The Relationship between Homocysteine Levels and Spontaneous Abortion in Iranian Women with Migraine

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Dear Editor-in-Chief

Spontaneous abortion (SA) imposes great emotional and financial costs to young couples and society (1). Some recent investigations have shown hyperhomocysteinemia as a risk factor for SA; however, there is controversy in this regard (2, 3). Due to the importance of SA in pregnant women, regarding scare and conflicting data on relationship between homocysteine levels and SA, and since high homocysteine levels in patients with migraine can increase characteristics of migraine attacks such as its severity, frequency, and duration (4-6), we aimed to investigate the association between serum levels of homocysteine and SA among women with migraine.

This cross-sectional study was conducted on 76 women with migraine, aged 25-45 yr, in Khorshid and Emam Mosa Sadr clinics affiliated to Isfahan University of Medical Sciences, Isfahan, Iran, during 2014. Migraine was diagnosed by a neurologist according to International Headache Society (*IHS*) criteria.

Patients suffering from migraine in a long time with current diagnosis of migraine with aura and a one-year history of severe, recurrent attacks (1 to 8 attacks per month) were selected. Patients with chronic heart disease, previous stroke incidence, chronic renal failure, and with history of

taking vitamin B supplements and history of abortion before migraine diagnosis were excluded from the study.

After getting approved by Ethical Committee of Isfahan University of Medical Sciences, and taking consent from all participants, we collected demographic characteristics (age, medical history, family history of migraine, taking of vitamin and mineral supplements and anti-migraine drugs intake) and SA information (occurrence and time of SA) from each patient. In this study, SA was considered as pregnancy that ends before 20th wk. Among 70 patients with migraine, 20 patients (28%) experienced SA. Mean homocysteine levels and the proportions of subjects with hyperhomocysteinemia were higher among patients with SA than those without (Table 1).

Multivariable odds ratio and 95% confidence intervals for the association between homocysteine levels and SA are presented in Table 2. In crude model, there was a significant positive relationship between homocysteine levels and SA (P=0.006). This association remained significant even after adjustment for potential confounding variables such as BMI, WC, family history of migraine and long-term anti-migraine drugs intake (P=0.034).

Table 1: Comparison of homocysteine levels and anthropometric measurements in patients with and without SA*

Variable	Patients with SA Mean (SD) or N (%)	Patients without SA Mean (SD) or N (%)	*P*-value
Age (years)	38.17 ± 6.51	33.05 ± 6.59	0.03
BMI (kg/m2)†	27.63 ± 4.40	26.09 ± 4.85	0.24
WC (cm)††	86.51 ± 7.77	82.84 ± 8.95	0.12
Homocysteine (μm/l)	8.95 ± 2.61	7.32 ± 2.07	0.008
Hyperhomocysteinemia‡	8 (40%)	6 (12%)	0.012
Family history of migraine	13 (65%)	30 (60%)	0.45
Drug consumption‡‡	19 (95%)	44 (88%)	0.34

*Spontaneous abortion
† Body Mass Index
††Waist Circumstance
‡Considered as homocysteine concentration higher than 10μm/l
‡‡long-term consumption of anti-migraine drugs such as corticosteroids and analgesics drugs

Stratified analysis by age revealed a significant positive association between homocysteine levels and SA among patients 35 yr and older (P=0.006). This relationship was significant even after adjustment for potential confounders (P=0.009). No significant relationship was found between homocysteine levels and SA among patients less than 35 yr.

Table 2: Results of logistic regression for association between homocysteine levels and SA*

Variable	Total		Age < 35		Age ≥35	
	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
Crude	1.41 (1.10-1.80)	0.006	0.91 (0.57-1.47)	0.70	1.58 (1.13-2.19)	0.006
Model 1	1.43 (1.09-1.88)	0.009	1.16 (0.59-2.32)	0.67	1.83 (1.21-2.76)	0.004
Model 2	1.43 (1.08-1.90)	0.012	1.14 (0.57-2.27)	0.70	1.80 (1.19-2.74)	0.006
Model 3	1.35 (1.02-1.79)	0.034	1.16 (0.59-2.27)	0.67	1.72 (1.14-2.58)	0.009

*Spontaneous abortion
Model 1: Adjusted for BMI and WC
Model 2: Additionally adjusted for family history of migraine
Model 3: Further controlled for long-term consumption of anti-migraine drugs such as corticosteroids and analgesics drugs

In spite of several studies, which assess this relationship between homocysteine levels and SA in other populations, this study examined this association among migraine patients. In consistent with our results, homocysteine level was associated with increased risk of SA (7). In addition, *w*omen with unexplained recurrent SA had high levels of serum homocysteine (6).

The high homocysteine levels are positively associated with SA among patients over 35 yr, without any significant association in patients below 35 yr old. A large number of studies have found a significant correlation between age and pregnancy loss. Therefore, high homocysteine levels in the older age range may increase the incidence of SA.

Conflict of Interests

The authors declare that there is no conflict of interests.

References

1. Eschenbach DA (2015). Treating spontaneous and induced septic abortions. *Obstet Gynecol*, 125 (5): 1042-8.

2. Lamont K, Scott NW, Jones GT, Bhattacharya S (2015). Risk of recurrent stillbirth: systematic review and meta-analysis. *BMJ*, 350: h3080.
3. Mascarenhas M, Habeebullah S, Sridhar MG (2014). Revisiting the role of first trimester homocysteine as an index of maternal and fetal outcome. *J Pregnancy*, 2014: 123024.
4. Micle O, Muresan M, Antal L, Bodog F, Bodog A (2012). The influence of homocysteine and oxidative stress on pregnancy outcome. *J Med Life*, 5(1): 68-73.
5. Sadeghi O, Nasiri M, Maghsoudi Z, et al (2015). Effects of pyridoxine supplementation on severity, frequency and duration of migraine attacks in migraine patients with aura: A double-blind randomized clinical trial study in Iran. *Iran J Neurol*, 14 (2): 74-80.
6. Nelen WL, Blom HJ, Steegers EA, et al (2000). Homocysteine and folate levels as risk factors for recurrent early pregnancy loss. *Obstet Gynecol*, 95(4): 519-24.
7. Kim NK, Choi YK, Kang MS, et al (2006). Influence of combined methylenetetrahydrofolate reductase (MTHFR) and thymidylate synthase enhancer region (TSER) polymorphisms to plasma homocysteine levels in Korean patients with recurrent spontaneous abortion. *Thromb Res*, 117: 653-8.

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