

## Can Hepatitis E Virus Be Considered as an Etiology of Cryptogenic Cirrhosis?

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**Date of Submission:** Oct 19, 2013

**Date of Acceptance:** Jan 14, 2014

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**How to cite this article:** Sohrabi M, Zamani F, Shirangi A, Ajdarkosh H, Kivani H, Mohamadnejad M. Can hepatitis E virus be considered as an etiology of cryptogenic cirrhosis? *Int J Prev Med* 2014;5:527-8.

### DEAR EDITOR,

Hepatitis E virus (HEV) is one of the main causes of endemic acute hepatitis, particularly in Asian and African countries.<sup>[1]</sup> The spectrum of clinical presentation is from asymptomatic to fulminate disease. A majority of infected patients recover completely, although mortality related to HEV infection is estimated to be 1% in the general population and even more common in pregnant women.<sup>[1,2]</sup> However, recently there have been several reports that HEV may evolve to a chronic form especially in immunocompromised patients.<sup>[3]</sup>

Although HEV has not been proven as an etiology of cryptogenic cirrhosis, some histologically studies illustrated that HEV may be associated to advanced fibrosis and cirrhosis in post solid organ transplantation<sup>[3]</sup> and among individual treated for non-Hodgkin's lymphoma's.<sup>[4]</sup> To investigate possible association of HEV infection and cryptogenic cirrhosis we conducted a cross-sectional study of patients with unknown etiology cirrhosis in Firoozgar Hospital, Tehran, Iran.

This study was conducted from 2009 to 2013. Cirrhosis was confirmed by histological examination. Patients with evidences of frank cirrhosis, who had contraindication for liver

biopsy, underwent transient elastography using Fibroscan (502 touch, Echoscence Co. France) to confirm cirrhosis. The liver stiffness score more than 40 kPa was considered as frank cirrhosis.<sup>[5]</sup> The control group was selected among matched healthy hospital staff without known hepatopathy. All participants had negative serologic markers for hepatitis B and C, negative anti-nuclear antibody and anti-smooth muscle antibody, normal serum iron profile, and normal serum ceruloplasmin levels.

A total of 50 patients were enrolled in each group. The mean age of cases and controls were  $51.6 \pm 5.7$  and  $41.89 \pm 6.7$  years, respectively. Twenty-seven (54%) cases and 27 (60%) control were male. Cirrhosis was confirmed with liver biopsy in 45 (90%) of the patients. The average serum levels of alanine transaminase (ALT), aspartate aminotransferase (AST), and alkaline phosphates (Alk.ph) among all patients were  $59.2 \pm 8.6$ ,  $73.9 \pm 12.6$  and  $280.4 \pm 126.3$ , respectively. Four (8%) and three (6%) of the patients and control group had positive HEV immunoglobulin G (IgG) antibody (HEV-Ab) respectively ( $P = 0.55$ ). The specimens which were positive for HEV IgG were tested for HEV-ribonucleic acid (RNA) using polymerase

chain reaction. None of the HEV-Ab positive patients were positive for HEV-RNA.

Among cirrhotic patients with available liver biopsy, there was no evidence regarding specific liver diseases. The mean grade of necroinflammation was 8.25 in the HEV-Ab positive group and 8.05 in the HEV-Ab negative group ( $P = 0.88$ ) and the mean liver stiffness in fibroscan was not different (KP = 52 vs. 54) in HEV-Ab positive and negative patients, respectively ( $P = 0.36$ ). We did not find any significant association between age or sex and presence of HEV-Ab in either group nor was there any association between ALT, AST and Alk.ph and the presence of HEV-Ab. One out of four patients with decompensate cirrhosis had positive HEV-Ab, and 3 of 45 patients (6.6%) with compensated cirrhosis had positive HEV-Ab ( $P = 0.85$ ).

There are few studies that focused on etiological impact of HEV on chronic liver diseases. A literature review of recent reports revealed that HEV infection is considered as a cause for chronic hepatitis, but this is mostly limited to patients with immune deficiency states.<sup>[6,7]</sup> Furthermore, the presence of anti-HEV-IgG in post-transplant and human immunodeficiency virus infected patients might put them at particular risk of developing liver failure.<sup>[6,7]</sup>

In this study, we evaluated HEV as potential etiology of cryptogenic cirrhosis and to our knowledge this is the first study that was done in this group of patients. The prevalence of HEV-Ab (IgG) was not significantly different in case and control groups. Furthermore, among cirrhotic patients, there was no correlation between compensated and decompensate disease based on the prevalence of

HEV-Ab. More studies with larger sample size are needed to determine whether HEV plays any role in the etiology of chronic liver disease.

## ACKNOWLEDGMENT

The authors would like to thank Ms Aten, Afsane Rahbari and all staff in GILDRC

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**Source of Support:** Nil, **Conflict of Interest:** None declared.