

**The effect of alcohol dehydrogenase gene polymorphisms
on alcohol consumption and chronic liver diseases in
Hungary**

By Reka Toth

**Department of Preventive Medicine, Public Health Research Group of the Hungarian
Academy of Sciences, Faculty of Public Health, Medical and Health Science Centre,
University of Debrecen**

Supervisor: Roza Adany, MD, PhD, DSc

**Doctoral school of Health Sciences
Doctoral program of Preventive Medicine and Public Health**

Summary

Although standardized death rates have recently declined, premature mortality from liver cirrhosis remains markedly higher in Hungary than in Western Europe, especially among males. Although the level of the alcohol consumption is the main determinant of chronic liver diseases, its risk is also affected by genetic factors. The aim of this study was to analyze the combined effect of the most frequent alcohol dehydrogenase (ADH) polymorphisms (Arg48His and Arg370Cys in ADH1B, Arg272Gln and Ile350Val in ADH1C) on the alcohol use habits, alcohol dependence and chronic liver diseases in Hungary. The study included men, aged 45-64 years. Altogether, 241 cases with chronic liver disease (CLD) 666 randomly selected controls without CLD were analyzed for all four polymorphisms. Associations between the polymorphisms, individually, and in combination, and excessive or problem drinking and CLD, were assessed using logistic regression.

In this study we have identified a novel mutation, called ADH1B Arg370His. The ADH1B*2 allele was associated with significantly lower odds ratio for variables describing drinking habits (frequency of drinking, alcoholism according to CAGE questionnaire). There was a significant association between ADH1B*2 and CLDs (OR=0.47; $p=0.003$), but it disappeared after adjusting for variables of the drinking pattern. Among heavy drinkers the presence of ADH1B*2 did not increase the risk of cirrhosis. The ADH1C Arg272Gln and Ile350Val showed almost complete linkage. The 272Gln/350Val allele increased the risk of frequent and problem drinking in homozygous form (OR=1.51, $p=0.028$, OR=1.780, $p=0.016$, respectively). The combined analysis showed that ADH1B 48His is protective against CLD but only when combined with the wild type ADH1C Arg272/Ile350 allele (OR=0.368, $p=0.019$).

The results obtained in the study help not only to clarify the effects of different ADH SNPs, but to better understand how these polymorphisms modify each other's effects in the development of alcoholism and chronic liver diseases. Our study helps to map the frequency and effect of allelic variants which lead to better understanding of the genetic composition of the Hungarian population. It can help in evolving public health programs more suitable to local specialties to lower the high level of cirrhosis and liver disease.

Keywords

Alcoholism, chronic liver disease, genetic epidemiology

Kulcsszavak

Alkoholizmus, krónikus májbetegségek, genetikai epidemiológia