Abstract

Correlation between Protease activated receptor 1 (*Par1*) polymorphism and recurrent abortion in Palestine

Recurrent abortion (RA), affects 5% of women in their reproductive age in the first trimester of pregnancy. Although there are many causes for RA, a definite reason for the repeated miscarriage is still unknown in half of the cases. During placental invasion period, the expression of human protease activated receptor 1 (PAR1) peaks *in vivo* between the 7th -10th weeks of gestation and completely shuts off thereafter. Also, PAR1 is crucial to many important processes involved in placentation, and its polymorphisms were found to correlate with different diseases and unfavorable pregnancy outcomes. For that we aimed to find out the correlation between *Par1* polymorphisms and RA.

Our case-control study included 175 females from the north and the center areas of Palestine with two or more consecutive first-trimester miscarriages as cases and 241 females with two or more normal ended deliveries from the same ethnic background as controls. The research was carried out at Al - Quds Nutrition and Health Research Institute, Al - Quds University, Abu- Dies (2009-2010). DNA was extracted from blood samples of participants and analyzed for polymorphisms in the 5′ regulatory region of *Par1*, namely -506 Insertion/ Deletion (I/D) (rs11267092) and -1426 C/T (rs32934). The -506 I/D was analyzed by size polymorphic Polymerase chain reaction (PCR). The -1426 C/T polymorphism was analyzed by Restriction Fragment Length Polymorphism (RFLP), High resolution melting (HRM) and by direct sequencing for quality control purposes. To make it technically easier we made major modifications on published techniques used to genotype these polymorphisms. Indeed, our results showed that our modified techniques are reliable and easier to implement than published ones, especially the HRM which is an inexpensive, time saving, and high throughput method of analysis.

The polymorphisms inspected in this study showed no deviation from Hardy – Weinberg equilibrium. The minor allele frequency I for the -506 I/D polymorphism was 0.328 and 0.376 for cases and controls respectively (allelic OR 0.8; 95% CI= 0.6 -1.1, p 0.155). The minor allele

frequency T for the –1426 C/T polymorphism was 0.012 and 0.009 for cases and controls respectively (allelic OR 1.3; 95% CI= 0.8 -8.0, p 1.0). Our results showed no association between *Par1* polymorphisms (rs11267092 and rs32934) and RA.

Although our results showed no association between the polymorphisms we tested and RA, we think our study is valuable since we developed easier techniques that can be used to screen for these polymorphisms where their presence is associated with other diseases. Moreover, we ruled out the possibility that these polymorphisms could have association with RA in our population, although association was found between them and different unfavorable pregnancy out comes, in addition to different diseases in different ethnic groups. Nonetheless, there is still an open question whether these or other polymorphisms in *Par 1* gene could have association with unfavorable pregnancy out comes, in our population, if analyzed on the fetus tissue and not maternal tissue only.