

# Behcet disease and pregnancy

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## Summary

**Purpose:** Behcet disease (BD) is a multisystemic vasculitis commonly diagnosed in reproductive years. The authors aimed to investigate the relationship between BD and pregnancy outcomes. **Materials and Methods:** In this multicenter retrospective survey study, the authors compared the pregnancy outcomes of BD patients with the healthy controls. **Results:** A total of 298 pregnancies of 94 patients with BD and 219 pregnancies of 95 healthy controls were evaluated. The mean birth weight of all babies of women with BD and the control group were 3,214 grams and 3,351 grams, respectively ( $p = 0.028$ ). The miscarriage rates were also higher in the BD group. The complication rates of pregnancy with hypertension, preeclampsia, preterm labour in the study group and the control group were 12.8% and 11.6%, respectively ( $p = 0.489$ ). **Conclusion:** The current study demonstrated that BD patients delivered smaller babies and they have higher miscarriage rates when compared to the healthy controls which might be due to the vasculitis of the placenta.

**Key Words:** Behcet Disease; Pregnancy outcome; Fetal outcome; Vasculitis.

## Introduction

BD is a multisystemic vasculitis with an unknown etiology. Its prevalence changes in-between different regions of the world and it is more prevalent on the ancient Silk Road.

BD might have many different clinical manifestations like mucocutaneous, ocular, and central nervous system involvement and therefore it is usually called a syndrome rather than a disease [1]. Unlike most of the other vasculitis syndromes, BD might affect both arterial and venous systems and all sizes of vessels [2].

Although BD is diagnosed commonly in the fertile period of life, there is little knowledge on the effects of BD on the pregnancy outcomes and the effects of pregnancy on the disease. The literature on this subject is limited to case reports and small sample-sized studies.

The authors aimed to investigate the relationship between BD and the pregnancy outcomes.

## Materials and Methods

This multicenter retrospective study was conducted in Dermatology Department of Tokat University Medicine Faculty, Dermatology Department of Canakkale Eighteen March University Medicine Faculty, Dermatology Department of Hatay Mustafa Kemal University Medicine Faculty, Dermatology Department of Afyon Kocatepe University Medicine Faculty, Dermatology Clinic of Ankara Kecioren Education and Research Hospital, and Dermatology Department of Elazig Firat University Medicine Faculty.

The local ethical committee approval was taken from Canakkale Eighteen March University and the permission of each institution where the study conducted was taken. Written consent of patients were taken before included into the study.

BD diagnosis was done according to the International Study Group Criteria [3]. Age-matched control group patients were chosen among the women who applied to the dermatology polyclinic with non-systemic diseases in the same period. Patients with other systemic diseases and women without any pregnancy history were excluded from the study.

Questionnaires were fulfilled by the dermatologists. Pregnancy and delivery histories of the patients were taken. The relationship between BD and pregnancy; maternal and fetal outcomes and the BD progression during the pregnancy were evaluated retrospectively.

Data were analysed with SPSS for Windows 11.5 (Statistical Package for Social Sciences). Continuous variables were evaluated for normal distribution by using Kolmogorov Smirnov Test. Descriptive statistics for continuous variables were done by mean  $\pm$  standard deviation and for nominal variables were done by Chi-square test. A  $p < 0.05$  was accepted as statistically significant.

## Results

A total of 298 pregnancies of 94 patients with BD and 219 pregnancies of 95 healthy control patients were evaluated. The number of the patients included from each hospital is summarized in Table 1.

Mean birth weight of all babies of women with BD and control group were 3,214 and 3,351 grams, respectively. Babies of women in the control group were significantly heavier than the babies of women with BD ( $p = 0.028$ ). The characteristic properties of BD group and control group are

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summarized in Table 2. Mean age of diagnosis of BD in the study group was  $32.29 \pm 9.43$  years.

Episiotomy infection was seen in two women with BD and transient neonatal lesions were seen in the babies of five women but none of them required treatment for the baby.

From 94 BD patients, 74 of them (78.7%) had no changes, 18 of them (19.2%) had exacerbation, and two of them (2.1%) had remission during the pregnancy.

The comparison of clinical manifestations of BD according to the menstrual cycle significantly correlated with clinical manifestations during the pregnancy. If a women had no changes during menstruation it might help to predict that she would not have changes in clinical manifestations during the pregnancy.

Complication ratios of pregnancy with hypertension, preeclampsia, preterm labour in the study group, and the control group were 12.8% and 11.6%, respectively ( $p = 0.489$ ). Still birth ratios were not significantly different between groups either.

## Discussion

In the current study, 298 pregnancies in 94 women with BD were compared with 219 pregnancies in 95 healthy controls and it was demonstrated that BD increased the miscarriage rates and birth weight when compared with the healthy controls, but BD did not increase the pregnancy complications. Pregnancy usually had no influence on the symptoms of BD.

Marshal *et al.* [4] evaluated 61 pregnancies in 23 women retrospectively. They compared them with 83 pregnancies of 30 women with recurrent oral ulcers and 61 pregnancies of 20 healthy women. They investigated the pregnancy complications, the fetal outcomes, and BD course during the pregnancy and the postpartum period. They found no significant difference among groups on the pregnancy complications and the fetal outcomes. The only serious complication was the Budd-Chiari Syndrome of a patient in the puerperium which might be coincidental, one patient had oral ulcer exacerbation, and one had recurrent episiotomy infection in the study group. They report no neonatal BD from 55 newborns in the study group. They concluded that even they had a small sample size perinatal outcome of BD patients were good, the clinical manifestation of the disease was not worsened by the pregnancy.

