

Effect of Threatened Miscarriage on Maternal Mood: A Prospective Controlled Chort Study

Düşük Tehdidinin Anne Ruh Hali Üzerine Etkisi: Prospektif Kontrollü Kohort Çalışması

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ABSTRACT Objective: Threatened abortion (TA) is a fairly common complication in early pregnancy and is a leading cause of maternal hospitalisation during pregnancy. Understanding the emotional impact, psychological aspects and psychiatric consequences of this fairly common complication of early pregnancy is therefore an important contribution to obstetric care and public health. However, prospective case-controlled studies specific to anxiety and depression disorders in patients with TA are very limited. The aim of this prospective case-control study was to investigate the possible relationship between anxiety, depression and TA and compare the prevalence of anxiety and depression levels in pregnant women complicated with and without TA. **Material and Methods:** A prospective study was conducted between September 2013 and August 2014. A total of 94 consecutive women with TA who were hospitalized and 120 healthy pregnant women without any signs and symptoms of miscarriage, were included in the study. Beck Anxiety Inventory (BAI) and Beck Depression Inventory (BDI) were administered to patients during the psychiatric interview. **Results:** The mean BAI scores in TA study and healthy control groups were 18.90 ± 10.52 and 8.24 ± 5.24 , respectively ($p < 0.001$). The mean BDI scores in TA study and healthy control groups were 18.07 ± 8.49 and 7.47 ± 6.22 , respectively ($p < 0.001$). **Conclusion:** The findings of this study indicated a potential link between TA and anxiety and depression disorders. Therefore, patients with TA during pregnancy should be evaluated in terms of anxiety and depression disorders as much as their medical conditions. Medical professionals should be sensitive to psychological consequences of TA.

Key Words: Abortion, threatened; anxiety; depression; pregnancy

ÖZET Amaç: Düşük tehdidi (TA) erken gebeliğin oldukça sık bir komplikasyonudur ve gebelik sırasındaki hastaneye yatışların önde gelen bir sebebidir. Erken gebelikteki bu oldukça yaygın komplikasyonun duygusal etkisini, psikolojik yönlerini ve psikiyatrik sonuçlarını anlamak bu nedenle obstetrik bakım ve halk sağlığı için önemli bir katkıdır. Bununla birlikte, TA hastalarında anksiyete ve depresyon bozukluklarına özgü prospektif vaka-kontrollü çalışmalar oldukça sınırlıdır. Bu prospektif vaka-kontrollü çalışmanın amacı düşük tehdidi ile olası anksiyete ve depresyon ilişkisini araştırmak ve anksiyete ve depresyon seviyelerini TA ile komplike olan ve olmayan gebe kadınlarda karşılaştırmaktır. **Gereç ve Yöntemler:** Eylül 2013 ile ağustos 2014 tarihleri arasında prospektif bir çalışma gerçekleştirildi. Toplam 94 TA'lı hastaneye yatırılan kadın ve düşük semptom ve bulgusu olmayan 120 sağlıklı gebe çalışmaya dahil edildi. Psikiyatrik görüşme sırasında katılımcılara Beck anksiyete ölçeği (BAI) ve Beck depresyon ölçeği (BDI) uygulandı. **Bulgular:** Ortalama BAI skoru TA ve sağlıklı kontrol grubunda sırasıyla $18,90 \pm 10,52$ ve $8,24 \pm 5,24$ idi, ($p < 0,001$). Ortalama BDI skoru TA ve sağlıklı kontrol grubunda sırasıyla $18,07 \pm 8,49$ ve $7,47 \pm 6,22$ idi, ($p < 0,001$). **Sonuç:** Bu çalışmanın bulguları TA ile anksiyete ve depresyon arasında potansiyel bir bağlantı göstermektedir. Bu nedenle, gebelikte TA hastaları tıbbi durumları kadar anksiyete ve depresyon açısından da değerlendirilmelidirler. Klinisyenler TA'nın psikolojik sonuçları konusunda duyarlı olmalıdırlar.

Anahtar Kelimeler: Düşük, tehdit; anksiyete; depresyon; gebelik

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Vaginal bleeding in early pregnancy is a very common complication and is seen in about 20–25% of pregnancies.¹ Threatened abortion (TA) is a condition characterized by vaginal bleeding before 20 weeks of pregnancy while the cervix is closed and an intrauterine viable fetus is confirmed by the ultrasound. The vaginal bleeding in TA is frequently slight and will subside spontaneously, but sometimes it may be more serious and severe. Only 50% of TA actually lead to complete miscarriage and pregnancy loss, but this risk is substantially lower if fetal cardiac activity has been confirmed.¹⁻⁴ After sonographic confirmation of an intrauterine viable fetus, 95% to 98% of threatened abortions continue beyond 20 weeks of gestation.⁵⁻⁷ Although the actual cause of the TA is frequently unclear, in most cases, the cause of the bleeding is due to a minor condition that requires no treatment.

