

## Association of ACE, PAI-1 and coagulation factor XIII gene polymorphisms with recurrent spontaneous abortion in Iranian patients

Soltangharaee H. (M.D.)<sup>1,2</sup>, Memariani T. (B.Sc.)<sup>1</sup>, Aarabi M (M.D.)<sup>1</sup>, Hantoushzadeh S. (M.D.)<sup>3</sup>, Arefi S. (M.D.)<sup>1,2</sup>, Aarabi M. (M.D.)<sup>4</sup>, Akhondi M.A. (Ph.D.)<sup>5</sup>, Modarresi M.H. (M.D., Ph.D.)<sup>3,6</sup>

1- Reproductive Biotechnology Research Center, Avesina Research Institute, ACECR, Tehran, Iran.

2- Avesina Infertility Clinic, Avesina Research Institute, ACECR, Tehran, Iran.

3- Faculty of Medicine, Medical Sciences/ Tehran University, Tehran, Iran.

4- Department of Clinical Pharmacology, Sheffield University, England.

5- Monoclonal Research Center, Avesina Research Institute, ACECR, Tehran, Iran.

6- Nanobiotechnology Research Center, Avesina Research Institute, ACECR, Tehran, Iran.

### Abstract

**Introduction:** Considering the 5% prevalence of abortion in women, its devastating psychological effects on affected people's lives and as tendency for clotting is one of the causes of recurrent spontaneous abortion (RSA), this study was designed to compare plasminogen activator inhibitor-1 (PAI-1), angiotensin converting enzyme (ACE) and blood coagulation factor XIII (FXIII) gene polymorphisms in Iranian patients with RSA and healthy women.

**Materials & Methods:** 120 patients with recurrent abortions (at least two) as cases and 112 healthy female controls without a history of abortion were entered into the study. In order to characterize PAI-1 (4G/5G), ACE (D/I) and FXIII (Val 34 Leu) polymorphisms, a polymerase chain reaction followed by digestion with restriction enzymes (PCR-RFLP) was designed. For the statistical analysis, SPSS software version 11.2 was used and t-test, Chi-square and Fisher's exact tests were calculated. P-values <0.05 were considered as significant.

**Results:** Homozygosity for PAI-1 4G polymorphism was seen in 16 cases, (14.4%), in contrast to two persons in the control group (2%), ( $p = 0.001$ ) and patients with homozygote 4G mutation were significantly more prone to RSA in contrast to others (OR: 8.2, % 95 CI: 1.8- 36.5). 38 patients, (29.5 %), and 25 people from the control group, (26.6%), were homozygote (D/D) for ACE polymorphism, depicting no statistically significant difference. Only two patients and one person from the control group had homozygosity (34leu) for FXIII polymorphism.

**Conclusion:** 4G/4G polymorphism for PAI-1 gene could be a thrombophilic mutation leading to abortion. Analysis of this mutation and other suspected factors such as MTHFR and FV Leiden is recommended in patients with RSA. In this study, there were no significant associations between ACE and FXIII with RSA.

**Key Words:** Recurrent spontaneous abortion (RSA), Thrombophilia, Plasminogen activator inhibitor-1, Angiotensin converting enzyme, Coagulation factor XIII.

**Corresponding Author:** Dr. Haleh Soltangharaee, Reproductive Biotechnology Research Center, Avesina Research Institute, P.O. Box: 19835-177, ACECR, Tehran, Iran.

**E-mail:** soltan@avesina.ac.ir