Jadaon *et al.* [5] evaluated 135 pregnancies of 31 BD women in their retrospective study. Mean age of the diagnosis was  $24.48 \pm 8.84$  years. Mean parity at the diagnosis was  $4.35 \pm 2.66$ . They formed an age, parity, and ethnic origin that matched the control group to compare the study group. When comparing the pregnancies of the same patients before and after BD diagnosis, the miscarriage ratios did not differ but the pregnancy complications increased after the diagnosis of BD. They showed that remission was more prevalent than exacerbation during the pregnancy and

Table 1. — *Distribution of the patients according to the hospitals.*

Institution	Behcet's group	Control group
Tokat University	26	26
Canakkale University	19	20
Hatay University	15	13
Afyon University	12	16
Ankara Kecioren Hospital	12	0
Elazig University	10	20
Total	94	95

Table 2. — *Demographic characteristics and obstetric outcomes of the groups.*

	BD	control	<i>p</i>
Age (years)	$39.65 \pm 10.03$	$40.07 \pm 10.09$	0.778
Gravida	$3.17 \pm 1.44$	$2.30 \pm 1.14$	<0.001
Parity	$2.56 \pm 1.06$	$1.93 \pm 0.93$	<0.001
Abortus	$0.55 \pm 0.87$	$0.33 \pm 0.61$	0.05
Ectopic pregnancies	$0.05 \pm 0.30$	$0.03 \pm 0.17$	0.552
Birth weight of			
first newborn (grams)	$3,153 \pm 575$	$3,373 \pm 541$	0.008
Mean birth weight of			
all newborns (grams)	$3,214 \pm 416$	$3,351 \pm 428$	0.028

patients tended to continue in the same direction after the delivery. They found that the pregnancy complications were more prevalent in BD group when compared to the control group. Neonatal outcomes including birth weight was not different between groups. They concluded that while maternal outcomes adversely affected from BD, neonatal outcomes did not change when compared with the control group. Remissions were five times more prevalent than exacerbations during the pregnancy and puerperium. They concluded that the pregnancy had no adversity but positive effects on BD, on the other hand, BD might have some adverse effects on the pregnancy outcomes including higher miscarriage rates [5].

The present authors demonstrated that neonatal birth weight was significantly lower in BD group unlike Jadaon *et al.* [5]. This difference might be because of the small sample size of the previous study. Like the previous studies [5], the miscarriage rates were higher in BD group in the current study.

In a study conducted in 2008 placentas of two patients were evaluated microscopically and it was demonstrated that both first trimester and term placentas of BD patients showed necrotizing villitis and neutrophil dominant infiltration. The authors excluded the infectious diseases both clinically and histologically [6]. As a result, higher miscarriage rates and lower birth weights in BD group in the current study can be explained by the vasculitis of the placenta. Even when a patient conceives in remission period, treatment might be used to decrease the miscarriage and the low birth weight rates especially in those who have poor obstetric history.

The course of BD during pregnancy changes among patients even in the different pregnancies of the same patient. Hamza *et al.* [7] evaluated 21 pregnancies of eight patients and while remission were seen in 12 pregnancies, exacerbations were seen in nine pregnancies. All exacerbations were seen in the dermatological manifestations such as erythema nodosum, genital aphthosis, necrotic pseudofolliculitis, and buccal aphthosis. In the retrospective study of Uzun *et al.* [8] the authors concluded that pregnancy did not affect BD markedly and BD did not increase the complications of pregnancy after analyzing 44 pregnancies of 28 patients. Jadaon *et al.* reviewed the literature and concluded that remission rate was 56.6% (83 pregnancies) and exacerbation rate was 35.6% (51 pregnancies) during pregnancy [5]. Bang *et al.* [9] demonstrated higher exacerbation ratio in their study. They evaluated 27 pregnant patients and demonstrated that the majority of exacerbations occurred in the first trimester. An interesting finding of the authors was that exacerbation was seen commonly in the mucocutaneous manifestations when compared with other types. Majority of our patients had neither remission nor exacerbation in the present study.

In a recent study Zhang *et al.* analyzed 334 BD patients and concluded that the mean age of onset was  $35.8 \pm 11.1$  years [10] which was concordant with the present study.

Neonatal BD is a very rare condition and almost always seen with the active maternal disease. It is manifested with oral ulcers, skin lesions, fever, and leukocytosis [11]. In the current study only five babies showed transient skin lesions which did not need to be treated.

The main factor that strengthens the present study is the large sample size. To the authors' knowledge, it is the largest sized study in the English literature. The main limitation of this study is its retrospective design. Because BD is a relatively rare disease and follow-up period must be very long, conducting a prospective study is not efficient. Previous studies were also performed in a retrospective manner. Because it is sometimes difficult to remember the specific symptom of a chronic disease or the treatment taken in a particular time like pregnancy, the authors only asked the general exacerbation or remission of the disease during pregnancy. Nearly every woman re-

members the birth weight of their babies even after a long time if they are delivered in a hospital. So such specific questions were asked to rule out bias.

## Conclusion

The authors demonstrated that BD patients deliver smaller babies and they have higher miscarriage rates when compared to the healthy controls. This might be because of the vasculitis of the placenta and more studies must be done on the subject to highlight the cause of the situation.

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