)	3245 (2000–4500)	**0,001**

BMI: Body mass index
Data are given as mean±standard deviation and median (minimum-maximum).
There is a statistically significant difference of p<0.05.

Table 2. Comparison of Outcomes of Pregnancies in Control and Case Group

	Threatened Abortion (n = 200)	Control (n = 200)	p value
Gestational diabetes (n, %)	12 (%6.0)	10 (%5.0)	0.215
Preeclampsia (n, %)	5 (%2.5)	4 (%2.0)	1.000
Placenta previa (n, %)	9 (%4.5)	9 (%4.5)	1.000
Abruptio placentae (n, %)	7 (%3.5)	4 (%2.0)	0.152
Preterm premature rupture of membrane (n, %)	22 (%11.0)	8 (%4.0)	**0.001**
Caesarean (n, %)	46 (%23.0)	48 (%24.0)	1.000
Vajinal delivery (n, %)	154 (%77.0)	152 (%76.0)	1.000
Preterm birth (n, %)	28 (%14.0)	12 (%6.0)	**0.001**
Macrosomia (n, %)	7 (%3.5)	5 (%2.5)	0.246
Newborn intensive care unit (n, %)	36 (%18.0)	14 (%7.0)	**0.001**
Stillbirth (n, %)	2 (%1.0)	2 (%1.0)	1.000

n: Number; %: Percentage; There is a statistically significant difference of p<0.05.

pregnancy was found to be longer in the control group, with a statistically significant difference (p=0.001) (Table 1). The fetal weight was observed to be lower in the group experiencing a threatened miscarriage, and this difference was found to be statistically significant (p=0.001) (Table 1). The incidence of neonatal intensive care was markedly elevated in the cohort exhibiting threatened miscarriage (p=0.001) (Table 2).

There was no significant difference between the two groups in terms of delivery parameters, specifically mode of delivery (p=1.000 and p=1.000) (Table 2). In the study group, there were 22 (11%) cases of PPROM, while the control group had 8 (4%) cases (Table 2). The incidence of preterm premature rupture of membranes (PPROM) was higher in the group with a high risk of miscarriage, and this difference was statistically significant ($p < 0.001$) (Table 2). Regarding preterm birth frequency, 28 (14%) patients were in the study group, while 12 (6%) patients were in the control group. The rate of preterm birth was significantly higher in the threatened miscarriage group, and this difference was statistically significant ($p < 0.001$) (Table 2). Although the rates of gestational diabetes, preeclampsia, placenta previa, abruptio placenta, and macrosomia were higher in the abortus imminens group, no statistically significant difference was found. Stillbirth rates were similar between the two groups, with no statistically significant difference observed (p=1.000) (Table 2).

DISCUSSION

This study evaluated the effects of threatened miscarriage on pregnancy outcomes, and the findings indicate that such pregnancies are associated with a significantly increased risk of preterm complications. Our study found no association between the incidence of threatened miscarriage and maternal age. However, Basama et al. (12) indicated that vaginal bleeding is more frequently observed in early gestational weeks as maternal age advances, while Yakıştıran B et al. (13) reported that women with threatened abortion tend to have a higher maternal age. In our study, the average gestational age at delivery was 36 weeks in the threatened miscarriage group, compared to 39 weeks in the control group, a difference that was statistically significant ($p < 0.01$). Similarly, Agarwal S et al. (14) found that the average gestational age was significantly lower in cases (35.29 ± 3.48 weeks) than in the control group (38.11 ± 4.77 weeks) ($p = 0.0002$).

