

베체트병이 합병된 임신에서 산모와 태아의 예후

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The outcome of pregnancy complicated by Behçet's disease

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Objective: The aim of this study is to investigate the effects of Behçet's disease (BD) on pregnancy outcome.

Methods: We evaluated pregnancies in women who had been diagnosed as BD prior to pregnancy. The medical records of 39 pregnancies in 27 women from May, 1991 to July, 2007 with underlying BD and 499 randomly selected normal pregnancies not associated with BD were retrospectively reviewed. Women with other connective tissue disorders like systemic lupus erythematosus or rheumatoid arthritis and medical illnesses such as diabetes mellitus or hypertension were excluded from the study. The statistical significance was defined as $P < 0.05$.

Results: The influence of BD on pregnancy and its outcome were studied in comparison with the normal group. The age, parity, spontaneous abortion rates, delivery weeks, cesarean section rates, premature rupture of membranes, preterm birth, fetal birth weights, APGAR scores, and intrauterine fetal death were compared. Majority of the women with BD were primiparae ($P < 0.001$), and intrauterine fetal death rates ($P < 0.001$) were significantly higher in the study group. The 1-minute APGAR score ($P < 0.005$) of 4 or less and 5-minute APGAR score ($P < 0.039$) of 7 or less appeared more in Behçet's group. The incidences of pregnancy complications including spontaneous abortion, premature rupture of membranes, preterm birth, and small for gestational age did not show statistically significant differences between the two groups.

Conclusion: The results show higher rates of primiparity, lower APGAR scores, and higher intrauterine fetal death rates in patients with BD which implies that the disease may adversely affect pregnancy. Therefore, it is important for pregnant women with BD to receive proper antenatal care and preconception counseling prior to pregnancy.

Key Words: Behçet's disease, Pregnancy outcome

Introduction

Behçet's disease (BD) is a multisystem inflammatory disorder characterized by recurrent oral and genital

ulcers and eye inflammation. It is most common in the Middle East and the Mediterranean regions, although it also affects Caucasians.¹⁻⁷ Turkey has the highest prevalence (80~370 per 100,000 cases). The prevalence in Japan, Korea, China, Iran, and Saudi Arabia ranges from 13.5 to 20 cases per 100,000 whereas it is lower in Western countries; 0.12~0.33 per 100,000 in the US.^{1,2} It was named after Behçet,

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a Turkish dermatologist who, in 1937, popularized this syndrome as a distinct clinical entity.¹ Since then, additional features such as arthritis, thrombophlebitis, erythema nodosum, gastrointestinal lesions, central nervous system lesions, epididymitis, vascular injuries, and hypercoagulability have been included in the variable patterns of the disease.¹ The vascular system, both arterial and venous, is affected in 25% of patients, and involvement of the pulmonary vascular tree has been reported in 5% of these patients.^{3,4,15,16.}

Vasculitis, clinicopathologic process characterized by inflammation and necrosis of blood vessels, and thromboembolic disease are known complications of BD and may be particularly problematic during pregnancy.⁸ These factors have been shown to be associated with pregnancy-related disorders or even failed pregnancies and may have harmful effects on the immediate and long-term health of the mother and the baby.

Although BD is mainly diagnosed during the fertile years, little is known about its influence on the outcome of gestation. The effect of pregnancy and the puerperium on the disease activity is also poorly understood. The objective of this study is to investigate the effects of BD on pregnancy outcome.

Materials and Methods

We evaluated the results of pregnancies and disease course in women who were diagnosed as having BD. The medical records of 39 pregnancies in 27 patients from May, 1991 to July, 2007 with underlying BD and 499 randomly selected normal pregnancies during the same period not associated with BD were retrospectively reviewed. Women with other connective tissue disorders like systemic lupus erythematosus or rheumatoid arthritis and medical illnesses such as diabetes mellitus or hypertension were

excluded from the study.

All pregnancies of the patients with BD were evaluated as a study group and were compared with the control group. The characteristics of the patients and the pregnancy outcome including age, parity, gestational age at delivery, spontaneous abortion history, cesarean section, premature rupture of membranes, preterm birth, fetal birth weights (small for gestational age), APGAR scores at 1 and 5 minutes, and intrauterine fetal death were investigated in this study.

Statistical analysis was performed using SPSS version 14.0 (SPSS Inc., Chicago, USA). The student's *t*-test was applied to compare the characteristics of the two groups and Chi-Square test and Fisher's exact test to examine the significance of the association among the categorical variables. Quantitative variables are presented as mean \pm standard deviation, and *P*-values less than 0.05 were considered significant.