It has been previously shown the negative emotional impact of miscarriage and pregnancy loss on maternal psychology. Several clinical studies reported that miscarriage causes mental distress such as depression, anxiety, anger, and grief.⁸⁻²⁰ All of these studies have focused on abortions which resulted with early pregnancy loss such as spontaneous abortion, induced abortion and recurrent abortion. However, there is no comprehensive study specific to psychological morbidities such as anxiety and depression disorders in patients with TA. After sonographic confirmation of fetal cardiac activity, nearly 95% to 98% of TA continue beyond 20 weeks of gestation and does not result in miscarriage or pregnancy loss.⁵⁻⁷

Understanding the emotional impact, psychological aspects and psychiatric consequences of this fairly common complication of early pregnancy is therefore an important contribution to obstetric care and public health. In literature, there are many studies investigating the psychological aspects and sequelae of miscarriage and early pregnancy loss, but prospective case-controlled studies specific to anxiety and depression disorders in patients with TA are limited. To the best of our knowledge, this is the first prospective case-controlled study on the relationship between TA and

psychiatric consequences during early pregnancy period. This study evaluated the current state of anxiety and depression disorders in patients with TA and compared the prevalence of anxiety and depression disorders with healthy pregnant controls. The aim of this prospective case-control study was to investigate the possible relationship between anxiety, depression and TA and compare the prevalence of anxiety and depression disorders in pregnant women complicated with and without TA.

MATERIAL AND METHODS

A prospective case-control study was performed at our Obstetrics and Gynecology Clinic of Kayseri Training and Research Hospital of Medicine, a tertiary referral centre in Turkey, between September 2013 and August 2014. The study was approved by the institutional ethics committee and all participants signed an informed consent form regarding to participate in the present study.

Ninety-four consecutive women with threatened miscarriage who were hospitalized in our Obstetric Inpatient Clinic for bed rest and 120 healthy pregnant women who admitted to our obstetric outpatient clinic for routine antenatal care without any signs and symptoms of miscarriage, and matched for age, parity and gestational age were included in the study. All patients included in the study had a singleton pregnancy.

Inclusion criteria for TA group were as follows: age 18 years or older; a single viable intrauterine pregnancy confirmed by precise date of the last menstrual period and an ultrasound scan; normal closed cervix on cervical examination; written approval and willingness to comply with the study. Our exclusion criteria for all groups were as follows: history of any pregnancy loss (e.g., spontaneous abortion, induced abortion, recurrent abortion and still births), history of any medical problem (e.g., endocrine abnormalities, gastrointestinal, cardiovascular and pulmonary system diseases) or psychiatric disorder (e.g., depression, anxiety, bipolar disorder, delirium, eating disorders, and psychotic disorder), multiple pregnan-

cies, history of any gynecological and obstetric pathology (e.g., uterine anomalies, placenta praevia, placental abruption, and preterm delivery), known obstetric complications such as nausea and vomiting during pregnancy, hyperemesis gravidarum, gestational hypertension, gestational trophoblastic disease and ectopic pregnancy, history of trauma during current pregnancy, congenital fetal anomalies, hydrops, intrauterine fetal deaths, any systemic diseases or medication (including antidepressant, anti-psychotic or other psychiatric drugs during the last 6 months) that would affect the test results, current or past history of illegal drug or narcotic use and cognitive incompetence which can make difficult to understand how to score The Beck Anxiety or Depression Inventory. Moreover, pregnancies under 4 weeks' of gestation and pregnancies over 20 weeks' of gestation were also excluded from the study. In addition, patients who refused the vaginal examination with transvaginal ultrasonography and vaginal speculum were also excluded from the study. Patients with recurrent admissions for TA to our Obstetric Inpatient Clinic were only recruited during their first hospitalization.

