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Missense *EPHX1*- rs1051740 Gene Polymorphism May Correlate to Pre-eclampsia: An *In Silico* Study

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Abstract

Epoxide hydrolase (EH) is a critical biotransformation enzyme that converts epoxides from aromatic compounds' degradation to trans-dihydrodiols that can be conjugated and excreted from the body. *EPHX1* is involved in the metabolism of xenobiotics and steroids and also plays a role in repair following oxidative injury. Mutations in this gene cause pre-eclampsia (PE), epoxide hydrolase deficiency, or increased epoxide hydrolase activity. *In silico* studies can help to identify the functional role of single nucleotide polymorphisms (SNPs) in the structure and stability of EPHX1 protein and to predict their relationship with PE. This study investigated, missense SNPs of the *EPHX1* gene and their effects on PE. At first, all missense SNPs of the *EPHX1* gene, located on chromosome 1q42.12, were monitored. Missense SNPs with a minor allele frequency (MAF)≥ 0.1 were selected in the NCBI-dbSNP database. The effect of the selected SNP based on functional, structural, and stability aspects of the protein was investigated by the following twelve online software: SIFT, Polyphen-2, PANTHER, SNPs&GO, PhD-SNP, Mutation Assessor, PROVEAN, I-mutant, iStable, MUpro, PSIPRED, and HOPE. Analysis of missense SNP by SIFT, Polyphen-2, PANTHER, and PROVEAN showed that rs1051740 (T>C, Tyr113His), could be a deleterious SNP for the function of *EPHX1*. The prediction of the effects of this SNP by I-mutant, IStable, MUpro, and PSIPRED also showed that substituting Tyr113His may decrease the stability of the protein. On the other hand, The HOPE analysis tool illustrated that the rs1051740 variant could disturb the protein motifs. Our findings suggest that the *EPHX1* gene may be involved in the development of PE and rs1051740 may have deleterious impacts on the function of this gene.

Keywords: Epoxide hydrolase 1, Genetic Polymorphism, *In silico* studies, Missense SNPs, Preeclampsia