



GG genotype of the PNPLA3 RS738409 polymorphisms is associated with NASH in Uzbek population

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Background

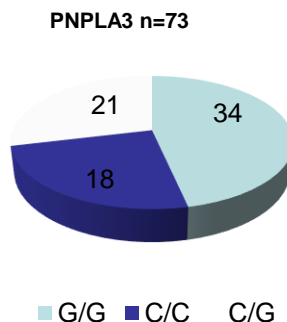
Nonalcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease and has an estimated incidence of 20%-30% in the general population and 67%-75% in the obese population. Genetic predisposition can play an important role in development of this disease. Nonsynonymous coding SNP rs738409 C/G (Ile148Met) in PNPLA3 gene has been found associated with the presence of NAFLD in a genome-wide association study. This association has been replicated in several cohorts of different ethnicity, but to date the assessment of this association has not been performed in the Central Asia populations.

Aims

The purpose of our research is to investigate the association between polymorphic variant of PNPLA3 gene (rs738409) and susceptibility to non-alcoholic fatty liver disease (NAFLD) in Uzbekistan.

Patients & Methods: In this case-control study, 73 patients a mean age of 55.1 diagnosed with NAFLD (48 patients with simple steatosis and 25 patients with non-alcoholic steatohepatitis (NASH)) and the age, gender and ethnically matched controls (n=37) were recruited. The diagnosis of NAFLD was verified on the basis of anamnesis, clinical and laboratory tests, and liver ultrasound. Genomic DNA was isolated and SNP genotyping was performed by using polymerase chain reaction with specific primers followed by restriction fragment length polymorphism analysis.

Our **result** showed significant association between GG genotype of the PNPLA3 rs738409 polymorphisms and NAFLD ($p=0.03$, OR = 2.99; 95% CI 1.21–7.42 for the additive model, Cochran-Armitage trend test; $p=0.02$, OR = 2.99; 95% CI 1.21–7.42 for the recessive model, Pearson's χ^2 test). Genotype frequencies of PNPLA3 rs738409 polymorphisms in a subset of patients with simple steatosis and NASH compare to the control group. Comparative analysis of resulting genotypes showed a slight increase of CG and GG genotypes among patient with simple steatosis, then among subjects of the control group, but this did not reach statistical significance. However, statistical analysis of genotype distribution between patients with NASH and controls showed a significant association between GG genotype and NASH assuming an additive model ($p<0,0001$, Cochran-Armitage trend test) and recessive model ($p<0,0001$, Pearson's χ^2 test).



Model of inheritance	Genotypes	Case s	Control s	χ^2	p	OR	
		n = 73	n = 37			value	95% CI
Additive model	C/C	31.5	45.9	4.82	0.03	0.54	0.24-1.22
	C/G	23.3	32.4			0.63	0.26-1.52
	G/G	45.2	21.6			2.99	1.21 - 7.42
Recessive model	C/C+C/G	54.8	78.4	5.84	0.02	0.33	0.13-0.83
	G/G	45.2	21.6			2.99	1.21 - 7.42

Conclusion: The present study, we confirm the association of PNPLA3 rs738409 GG genotype with susceptibility to NAFLD. After stratification into the two main subtypes of NAFLD, the risk genotype GG was found to be significantly associated with susceptibility to NASH. We also found that the GG genotype is not associated with simple steatosis in Uzbek population

References:

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