Original Article

Combination of Thrombophilic Gene Polymorphisms as a Cause of Increased the Risk of Recurrent Pregnancy Loss

Raheleh Torabi [1], Saeed Zarei [2], Hojjat Zeraati [3], Amir Hassan Zarnani [4, 5], Mohammad Mehdi Akhondi [6], Reza Hadavi [2], Elham Savadi Shiraz [6], Mahmood Jeddi-Tehrani [2*]

1- Department of Medical Genetics, National Institute for Genetic Engineering and Biotechnology (NIGEB), Tehran, Iran
2- Monoclonal Antibody Research Center, Avicenna Research Institute, ACECR, Tehran, Iran
3- Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran
4- Nanobiotechnology Research Center, Avicenna Research Institute, ACECR, Tehran, Iran
5- Immunology Research Center, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran
6- Reproductive Biotechnology Research Center, Avicenna Research Institute, ACECR, Tehran, Iran

Abstract

Background: Recurrent pregnancy loss is (RPL) a heterogeneous condition. While the role of acquired thrombophilia has been accepted as an etiology for RPL, the contribution of specific inherited thrombophilic gene polymorphisms to the disorder has been remained controversial.

Methods: One hundred women with a history of two or more consecutive abortions and 100 women with at least two live births and no miscarriages were included in the study and evaluated for the presence of 11 thrombophilic gene polymorphisms (Factor V LEIDEN, Factor V 4070 A/G, Factor V 5279 A/G, Factor XIII 103 G/T, Factor XIII 614 A/T, Factor XIII 1694 C/T, PAI-1 -675 4G/5G, ITGB3 1565 T/C, β-Fibrinogen -455G/A, MTHFR 677 C/T, MTHFR 1298 A/C) using PCR-RFLP technique. The data were statistically analyzed using Mann-Whitney test and logistic regression model.

Results: There was no relation between factor XIII 103G/T gene polymorphism with increased risk of RPL. However, the other 10 gene polymorphisms were found to be associated with increased/decreased risk of RPL. Multiple logistic regression model for analyzing the simultaneous effects of these polymorphisms on the risk of RPL showed that six of these 11 polymorphisms (Factor V 1691G/A, Factor V 5279A/G, Factor XIII 614A/T, β-Fibrinogen -455G/A, ITGB3 1565T/C, and MTHFR 1298A/C) were associated with RPL.

Conclusion: It is possible to calculate the risk of abortion in a patient with RPL by determining only six of the 10 polymorphisms that are individually associated with RPL.

** Corresponding Author:*
Mahmood Jeddi-Tehrani, Department of Immunochemistry, Monoclonal Antibody Research Center, Avicenna Research Institute, ACECR, P.O. Box: 19835-1177, Daneshjo Blvd., Velenjak, Tehran, Iran
E-mail:
mahjed@yahoo.com

Received: Dec. 13, 2011
Accepted: Feb. 18, 2012

Keywords: PCR-RFLP, Recurrent pregnancy loss, Thrombophilic gene.
To cite this article: Torabi R, Zarei S, Zeraati H, Zarnani AH, Akhondi MA, Hadavi R, et al. Combination of Thrombophilic Gene Polymorphisms as a Cause of Increased the Risk of Recurrent Pregnancy Loss. J Reprod Infertil. 2012;13(2):89-94.

Introduction

Inherited thrombophilia is a risk factor for pregnancies leading to reproductive disorders and recurrent pregnancy loss (RPL). A number of thrombophilic gene polymorphisms that are suspected to associate with RPL, have been reported (1).

The most common polymorphism studied for association with RPL is Factor V (1q23) (FV) Leiden (2). FV Leiden may cause thrombosis by decreasing the sensitivity of FV to inactivation by activated protein C, leading to increased generation of thrombin. Activated protein C resistance (APCR) is the inability of protein C to cleave Factor Va, which allows for longer duration of

23. Ruzzi L, Ciarafoni I, Silvestri L, Semeraro ML, Abeni D. Association of PLA2 polymorphism of the ITGB3 gene with early fetal loss. Fertil Steril. 2005;83(2):511-2.
24. Yilmaz S, Bayan K, Tüzün Y, Batun S, Altintaş A. A comprehensive analysis of 12 thrombophilic mu