Results

Twenty-seven patients with BD who had 39 pregnancies were compared with randomly selected 499 normal pregnancies in the control group. The general characteristics of the patients and pregnancy outcomes were studied in comparison. As seen in Table 1, the maternal mean age at pregnancy and the gestational weeks at delivery showed no significant difference. However, the rate of primiparity (66.7%) over multiparity (33.3%) in women with BD was significantly higher ($P < 0.001$) than the rate (15.6% over 84.4%) in the control group.

The pregnancy outcome in women with BD was compared with the control group, and the pregnancy complications including spontaneous abortion (17.9% vs. 13.6%), premature rupture of membranes (10.3% vs. 7.6%) and preterm birth (15.4% vs. 12%) tend to occur more frequently in BD patients than in normal

Table 1. Patient characteristics and pregnancy outcome in women with Behcet's disease compared with the control group

	Behcet's group (n=39)	Control group (n=499)	P-value
Maternal age (years)	29.8±4.3	30.7±4.2	0.182
Parity			
Primiparity	26 (66.7%)	78 (15.6%)	<0.001*
Multiparity	13 (33.3%)	421 (84.4%)	
Gestational age at delivery (weeks)	37.4±4.8	38.1±3.2	0.369
Spontaneous abortion history	7 (17.9%)	68 (13.6%)	0.453
Premature rupture of membranes	4 (10.3%)	38 (7.6%)	0.554
Cesarean section	17 (43.6%)	226 (45.3%)	0.837
Preterm birth	6 (15.4%)	60 (12%)	0.538
Intrauterine fetal death	3 (7.7%)	3 (0.6%)	<0.001*
Fetal birth weight (grams)	2,955±789	3,151±678	0.087
Small for gestational age	5 (12.8%)	47 (9.4%)	0.489
APGAR score (1 min)			
≤4	6 (20.7%)	26 (5.2%)	0.005*
≥5	23 (79.3%)	473 (94.8%)	
APGAR score (5 min)			
≤7	6 (20.7%)	42 (8.4%)	0.039*
≥8	23 (79.3%)	457 (91.6%)	

*P-value<0.05 by Student's *t*-test, Chi-square test (Fisher's exact test).

pregnancies though the differences did not reach the statistically significant value. As for neonates, APGAR scores at 1 ($P<0.005$) and 5 ($P<0.039$) minutes after birth were distinctively lower in Behçet's group. The 1-minute APGAR score of 4 or less (20.7% vs. 5.2%) and 5-minute APGAR score of 7 or less (20.7% vs. 8.4%) appeared more frequently in Behçet's group. Moreover, 3 (7.7%) intrauterine fetal death were observed in 39 pregnancies in the study group as compared with 3 (0.6%) out of 499 pregnancies in the control group ($P<0.001$). Intrauterine fetal death rate was significantly higher in BD group. There were no significant differences in cesarean section rates and fetal birth weights.

Discussion

The prevalence of BD is known to be high in Japan, China, Turkey, Tunisia, and the Mediterranean and

the Middle Eastern countries and the prevalence of BD in Korea also has been reported as high.^{5,6} Since BD is mainly diagnosed during the reproductive periods of life, it is important to have knowledge regarding its influence on the outcome of gestation in women with BD.⁷

The outcome of pregnancy in BD patients has not yet been widely investigated. Hamza et al. studied 21 pregnancies in eight women with BD and did not find miscarriages, prematurity, or perinatal death in any of the cases.^{10,13,14} Marsal and colleagues could not find any unfavorable influence on pregnancy outcome, labor, and neonatal outcome in BD patients as compared with healthy women.¹¹ In contrast, Guzman and co-workers reported a case in which a woman with BD had ruptured membranes and evidence of fetal distress at 36 weeks and subsequently delivered a severely growth-restricted fetus (<3%).¹² Jadaon et al. showed an increase in miscarriages and pregnancy

complication rates in BD as compared with the controls, which they explained by the vasculitic process underlying BD, as well as by blood hypercoagulability that takes place during pregnancy in BD.¹

We studied the relationship between pregnancy and BD by analyzing retrospectively maternal complications of pregnancy and fetal outcome, comparing the pregnancies complicated by BD with the normal pregnancies of healthy women. Unlike most of the previous studies, our data, although the limited number of cases and the absence of prospective studies made it difficult to draw an affirmative conclusions, showed higher rates of primiparity, lower APGAR scores of the infants at birth, and higher intrauterine fetal death rates in patients with BD, suggesting that the disease may adversely affect pregnancy and especially

fetal outcome.^{9,13,14} The apparently lower multiparity in BD patients implies that there is a notable difference in the risk for pregnancy outcome between the two groups. The higher tendency of spontaneous abortion, premature rupture of membranes, preterm delivery, and low fetal birth weight featuring small for gestational age in BD group also advocates the conclusion.

The pregnancy complicated by BD should be monitored closely for evidence of possible adverse outcome such as intrauterine fetal death, and for increase of intrauterine growth restriction and fetal compromise as in pregnancies complicated by similar connective tissue disorders. It is important for pregnant women with BD to receive proper antenatal care and pre-conception counseling prior to pregnancy.