Given the correlation between miscarriage risk and preterm delivery found in previous studies, it is reasonable to hypothesize that pregnancies with miscarriage risk will have lower mean gestational age and birth weight compared to those without such risk (2, 6, 14, 15, 16, 17). In our study, the distribution of gravida and parity was found to be similar between the groups, aligning with the existing literature (18-20). First trimester bleeding is suggested as an indicator of underlying placental dysfunction potentially leading to adverse outcomes such as preterm delivery, PPROM, and placental abruption later in pregnancy (6). This association between early pregnancy hemorrhage and preterm labor has been confirmed by other researchers, including Ahmed et al. (21) and Amirkhani et al. (22), who demonstrated a significantly higher risk of preterm delivery in patients with bleeding. Conversely, Strobino et al. (23) found no correlation between threatened miscarriage and preterm labor. Despite this, our study observed an elevated risk of preterm delivery, consistent with the hypothesis that the disruption of the chorionic amniotic plane due to adjacent hemorrhage could increase membrane rupture susceptibility (6). Similarly, Agarwal et al. (14) and Rai et al. (24) reported a significantly increased risk of PPROM and preterm delivery in women experiencing early pregnancy bleeding. Saraswat et al. (2) also highlighted in their meta-analysis that the study group had a higher likelihood of PPROM and preterm labor, aligning with our findings.

Moreover, both preterm delivery and PPROM are associated with low birth weight, as seen in studies by Rai et al. (24) and Patel et al. (25). Our findings corroborate this, with lower fetal weight linked to preterm labor. Consequently, complications like respiratory distress have led to an increased admission of low birth weight neonates to the neonatal intensive care unit (NICU) (26). Consistent with studies on women diagnosed with abortus imminens, we observed that infants born from these pregnancies were more likely to require NICU admission, with this need being statistically significant ($p<0.05$).

Although some studies, such as those by Evrenos et al. indicate higher rates of gestational diabetes mellitus (GDM) in pregnancies with threatened abortion, our study found no significant difference in GDM incidence between the groups (1). Similarly, while Weiss et al. (6) suggested an elevated risk of preeclampsia in pregnancies at risk of miscarriage, our study, in line with Saraswat et al. (2) and Kanmaz AG et al. (27), showed no significant change in preeclampsia incidence.

Regarding mode of delivery, our study did not reveal an increase in cesarean section rates in pregnancies with miscarriage risk, consistent with findings by Saraswat L. et al. (2) and Davari-Tanha et al. (28). In terms of placental complications, such as placenta previa and placental abruption, our findings showed no statistically significant differences between the groups, aligning with some studies while contrasting with others like those of Johns et al. (29).

Furthermore, the incidence of macrosomia and stillbirths in pregnancies at risk of miscarriage was comparable to the control group. Although discrepancies exist in the literature regarding stillbirth frequency in such pregnancies, our findings support those studies identifying an increased need for NICU admission in cases of first trimester bleeding ($p<0.001$). Given the elevated prevalence of complications directly affecting the fetus, such as preterm birth and miscarriage, it is reasonable to anticipate higher NICU admission rates in pregnancies deemed at risk, as our study and others (2, 19) have shown.

Currently, definitive information is lacking about complications pregnant women may encounter later in gestation when experiencing a threatened miscarriage in the first trimester. Nonetheless, our study contributes valuable data to the existing literature, being one of the few single-center studies with a large sample size that compares pregnancy complications between women with and without miscarriage risk. Although the retrospective nature of our study is a limitation, rigorous patient selection criteria were employed to minimize bias.

CONCLUSIONS

Threatened abortion is an important condition in predicting poor obstetric outcomes in terms of both maternal and fetal outcomes. The incidence of preterm labor and PPROM has increased in the prognosis of abortus imminens cases. In clinical practice, pregnant women should be informed and closely monitored in the follow-up of abortus imminens cases.

Ethics Committee Approval
The study has been granted ethical approval by the non-interventional ethics committee of Nigde Omer Halisdemir University Faculty of Medicine, under decision number 2022/109.

Informed Consent
Informed consent forms were obtained from all participants in the study.

Author Contributions
Concept-IT; Design-IT, EK; Supervision-IT; Resources-IT, EK; Materials-IT; Data Collection and/or Processing-IT; Analysis and/or Interpretation-IT, EK; Literature Search-IT, EK; Writing Manuscript-IT, EK; Critical Review-IT, EK.

Declaration of Interests
The authors declare that there is no conflict of interest.

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