Synopsis

Recurrent early pregnancy loss (REPL) is defined as the occurrence of three or more miscarriages before the end of first trimester. In this study, we tried to analyze the relationship between genetic variants in different genes and the risk of REPL. Polymorphisms in CYP1A1 and CYP2D6 showed a significant association. Novel intronic variant of eNOS showed a significant association in homozygous condition. Larger repeat numbers of TTTA repeat of CYP19, even though present at a low frequency showed a significant difference in their distribution. Androgen receptor CAG repeat numbers also exhibited a strong correlation with a normal pregnancy outcome. Smaller repeat numbers were found to be associated with REPL. Randomness of X chromosome inactivation process was assessed to account for the X-chromosomal factors in REPL. A very significant difference was seen in the degree of skewing. Women with a biased X inactivation was gifted with successful pregnancy outcome. A significant relationship between the length of CAG repeats of androgen receptor and the choice of X inactivation was observed. X chromosomes with shorter repeats were selectively subjected to inactivation at a significant level irrespective of being case or control. A novel polymorphism was detected in the cannabinoid metabolizing enzyme, anandamide hydrolase. This variation appears to decrease the expression by possessing a less preferred codon. Polymorphisms in FVL, prothrombin and MTHFR failed to show any relationship to REPL.

Platelet proteomic analysis revealed the over expression of FSD1-like protein and a variable region of IgM heavy chain. They possibly enhance platelet activation, aggregation followed by depletion leading to the risk of pregnancy failure.