POLYMORPHISMS ASSOCIATED WITH LIVER FIBROSIS AND HEPATOCELLULAR CARCINOMA IN PATIENTS WITH CHRONIC HEPATITIS C

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Introduction: Chronic hepatitis C virus (HCV) infection is a major cause of progressive liver disease, such as cirrhosis and hepatocellular carcinoma. Host genetic diversities, including epidermal growth factor (EGF), interleukin-28B (IL-28B), patatin-like phospholipase domain containing 3 gene (PNPLA3), and transforming growth factor-β (TGF-β) gene polymorphisms, have been associated with fibrosis severity and hepatocarcinoma development in hepatitis C. However, the combinatorial association of these polymorphisms in a Brazilian population with chronic hepatitis C is unknown. Objective: To investigate the association of EGF rs4444903, IL-28B rs12979860 and rs8099917, PNPLA3 rs738409, and TGF-β codon 25 gene polymorphisms with fibrosis severity and hepatocarcinoma development in a cohort of Brazilian patients. Material and Methods: DNA was obtained with Salting-Out methodology from blood samples of 85 patients infected with HCV genotype 1. Amplified products of IL-28B, TGF-β, EGF and PNPLA3 single nucleotide polymorphisms (SNPs) were genotyped by Sanger sequencing. Liver tissue was analyzed at baseline and ten years after pegylated interferon-ribavirin treatment by biopsy and/or transient elastography (Fibroscan). Fibrosis severity was stratified as: mild (F0-F3) and severe (F4-F6). Discussion and Results: At baseline, 35% of the patients were classified as mild fibrosis and 65% as severe fibrosis, median age was 52 years old, and 46% were male. TGF-β and IL-28B SNPs were genotyped in all patients. EGF and PNPLA3 SNP-genotyping are under process. We found significant association in TGF-β codon 25 polymorphism with grade of fibrosis: genotype GG was more frequently found in patients with severe fibrosis (91%) when comparing with those with mild fibrosis (66%). No association was observed for IL-28B. Conclusions: We found association of TGF-β polymorphism with fibrosis severity, and others markers are being analyzed. Identification of molecular markers for disease progression in hepatitis C can impact disease management and treatment.

Key-words: IL-28B, TGF-β, EGF, PNPLA3