Threatened abortion is defined as a history of vaginal bleeding before the twentieth week of pregnancy while the cervix is closed and an intrauterine fetal cardiac activity is confirmed by the ultrasound. Diagnosis of TA was made based on the clinical criteria and other causes of vaginal bleeding, such as cervical polyps, cervicitis, cervical erosion and other gynecological pathologies were excluded. All patients who met eligibility criteria were sequentially recruited by research coordinator (U.A.) at the study site. All participants were informed about the study and gave their informed written consents for study participation. After informed consent, the participant completed an enrollment questionnaire assessing sociodemographic characteristics and medical information. The final study group was composed of 214 subjects. Each subject underwent a comprehensive medical and obstetric examination along with obstetric ultrasound to confirm the intrauterine pregnancy as well as to exclude any relevant obstetric pathology

(e.g., twin pregnancy, molar pregnancy or missed abortion). Gestational age was determined with ultrasound screening on the basis of the last menstrual period. All obstetric procedures and study informing were performed by a single obstetrician (U.A.) to avoid interobserver variability. After recording the socio-demographic and clinical characteristics of participants in the obstetric clinic, patients were referred to the psychiatry department. All of the psychiatric interviews were conducted by a single experienced psychiatrist (Y.H.) to avoid possible observer-dependent factors (counseling, patient preparation, moral and psychological support). Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) (SCID-I), was used to evaluate the anxiety and depression. Beck Anxiety Inventory (BAI) and Beck Depression Inventory (BDI) were administered to patients during the psychiatric interview and were evaluated by the same psychiatrist.

MEASURES

SCID-I is a semi-structured interview instrument used to establish Axis I psychiatric disorders according to DSM-IV criteria.²¹ This instrument is widely used in clinical practice and for research purposes all over the world. The interview instruments have been standardized for Turkish populations.²² In this study, we used The Beck Anxiety Inventory and The Beck Depression Inventory.

The Beck Anxiety Inventory (BAI): The BAI is a 21-item multiple-choice self-report inventory that measures the severity of anxiety with a 0-3 scoring system.²³ The total score ranges 0-63. Higher total scores indicate more severe anxiety symptoms. The Turkish version of the BAI used in this study has been validated in Turkish populations.²⁴

The Beck Depression Inventory (BDI): The BDI is a 21-item multiple-choice self-report inventory that measures the severity of depression with a 0-3 scoring system (0="least" and 3="most").²⁵ The total score is obtained by the sum

of all BDI item scores. The total score ranges 0-63 with higher scores indicating more severe depressive symptoms. The Turkish version of the BDI used in this study has been validated in Turkish populations.²⁶ Scores from 0 to 9 represent no depression, scores of 10 to 16 indicate mild depression, scores of 17 to 29 indicate moderate depression, and scores of 30 to 63 indicate severe depression.²⁷ Questionnaire takes approximately 15 minutes to fill. However, this period may vary depending on the patient's level of education.

STATISTICAL ANALYSIS

Continuous variables were expressed as mean±standard deviation and median (minimum-maximum), whereas categorical variables were denoted as numbers or percentages where appropriate. Kolmogorov-Smirnov Goodness of Fit test was used to test the distribution of data. Because the distributions were not normal, Mann Whitney U Test was used to compare the variables. Chi-square Test was used for the comparison of the categorical data. Collected data were analyzed by Statistical Package for Social Sciences version 15.0 (SPSS Inc., Chicago, IL, USA). Two-tailed p value less than 0.05 was accepted to be statistically significant.

RESULTS

In the present study, 337 patients were enrolled, but 214 patients were eligible for inclusion and 223 patients were excluded, of which 28 refused to participate in the study and 95 did not meet the inclusion criteria. Our analyses included a total of 214 patients who fulfilled the inclusion criteria. A total of 94 women with TA and 120 healthy pregnant women completed the survey.

The mean age was 27.11±6.29 years in TA group and 25.50±5.24 years were in the healthy control group. The various demographic and clinical characteristics for each of the groups were shown in Table 1. There was no statistically significant difference among the 2 study groups in terms of mean age, gravidity, parity, gestational age and body mass index (BMI) which are listed in Table 1. All of the participants were married and were in the first trimester of gestation.

The mean BAI scores in TA study and healthy control groups were 18.90±10.52 and 8.24±5.24, respectively. The mean BDI scores in TA study and healthy control groups were 18.07±8.49 and 7.47±6.22, respectively. Mean BAI and BDI scores significantly differed between two groups ($p<0.001$). Mean BAI and BDI scores of the participants in two groups were presented in Table 2.

Among the 94 women in the TA study population, 10 (10.6%) of patients had minimal anxiety (BAI score, 0-7), 33 (35.1%) mild (BAI score, 8-15), 30 (31.9%) moderate (BAI score, 16-25) and 21 (22.3%) had severe anxiety (BAI score, 26-63). A total of 51 (54.2%) women in TA group had BAI score of ≥ 16 and were classified as moderate or severe anxiety disorder. In healthy control group, 58 (48.3%) of patients had minimal anxiety, 50 (41.7%) mild, 12 (10.0%) moderate, and 0 (0.0%) had severe anxiety. On the other hand, only 10% of patients in the control group had moderate or severe anxiety.

