

# In Slovenian patients with primary biliary cirrhosis genetic polymorphism of glutathione S-transferase (GSTP1) contribute to higher prevalence of concomitant autoimmune thyroid disease

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## AIM OF STUDY

Glutathione S-transferases (GST) are a large family of isoenzymes that catalyse conjugation reactions of reduced glutathione. However GST-mu 1 (GSTM1), GST-theta 1 (GSTT1) and GST-pi 1 (GSTP1) also play an important role in cellular protection against damage caused by reactive oxygen species. Genetic polymorphisms of genes coding for these enzymes alter enzyme activity by reducing antioxidant defense mechanisms, which are known to contribute to the pathogenesis of many autoimmune diseases. Primary biliary cirrhosis (PBC) is a rare autoimmune liver disease, characterized by progressive destruction of small intra-hepatic bile ducts and gradual development of biliary cirrhosis. PBC is frequently associated with autoimmune thyroid disease (AITD), which reportedly affects 15 to 25 percent of patients with PBC. The aim of our research was to determine the influence of *GSTM1*, *GSTT1* and *GSTP1* polymorphisms on concomitant AITD in Slovenian PBC patients.

## METHODS

The study population consisted of 92 patients (91 females and 1 male) with PBC. All the patients were examined for the presence of thyroid disease. AITD was diagnosed in patients with positive specific thyroid autoantibodies and with characteristic hypoechoic ultrasound pattern. Polymorphic *GSTM1* and *GSTT1* genes deletions (null alleles) were identified using multiplex PCR. Both genes were simultaneously amplified in a single-step PCR reaction together with the beta-globin gene as the internal positive control and PCR products were visualized on a 2% agarose gel stained with ethidium bromide. Custom TaqMan SNP genotyping assays were used to determine *GSTP1* Ile105Val and Ala114Val polymorphisms. Statistical analysis (Pearson Chi-Square, Fisher's Exact Test, Odds Ratio, 95% Confidence Interval) were performed using IBM SPSS Statistics version 20.0.

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## RESULTS

Among 92 PBC patients AITD was confirmed in 30 (32.6%) and excluded in 62 (67.4%). *GSTMI* null and *GSTTI* null allele and *GSTPI* Ala114Val frequency distribution did not differ between PBC patients with and without concomitant AITD. *GSTPI* Ile105Val genotype distribution significantly differed between PBC patients with and without concomitant AITD (Pearson  $p=0.007$ ). In particular, PBC patients with homozygous *GSTPI* 105Val/105Val genotype had significantly higher risk for concomitant AITD (Pearson  $p=0.005$ , Fisher  $p=0.010$ , OR=8.500, 95% CI=1.571-45.979). (Table 1).

## CONCLUSIONS

Our results suggest that the presence of *GSTPI* 105Val allele may contribute to higher prevalence of AITD in PBC patients.