



Serum Folic Acid Levels in Women With Recurrent Early Pregnancy Loss

Şahin ZETEROĞLU¹, Yusuf ÜSTÜN¹, Yaprak ENGİN-ÜSTÜN¹, Ümit ZETEROĞLU², Murat KARAYEL³

¹Department of Obstetrics and Gynecology, Faculty of Medicine, Yüzüncü Yıl University, Van, Turkey

²3rd Maternity and Women Health Clinic, İzmir Atatürk Training Hospital, İzmir, Turkey

³Van Maternity Hospital, Van, Turkey

Abstract

Objective: The aim of the study was to compare the folate status of women with spontaneous recurrent abortion with healthy pregnant women of similar gestational age.

Materials and Methods: Sixteen women with recurrent spontaneous abortions and 25 consecutive women attending their antenatal visits in the first trimester of pregnancy were enrolled into the study. We measured serum folate levels.

Results: There were no significant differences between two groups in age and body mass index. We observed a significant decrease in median serum folate concentrations in women with spontaneous recurrent early pregnancy losses.

Conclusion: Decreased serum folic acid levels might have an important role in etiology of recurrent early pregnancy loss.

Key words: recurrent pregnancy loss, folic acid, spontaneous abortion

Özet

Rekürren Erken Abortusu Olan Kadınlarda Serum Folik Asit Düzeyleri

Amaç: Aynı gestasyonel yaştaki, rekürren spontan abortusu olan gebeler ile sağlıklı gebeliği olan kadınlardaki folat düzeyini karşılaştırmak.

Materyal ve Metot: Çalışmaya, ilk trimesterde başvuran rekürren spontan abortusu olan 16 kadınla sağlıklı gebeliği olan 25 kadın dahil edildi. Serum folik asit düzeyleri ölçüldü.

Sonuçlar: Gruplar arasında yaş ve vücut kütle indeksi açısından anlamlı farklılık olmadığı saptandı. Rekürren spontan abortusu olan kadınlarda medyan serum folat konsantrasyonunun anlamlı olarak daha düşük olduğu saptandı.

Tartışma: Düşük serum folat düzeyi rekürren spontan abortusların etiolojisinde önemli bir role sahip olabilir.

Anahtar sözcükler: rekürren abortus, folik asit, spontan abortus

Introduction

About 40% of pregnancies are spontaneously aborted (1). In certain women, spontaneous abortion is habitual. Multiple mechanisms are said to play a role in the etiology of spontaneous and recurrent abortions. It is now widely accepted that spontaneous recurrent abortion is a heterogeneous condition, with several etiological factors such as immunological disorders, structural uterine anomalies, chromosomal anomalies, and endocrinological defects (2). In most cases, however, the underlying cause is not apparent and the condition is therefore considered unexplained.

The aim of the study was to compare the folate status of women with spontaneous recurrent abortion with healthy pregnant women of similar gestational age.

Materials and Methods

Sixteen women with recurrent spontaneous abortions and 25 consecutive women attending their antenatal visits in the first trimester of pregnancy were enrolled into the study. Recurrent early pregnancy loss was defined as at least three consecutive spontaneous early pregnancy losses within 16 weeks after the last menstruation (excluding ectopic and molar pregnancies). Women were excluded if they had vitamin supplementation within six months before the trial. Controls had no spontaneous abortion, and no folic acid supplementation for six months. Blood samples for both groups were collected in the fasting state. We measured serum folate levels. Concentrations of folate were determined by enzyme linked assays.

Corresponding Author: Şahin Zeteroğlu, MD
Yüzüncü Yıl Üniversitesi Tıp Fakültesi
Kadın Hastalıkları ve Doğum AD, 65200 Van, Türkiye
Tel: 0 432 216 47 10/ 1163; 0 532 424 09 19
E-mail: zeteroglu@artemisonline.net

**Table 1. Demographic data and folate status of the groups**

	Study group (n=16)	Control group (n=25)	P value
Age (year)	27.75±8.00	26.56±3.95	0.52
BMI (kg/m ²)	24.82±4.15	23.96±3.85	0.50
Folate status (ng/mL)	6.43±5.04	8.96±4.90	0.04
Gestational age (week)	11.38±4.21	11.08±3.63	0.81

Results were given as mean ± standard deviation. Because of the normal distribution of variables, Student's t-test was used for statistical analysis. $P < 0.05$ was considered to be significant.

