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Short communication

Genotype and allele frequencies of *ABCB1* C1236T, G2677A/T and C3435T variants in the Kosovo population

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Introduction

Pharmacogenomics has become an important component of precision medicine by facilitating the optimization of drug therapy according to an individual's genetic profile. Genetic variability contributes significantly to differences in drug efficacy, safety, and therapeutic outcomes among individuals (Relling & Evans, 2015; Roden et al., 2019). In addition to drug-metabolizing enzymes, membrane transport proteins have been recognized as important determinants of pharmacokinetic variability.

One of the most extensively investigated transporters is P-glycoprotein, encoded by the ATP-binding cassette subfamily B member 1 (*ABCB1*) gene. P-glycoprotein functions as an ATP-dependent efflux transporter involved in the absorption, distribution, and elimination of numerous therapeutic agents (Fromm, 2003). Among the most frequently studied *ABCB1* variants are C1236T (rs1128503), G2677A/T (rs2032582), and C3435T (rs1045642), which have been associated with altered transporter activity and variability in drug response (Cascorbi, 2006). Since the distribution of these variants differs among populations, population-specific pharmacogenetic studies are necessary. The aim of this study was to determine the genotype and allele frequencies of *ABCB1* C1236T, G2677A/T, and C3435T polymorphisms in a Kosovo population sample.

Materials and methods

A total of 234 unrelated individuals of Kosovo origin were included in this cross-sectional study. Peripheral blood samples were collected following informed consent procedures and in accordance with ethical principles for biomedical research. Genomic DNA was isolated from peripheral whole blood using the Nextractor NX-48S automated extraction system according to the manufacturer's protocol. Genotyping of *ABCB1* C1236T (rs1128503), G2677A/T (rs2032582), and C3435T (rs1045642) polymorphisms was performed using TaqMan® SNP Genotyping Assays and real-time polymerase chain reaction (RT-PCR). Allelic discrimination analysis was conducted using MxPro software. Genotype and allele frequencies were calculated by direct counting. Hardy–Weinberg equilibrium (HWE) was evaluated using the chi-square test. Statistical significance was defined as $p < 0.05$.

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Results and discussion

Among the 234 subjects included in the study, the heterozygous genotype was the most prevalent for all three investigated *ABCB1* polymorphisms. For *ABCB1* C3435T (rs1045642), the CT genotype was observed in 124 individuals (53.0%), followed by the CC genotype in 62 individuals (26.5%) and the TT genotype in 48 individuals (20.5%). The frequencies of the C and T alleles were 53.0% (n = 248) and 47.0% (n = 220), respectively, and the genotype distribution was consistent with Hardy–Weinberg equilibrium ($\chi^2 = 0.95$, $p > 0.05$). Similarly, for *ABCB1* C1236T (rs1128503), the CT genotype was the most common, occurring in 118 individuals (50.4%), while the CC and TT genotypes were detected in 82 (35.0%) and 34 (14.5%) subjects, respectively. The C allele frequency was 60.3% (n = 282), whereas the T allele frequency was 39.7% (n = 186). The observed genotype distribution did not deviate significantly from Hardy–Weinberg equilibrium ($\chi^2 = 0.65$, $p > 0.05$). Genotyping of *ABCB1* G2677T (rs2032582) was successfully completed in 229 participants, while five samples (2.1%) could not be genotyped. Among successfully genotyped individuals, the GT genotype was the most frequent, observed in 103 subjects (45.0%), followed by the GG genotype in 83 subjects (36.2%) and the TT genotype in 43 subjects (18.8%). The frequencies of the G and T alleles were 58.7% (n = 269) and 41.3% (n = 189), respectively. The genotype distribution was also consistent with Hardy–Weinberg equilibrium ($\chi^2 = 1.19$, $p > 0.05$), indicating that all three polymorphisms were in genetic equilibrium within the studied population.

The genotype and allele frequencies of the ABCB1 C1236T, G2677T, and C3435T polymorphisms observed in the present study were comparable to those previously reported in Balkan and other European populations. In particular, the predominance of heterozygous genotypes and the balanced distribution of alleles are consistent with findings reported in the Macedonian population by (Naumovska et al., 2014). Similarly, the higher frequencies of the C allele for C1236T and C3435T and the G allele for G2677T are in agreement with data reported for Caucasian populations (Fung & Gottesman, 2009). The absence of the A allele at rs2032582 is also consistent with its low prevalence among European populations (Sakaeda et al., 2002). Overall, these findings indicate that the Kosovo population shares a similar ABCB1 genetic profile with neighboring Balkan populations and provide baseline data for future pharmacogenetic studies.

Conclusion

The present study determined the genotype and allele frequencies of ABCB1 C1236T (rs1128503), G2677T (rs2032582), and C3435T (rs1045642) polymorphisms in a Kosovo population. Heterozygous genotypes were the most prevalent variants, and allele distributions were comparable to those reported in other Balkan and European populations. These findings demonstrate substantial genetic variability within the ABCB1 gene and provide important baseline pharmacogenetic data for future studies investigating the influence of ABCB1 polymorphisms on drug response and personalized therapeutic approaches in Kosovo.

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