TABLE 1: Some demographic and clinical characteristics of groups.

	TA Study Group (Mean±SD) (n=94)	Healthy Control Group (Mean±SD) (n=120)	p
Age	27.11±6.29	25.50±5.24	0.083*
BMI	25.83±6.76	24.65±6.38	0.090*
Gravidity	2.41±1.31	2.20±1.16	0.229*
Parity	1.20±1.02	1.06±0.97	0.289*
Gestational age	7.88±2.87	7.48±2.41	0.412*

* Mann Whitney U Test.

TA: Threatened abortion; BMI: Body mass index.

TABLE 2: Comparison of the mean BAI and BDI scores of threatened abortion and control groups.

	TA Study Group (Mean±SD) (n=94)	Healthy Control Group (Mean±SD) (n=120)	p
Mean BAI Score	18.90±10.52	8.24±5.24	<0.001*
Mean BDI Score	18.02±8.49	7.47±6.22	<0.001*

* Mann Whitney U Test.

TA: Threatened abortion; BAI: The Beck Anxiety Inventory; BDI: The Beck Depression Inventory.

The prevalence of anxiety and depression disorders of patients in each group according to anxiety degree were shown in Table 3. The distribution of patients in TA group according to depression degree was as follows: 8 (8.5%) of patients had no depression (BDI score, 0-9), 41 (43.6%) mild (BDI score, 10-16), 37 (39.4%) moderate (BDI score, 17-29) and 8 (8.5%) had severe depression (BDI score, 30-63). In healthy control group, 86 (71.7%) of patients had no depression, 23 (19.2%) mild, 10 (8.3%) moderate, and 1 (0.8%) had severe depression. A total of 45 (47.9%) women in TA group had BDI score of ≥ 17 and were classified as moderate or severe depression disorder. In the other words, only 9.1% of patients in the healthy control group had moderate or severe depression. There was a significant difference in the magnitude of mean BAI and BDI scores between two groups ($p < 0.001$). In other words, patients with TA had significantly higher BAI and BDI scores than healthy controls.

DISCUSSION

Threatened miscarriage is a fairly common complication in early pregnancy and is a leading cause of maternal hospitalisation during pregnancy. It affects approximately 20-25% of all clinically recognised pregnancies.¹ In this present study, we investigated the possible relationship between anxiety, depression and TA and compared the preva-

lence of anxiety and depression disorders in patients with and without TA. The most important finding of this study is that roughly half of the patients with TA had moderate or severe anxiety and depression disorder, and these prevalence rates were higher than the rates for healthy control subjects.

Over the past three decades, numerous studies have been published indicating the negative emotional impact of miscarriage and pregnancy loss on maternal psychology. Most of these studies reported a statistically significant associations between miscarriage and pregnancy loss and maternal psychological morbidities. There is increasing evidence that miscarriage causes maternal mental distress such as depression, anxiety, anger, and grief.⁸⁻²⁰ In the literature, all of these studies investigating the association between anxiety, depression and miscarriage have focused on abortions that resulted in fetal loss such as spontaneous abortion, induced abortion and recurrent abortion. However, there is no comprehensive, prospective case-controlled study specific to emotional and psychological consequences such as anxiety and depression disorders in patients with TA. Threatened miscarriage is different from other types of abortion, because after the documentation of a living embryo, 95% to 98% of threatened abortions do not miscarry and continue beyond 20 weeks of gestation.⁴⁻⁷ In 1989, Friedman and Gath analyzed 67 women who had spontaneous abortion four weeks ago to determine the prevalence of depressive disorder following miscarriage. They reported that up to 50% of women developed depressive disorder following miscarriage and depressive symptoms were significantly associated with a history of previous spontaneous abortion.⁸

Recently, Chojenta et al., using the data of the Australian Longitudinal Study on Women's Health (ALSWH) which is a prospective cohort study investigating the health of over 40 000 Australian women, reported that women with a previous pregnancy loss were more likely to experience sadness or low mood, and excessive worry during a subsequent pregnancy.¹⁸ In a systematic review, Geller et al. reviewed the literature regarding anxiety symptomatology and disorders following

TABLE 3: The prevalence of anxiety and depression disorders in groups.