References

1. Jadaon J, Shushan A, Ezra Y, Sela HY., Ozcan C, Rojansky N. Behçet's disease and pregnancy. *Acta Obstet Gynecol Scand* 2005; 84: 939-44.
2. Hurt WG, Cooke CL, Jordan WP, Bullock JP, Rodriguez GE. Behçet's syndrome associated with pregnancy. *Obstet Gynecol* 1979; 53(3 Suppl): 31S-3S.
3. Michelson JB, Friedlaender MH. Behçet's disease. *Int Ophthalmol Clin* 1990; 30: 271-8.
4. Klipple GL, Riordan KK. Rare inflammatory and hereditary connective tissue diseases. *Rheum Dis Clin North Am* 1989; 15: 383-98.
5. Chajek T, Fainaru M. Behçet's disease. Report of 41 cases and a review of the literature. *Medicine (Baltimore)* 1975; 54: 179-96.
6. Bang D, Lee JH, Lee ES, Lee S, Choi JS, Kim YK, et al. Epidemiologic and clinical survey of Behçet's disease in Korea: the first multicenter study. *J Korean Med Sci* 2001; 16: 615-8.
7. Bang D, Chun YS, Haam IB, Lee ES, Lee S. The Influence of pregnancy on Behçet's disease. *Yonsei Med J* 1997; 38: 437-43.
8. Ramsey-Goldman R. The effect of pregnancy on the vasculitides. *Scand J Rheumatol Suppl* 1998; 107: 116-7.
9. Uzun S, Alpsoy E, Durdu M, Akman A. The clinical course of Behçet's disease in pregnancy. *J Dermatol* 2003; 30: 499-502.
10. Hamza M, Eleuch M, Zribi A. Behçet's disease and pregnancy. *Ann Rheum Dis* 1988; 47: 350.
11. Marsal S, Falga C, Simeon CP, Vilardell M, Bosch JA. Behçet's disease and pregnancy relationship study. *Br J Rheumatol* 1997; 36: 234-8.
12. Guzelian G, Norton ME. Behçet's syndrome associated with intrauterine growth restriction: a case report and review of the literature. *J Perinatol* 1997; 17: 318-20.
13. Gül U. Pregnancy and Behçet's disease. *Arch Dermatol* 2000; 136: 1063-4.
14. Ferraro G, Lo Meo C, Moscarelli G, Assennato E. A case of pregnancy in a patient suffering from the Behçet Syndrome: immunological aspects. *Acta Eur Fertil* 1984; 15: 67-70.
15. Espinosa G, Cervera R, Reverter JC, Tàssies D, Font J, Ingelmo M. Vascular involvement in Behçet's disease. *Isr Med Assoc J* 2002; 4: 614-6.
16. Krause I, Weinberger A. Vasculo-Behçet's disease. *Isr Med Assoc J* 2002; 4: 636-7.

= 국문초록 =

목적: 본 연구는 베체트병이 합병된 임신에서 산모와 태아의 예후에 관하여 알아보고자 하는 것이다.

연구 방법: 1991년 5월부터 2007년 7월까지 본원에서 베체트병으로 진단된 39명의 산모와, 같은 기간 동안 무작위 추출된 499명의 정상 산모를 대상으로 후향적으로 의무기록을 분석하여 연구되었다. 전신성홍반성루프스 또는 류마티스관절염과 같은 다른 결체조직 질환과 고혈압, 당뇨와 같은 내과적 질환이 동반된 경우는 본 연구에서 제외되었다.

결과: 베체트병이 합병된 임신에서의 예후와 정상 임신에서의 예후를 연구하기 위해 산모의 나이, 산과력, 유산율, 분만주수, 제왕절개술여부, 조기양막파수 여부, 조산, 출생 시 체중, APGAR 점수, 자궁 내 태아사망률을 비교 분석하였다. 정상 산모에 비해 베체트병을 진단받은 산모에서 초산모의 비율이 더 많았고 ($P<0.001$), 1분 APGAR 점수가 4점 이하인 경우 ($P<0.005$)와 5분 APGAR 점수가 7점 이하인 경우 ($P<0.039$)가 더 빈번하게 나타났으며, 자궁내 태아사망의 발생빈도가 유의하게 ($P<0.001$) 증가됨을 확인하였고, 기타 산과적 합병증은 차이가 없었다.

결론: 베체트병은 산모와 태아에게 부정적 영향을 줄 가능성이 있으므로, 베체트병으로 진단된 여성이 임신을 원하는 경우 더욱 주의 깊은 임신 전 상담이 필요하며, 임신 후에는 좀 더 적극적인 산전진찰이 필요하다고 할 수 있을 것이다.

중심단어: 베체트병, 임신예후
