The Association of Soluble Epoxide Hydrolase Genetic Variants with Hypertensive Diabetic Patients Type II

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Abstract

Background: Human soluble epoxide hydrolase is responsible for inactivation of epoxyeicosatrienoic acids, which play a major role in cardiovascular homeostasis. Genetic variants on *EPHX2* gene are associated with cardiovascular complications, such as hypertension, among different ethnic groups. However, there are no reports regarding the association of *EPHX2* genotype with hypertension among diabetic type II (T2D) patients of Middle Eastern Jordanian origin.

Aim: The current study aims to find out the association of *EPHX2* allele, genotype and haplotype with T2D and hypertension among Jordanian diabetic patients.

Methods: Ninety three genomic DNA samples of non-diabetic controls and 97 samples from T2D patients were genotyped for *EPHX2 rs4149243*, *rs2234914* and *rs751142* genetic variants. Among the diabetic patients, 50 were diagnosed with hypertension in addition to T2D. The DNA samples were amplified using polymerase chain reaction

(PCR). Then, these PCR products were sequenced using Applied Biosystems Model (ABI3730x1).

Results: It is found that there was no significant (P>0.05) association of *EPHX2 rs4149243*, *rs2234914* and *rs751142* allele, genotype and haplotype with the incidence of T2D and hypertension. Additionally, there was no association (P>0.05) between these *EPHX2* genetic variants with the baseline total cholesterol, low density lipoprotein, high density lipoprotein and triglycerides among both non-diabetic and diabetic volunteers. However, we found, in the current study, an inter-ethnic variation (χ^2- test, p value<0.05) in the allele frequency of *EPHX2 rs4149243* and *rs2234914* variants between Jordanians and other ethnic populations. The allele frequency of *rs4149243* variant was significantly different (p-value<0.05) in comparison with the frequencies reported among Africans, Americans, Asians, and Europeans. In addition, *rs751142* allele frequency in Jordanians was significantly different (p-value<0.05) in comparison with Africans, Italian-European, and Asians except with Pakistani group. This study also used *in silico* Berkely Drosophila Genome Project software to predict the effect of *EPHX2* intronic variants on the splicosome formation. This software predicted that the intronic SNP *rs4149243* can alter the splicing of intron 7 which is on the recognition site of one of the splicing sites of intron 7.

Conclusion: *EPHX2 rs4149243*, *rs2234914* and *rs751142* genetic variants do not play a role in the development of T2D and hypertension diseases among Jordanian T2D patients. In addition, this study is the first report regarding the inter-ethnic variation in the allele frequency of these studied genetic variants, between Jordanians and other ethnic groups. These findings may increase our understanding of the role of

EPHX2 genetic variants in the development of chronic diseases among different ethnic populations. Further clinical studies with larger sample size are needed to find out the association of other functional *EPHX2* variants with cardiovascular diseases in Jordan.

Keywords: Diabetes**,** *EPHX2* gene, genetic variants, hypertension, Jordanians.