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ORIGINAL ARTICLE

The Role of Interleukin-17 and Toll-Like Receptor 4 Gene Polymorphisms in Patients with Hepatitis C Virus and Hepatocellular Carcinoma

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ABSTRACT

Key words:
Hepatocellular carcinoma; Hepatitis C virus; TLR4; IL-17

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Background: *Hepatocellular carcinoma (HCC) is a global health problem. HCC is the fourth common malignancy in Egypt. It is a crucial medical need to predict hepatocellular carcinoma development in cirrhotic liver patients.* ***Objectives:*** *this study aims to investigate the association between TLR4 gene polymorphism (rs2149356) and the probability of HCC development among chronic hepatitis C virus infected patients and clarify the role of serum IL-17 in patients with end stage liver disease and HCC in HCV infected patients.* ***Methodology:*** *the study included 25 patients with chronic hepatitis C infection, 25 patients with chronic hepatitis C infection and HCC, and 25 apparently healthy control subjects as controls. All participants undergone full clinical and laboratory assessment. TLR4 (rs2149356) G/T polymorphism genotyping by PCR-RFLP (polymerase chain reaction - restriction fragment length polymorphism) and serum IL-17 detection by ELISA (enzyme-linked immunosorbent assay).* ***Results****: TLR4 (rs2149356) GG genotype was significantly associated with chronic HCV with HCC patients (72%) and chronic HCV patients (48%), while GT genotype was associated with healthy controls (48%) (P-value <0.001). Serum IL-17 was significantly elevated in chronic HCV with HCC patients than chronic HCV and control subjects (P-value <0.001). Serum IL-17 was an excellent predictor for HCC development at a cut-off value of 128.1 pg/dL with 96% sensitivity and 82% specificity.* ***Conclusion****: TLR4 (rs2149356) polymorphism and IL-17 have an important role in immunopathogenesis of HCC in chronic HCV infected patients.*

INTRODUCTION

Hepatocellular carcinoma (HCC) is a worldwide health problem with variable epidemiology from place to place. It is the fourth common malignancy in Egypt.[1] The major predisposing factors for HCC are Hepatitis B (HBV) or C (HCV) viruses infection, co-infection of hepatitis viruses with human immunodeficiency virus (HIV), aflatoxin-B1 (AFB1) exposure, alcohol abuse, nonalcoholic steatohepatitis (NASH), nonalcoholic fatty liver disease (NAFLD), diabetes, obesity, family history, genetic factors and metabolic syndrome.[2,3] In most cases; HCC develops on top of chronic inflammation and cirrhosis caused mainly by hepatitis viral infection, with chronic HCV infection is considered the main cause for HCC development.[4] Chronic hepatic inflammation is characterized by continues over expression of pro-inflammatory cytokines with recruitment of immune cells to the liver tissue. Even though the immune activation helps to clear viral infection and restore hepatic tissue function, such prolonged immune response may lead to replacement of hepatic parenchyma by fibrotic tissue and distortion of its vasculature causing hepatic cirrhosis and probably HCC.[5–7]

The innate immune response was described in HCV infection with the upregulation of interferon stimulated genes (ISGs).[8] Innate immune response is the primary defense mechanism against pathogens mediated by common pathogen-derived signals such as lipopolysaccharide (LPS) in gram negative bacteria and viral DNA that can be recognized by toll-like receptors