Association of glucokinase regulatory gene polymorphisms with risk and severity of non-alcoholic fatty liver disease: an interaction study with adiponutrin gene.


Author information

• The Pharmacogenomics Laboratory, Department of Pharmacology, Faculty of Medicine, University of Malaya, 50603, Kuala Lumpur, Malaysia, tanhwali@yahoo.com.

Abstract

BACKGROUND:

Recent genome-wide association studies demonstrated an association between single nucleotide polymorphisms (SNPs) on the glucokinase regulatory gene (GCKR) with hepatic steatosis. This study attempted to investigate the association of GCKR rs780094 and rs1260326 with susceptibility to non-alcoholic fatty liver disease (NAFLD) and its severity.

METHODS:

The genotypes were assessed on 144 histologically confirmed NAFLD patients and 198 controls using a Sequenom MassARRAY platform.

RESULTS:

The GCKR rs1260326 and rs780094 allele T were associated with susceptibility to NAFLD (OR 1.49, 95% CI 1.09-2.05, p = 0.012; and OR 1.51, 95% CI 1.09-2.09, p = 0.013, respectively), non-alcoholic steatohepatitis (NASH) (OR 1.55, 95% CI 1.10-2.17, p = 0.013; and OR 1.56, 95% CI 1.10-2.20, p = 0.012, respectively) and NASH with significant fibrosis (OR 1.50, 95% CI 1.01-2.21, p = 0.044; and OR 1.52, 95% CI 1.03-2.26, p = 0.038, respectively). Following stratification by ethnicity, significant association was seen in Indian patients between the two SNPs and susceptibility to NAFLD (OR 2.64, 95% CI 1.28-5.43, p = 0.009; and OR 4.35, 95% CI 1.93-9.81, p < 0.0001, respectively). The joint effect of GCKR with adiponutrin rs738409 indicated greatly increased the risk of NAFLD (OR 4.14, 95% CI 1.41-12.18, p = 0.010). Histological data showed significant association of GCKR rs1260326 with high steatosis grade (OR 1.76, 95% CI 1.08-2.85, p = 0.04).

CONCLUSION:

This study suggests that risk allele T of the GCKR rs780094 and rs1260326 is associated with predisposition to NAFLD and NASH with significant fibrosis. The GCKR and PNPLA3 genes interact to result in increased susceptibility to NAFLD.