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## POTASSIUM CHANNEL GENES KCNQ1, KCNE1/2, KCNH2 (HERG) MUTATIONS IN PATIENTS WITH ATRIAL FIBRILLATION IN KAZAKHSTAN

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**Background:** Atrial fibrillation (AF) is a common arrhythmia of substantial public health importance, a major risk factor for stroke, heart failure, and other cardiovascular morbidities. Recent evidence demonstrates a heritable component underlying AF, and genetic discoveries have identified common variants associated with the arrhythmia.

**Aim:** This study aims to report the spectrum of KCNQ1, KCNE1, KCNE2, KCNH2 (HERG) mutations in Kazakhstani patients with AF.

**Methods:** Patients with AF were recruited at National Research Center for Cardiac Surgery, Nur-Sultan, Kazakhstan. Genomic DNA of the 104 cases with AF and 87 healthy relatives were analyzed for mutations in all protein-coding exons and their flanking splice site regions of the genes KCNQ1, KCNE1, KCNE2 and KCNH2 (HERG) using targeted next generation sequencing and validated by bidirectional Sanger sequencing.

**Results:** In total, a disease-causing mutation was identified in 59 of the 104 (56.5%) index cases. Of these, altered sequence variants in the KCNQ1 gene accounted for 14.5 % of the mutations, whereas a KCNE1 mutation accounted for 43.5 % of the mutations, KCNE2 for 1.4% and KCNH2 for 40.6%. The majority of the distinct mutations were found in a single case (80 %), whereas 20 % of the mutations were observed more than once. We found two sequence variants in KCNQ1 exon 13 (S546S G1638A) and exon 16 (Y662Y C1986T) in 15 patients (14.5 %). In KCNE1 gene in exon 3 mutation, S59G A280G was observed in 42 of 104 patients (43.5%) and KCNE2 exon 2 T10K C29A in 1 patient (1.4 %). Screening KCNH2 (HERG) gene revealed sequence variants C789A (I263N), T1467C (I489I), C1539T (F513F) in exon 6, G2832T (E944D) in exon 12 and (R1047L G3541T), C3153T (R1051R) in exon 13. Genetic cascade screening of 87 relatives to the 104 index cases with an identified mutation revealed 26.9 % mutation carriers who were at risk of cardiac events such as syncope or sudden unexpected death.

**Conclusion:** In this cohort of Kazakhstani index cases with AF, a disease-causing mutation in potassium channel genes KCNQ1, KCNE1/2, KCNH2 (HERG) was identified in 56.5 % of the referred patients.

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