Psychiatric Disorders, n (%)	TA Study Group (n=94)	Healthy Control Group (n=120)	p
Anxiety			
Minimal	10 (10.6)	58 (48.3)	<0.001*
Mild	33 (35.1)	50 (41.7)	<0.001*
Moderate	30 (31.9)	12 (10.0)	<0.001*
Severe	21 (22.3)	0 (0.0)	<0.001*
Depression			
No	8 (8.5)	86 (71.7)	<0.001*
Mild	41 (43.6)	23 (19.2)	<0.001*
Moderate	37 (39.4)	10 (8.3)	<0.001*
Severe	8 (8.5)	1 (0.8)	<0.001*

* Chi-square Test.

TA: Threatened abortion.

miscarriage.²⁸ Authors reported that miscarrying women are at increased risk for anxiety symptoms immediately following miscarriage and continuing until approximately 4 months post-loss. In 2011, another systematic review conducted by Coleman analyzed the studies published between 1995 and 2009 to measure the association between abortion and indicators of adverse mental health. The results revealed that abortion is a statistically validated risk factor for the development of various psychological disorders.¹⁹ Neugebauer et al. performed a prospective analysis of 459 pregnant women.¹¹ In this prospective case-control study, data of 229 patients with spontaneous abortion and 230 control women were analyzed and it was found that 10.9% of women with sporadic miscarriages experienced at least one episode of major depression. In another study, Craig et al. reported depression disorders in 33% of patients with recurrent miscarriages.²⁰

In our study, the current prevalence rate of moderate and severe anxiety and depression disorder in patients with TA was 54.2% and 47.9%, respectively. Patients with TA displayed higher rates of anxiety and depressive symptoms than healthy controls. We found no published reports including a comparison of prevalence rates of anxiety and depression disorders between patients with TA and healthy controls. However, to make a comparison between our study findings and the above-mentioned study findings is difficult because all previous studies have focused on abortions that resulted in fetal loss. Although the present study was different from the previous studies, the results of these previous studies were similar to our findings when a comparison was made. The most comprehensive review evaluating psychological morbidity following miscarriage was conducted by Lok and Neugebauer in 2007.²⁹ In this comprehensive review, there were numerous studies showing the association between miscarriage and anxiety or depression disorders. The prevalence of major depressive disorder among the miscarrying women in the Friedman's study was 48%.⁸ Garel et al. reported a similar prevalence, with 51% of their studied population for major depression.¹⁰ However, lack of gestational age-matched healthy control group was

the potential limitation of the both studies. In many other studies, elevated anxiety and depressive symptoms were reported in 10-55% of miscarrying women shortly after miscarriage.^{10,13,14}

There are some limitations to our study. The data collection from a single obstetrics clinic from one geographic region is the potential limitation of the study. Therefore, the generalizability of our findings is limited. The absence of longitudinal data as well as control data on psychological symptoms pre-conceptionally, after recovery from illness and postpartum is another limitation of this study. In this current study psychological distress scores were obtained in only physical illness period in the first trimester of gestation. This study has many strengths. The major strength of this study was its prospective nature and the inclusion of a control group of healthy pregnant women without TA. Other important strengths of the study include wide and strict exclusion criteria, and the use of both psychiatric interviews and self-report measures standardized for study populations to assess anxiety and depression scores. In addition, all psychiatric interviews were performed by a single experienced psychiatrist (YU) to avoid possible observer-dependent factors.

Anxiety and depressive disorders are the most common psychiatric conditions among the miscarrying women. The current literature suggests that TA can induce anxiety and depression reaction as substantial as pregnancy loss. For pregnant women, the possibility of pregnancy loss is always been a source of psychological distress. Pregnant women are often unprepared for this traumatic possibility. Therefore, given the often sudden and unexpected nature of the event, TA could be cause a range of psychological reactions, ranging from grief to anxiety and depression. Women with TA are most concerned about the possible causes for their bleeding and the possible pregnancy outcomes. Yet, while a significant amount of research has focused on psychological aspects and sequelae of miscarriage which resulted with early pregnancy loss, any comprehensive study does not exist on the psychological dimension and psychiatric consequences in patients with TA.

In conclusion, approximately one-half of patients with TA suffered some form of moderate or severe anxiety and depression disorder. The psychological distress associated with TA was a direct consequence rather than a cause of TA. The findings of this study indicated a potential link between TA and anxiety and depression disorders. Therefore, patients with TA during pregnancy should be evaluated in terms of anxiety and depression disorders as much as their medical conditions. Medical professionals should be sensitive to psychological

consequences of TA. Psychiatric counseling may be helpful in patients with TA to assess the anxiety and depression degree and provide optimal management, care and support for these patients. However, further larger scale, prospective controlled and homogeneous studies are needed to confirm these results.

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