Beyond Diabetes Mellitus: Close Pathological Association of Mutations of the *KCNQ1* Gene with Other Systemic Disorders

Dear Editor,

I read with great interest the recent article by Saif et al[1] in a recent issue of your esteemed journal. The article is highly thought provoking. Interestingly, the past few years have seen the identification of a number of pathological conditions resulting because of mutations in the *KCNQ1* gene.

For instance, increased disease severity is seen in patients with Long QT syndrome (LQTS) who demonstrate 3' UTR single nucleotide polymorphisms such as rs8234 in the *KCNQ1* gene.[2] In fact, there is an increased risk of mortality in individuals with type-1 LQTS who exhibit cytoplasmic loop mis-sense mutations of the *KCNQ1* gene.[3] Certain mutations of the *KCNQ1* gene may also result in left ventricular non-compaction in patients with LQTS.[4]

Similarly, familial atrial fibrillation may occur because of the V141M mutation of the *KCNQ1* gene.[5] The L203P variant of the *KCNQ1* gene may result in Torsades de pointes in patients, especially those with underlying Steinert syndrome, while the G643S variant predisposes patients with underlying myocardial ischaemia to developing Torsades de pointes.[6,7] *KCNQ1* gene polymorphisms may also play a pathological role in the development of Romano-Ward syndrome and Jervell and Lange-Nielsen syndromes.[8] The rare Jervell and Lange-Nielsen syndrome occurs because of the p.S277del/c.921G>A mutation of the *KCNQ1* gene.[9]

Similarly, an increased predisposition to develop "new onset diabetes" after tacrolimus-treated renal transplantation is seen in patients who demonstrate the rs2237895 single nucleotide polymorphisms of the *KCNQ1* gene.[10] Interestingly, the rs2074196 polymorphism of the *KCNQ1* gene increases the risk of developing gestational diabetes mellitus.[11] An increased risk of developing nephropathy is also seen in diabetic patients who exhibit the T allele of rs2237897 polymorphism.[12]

Clearly, mutations in the *KCNQ1* gene are associated with a range of pathological conditions ranging from familial atrial fibrillation to Jervell and Lange-Nielsen syndrome. Further studies are needed to identify any other similar associations.

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