Results

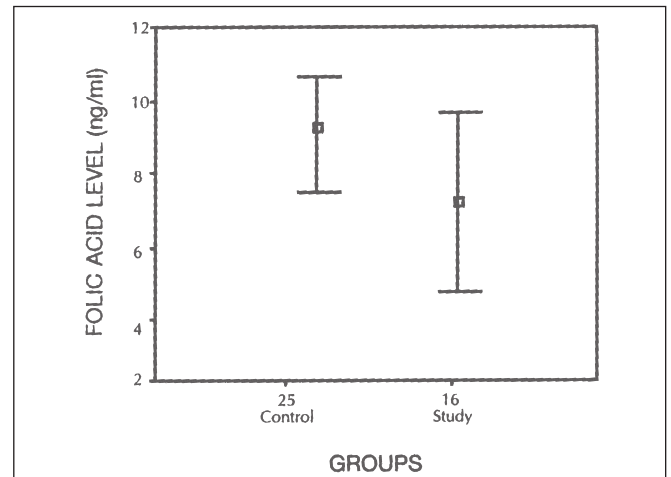
There were no significant differences between two groups in age and body mass index. The gestational period was not significantly different between normal pregnancy and study group (Table 1).

The distribution of the serum concentrations of folate in both women with recurrent spontaneous abortion and controls is depicted in Figure 1. We observed a significant decrease in median serum folate concentrations in women with spontaneous recurrent early pregnancy losses ($p=0.04$).

Discussion

Folic acid is an essential micronutrient. Our study has shown a significant decrease in serum plasma folate levels in the group of patients with recurrent early pregnancy loss. So our study revealed that decreased serum folic acid levels might have an important role in etiology of recurrent early pregnancy loss. But Neiger et al. concluded that low folate concentrations did not appear to be associated with an increased risk of pregnancy loss and adverse outcome (3). Sutterlin et al. also indicated that folic acid and vitamin B₁₂ deficiency was not a common metabolic disorder among women with recurrent spontaneous abortion, implying that these two vitamins did not play an important role in the etiology of habitual abortion, but they investigated folate concentrations in those women, not during, but after their pregnancies (4). Reznikoff-Etievant et al. noticed no difference between early recurrent abortion cases and controls for folate (5).

Although our results are not consistent with the results of these studies, there are many other studies supporting our results. Martin et al. observed a significant association between threatened abortion and reduced serum folate concentrations (6). Pietzrik et al. found low concentrations of serum folate in habitually aborting gravidas than in controls

**Figure 1. Distribution of folate status in both groups**

(-3.1 ng/mL) and in first-trimester aborters than in controls (-2.3 ng/mL) (7). Nelen et al. also observed statistically significant lower median serum folate concentrations in women who had spontaneous recurrent early pregnancy loss (8). In several reports, other sensitive markers of folate metabolism such as plasma total homocysteine were found to be elevated in recurrent early pregnancy loss (9,10).

The differences of these results are probably due to small samples or selection of controls. Larger randomised controlled trials are needed for further detailed information.

References

1. Abir R, Ornoy A, Hur HB. The effects of sera from women with spontaneous abortion on the in vitro development of early somite stage rat embryos. *Am J Reprod Immunol* 1994;32:73-81.
2. Bulletti C, Flamingi C, Giacomucci E. Reproductive failure due to spontaneous abortion and recurrent miscarriage. *Hum Reprod Update* 1996;2:118-36.
3. Neiger R, Wise C, Contag SA. First trimester bleeding and pregnancy outcome in gravidas normal and low folate levels. *Am J Perinatal* 1993;10:460-2.
4. Sutterlin M, Bussen S, Ruppert D, Steck T. Serum levels of folate and cobalamin in women with recurrent spontaneous abortion. *Hum Reprod* 1997;12(10):2292-6.
5. Reznikoff-Etievant, Zittoun J, Vaylet C, Pierre P, Milliez J. Low vitamin B₁₂ level as a risk factor for very early recurrent abortion. *Eur J Obstet Gynecol Reprod Biol* 2002;104:156-9.
6. Martin RH, Harper TA, Kelso W. Serum folic acid in recurrent abortion. *Lancet* 1965;1:670-2.
7. Pietzrik K, Prinz R, Reusch K, Bung P, Malmann P, Chronides A. Folate status and pregnancy outcome. *Ann N Y Acad Sci* 1992; 669:371-3.
8. Nelen WL, Blom HJ, Steegers EA, Heijer MD, Thomas CM, Eskes TK. Homocysteine and folate levels as risk factors for recurrent early pregnancy loss. *Obstet Gynecol* 2000;95:519-24.
9. Steegers-Theunissen RPM, Boers GHJ, Blom HJ, Trijbels FJM, Eskes TKAB. Hyperhomocysteinemia and recurrent spontaneous abortion or abruptio placentae. *Lancet* 1992;339:1122-3.
10. Quere I, Bellet H, Hoffet M, Janbon J, Mares P, Gris JC. A woman with five consecutive fetal deaths: Case report and retrospective analysis of hyperhomocysteinemia prevalence in 100 consecutive women with recurrent miscarriages. *Fertil Steril* 1998;69:152-4.