Reply to Letter entitled "Hepatitis E in Decompensated Alcoholic Cirrhosis" by Renou et al.

The report of Renou et al adds to our growing understanding of the complex epidemiology of HEV infection amongst individuals residing in industrialized countries. HEV is a single stranded RNA virus that can be spread through contaminated drinking water, blood products and as a zoonosis from infected animals. Acute HEV genotype 1 or 2 infection is a leading cause of acute hepatitis and jaundice worldwide as well as acute liver failure (ALF) in endemic countries, particularly in pregnant women. In addition, acute HEV has been implicated in 20 to 60% of hospitalized patients presenting with acute-on chronic liver failure in some developing countries (1). Sporadic acute HEV genotype 3 infection presumably transmitted from contaminated food or dairy products also accounts for some cases of icteric hepatitis in selected regions of Europe such as Wales, Southwest France, and Denmark but is exceedingly rare in most western countries (2). In support of this, only 3 of the 681 (0.4%) adult Americans with ALF from our multicenter, prospective study were anti-HEV IgM positive over a 13 year time span and none of our cases were pregnant nor had detectable HEV RNA (3). Other studies in the US have also failed to implicate HEV as a significant cause of acute or chronic hepatitis in HIV + or solid organ transplant patients. Lastly, the seroprevalence of detectable anti-HEV IgG is declining in the US and other western countries for unclear reasons.

Renou et al now report that only 3 of 181 (1.6%) hospitalized patients with decompensated alcoholic liver disease enrolled in a multicenter French cohort study had a weakly positive anti-HEV IgM and all of them were HEV RNA (-). In addition, anti-HEV IgG seropositivity (34%) was not associated with the severity of liver disease or clinical outcomes. The findings of Renou et al are in keeping with a recent report from the HALT-C study group that also failed to implicate unsuspected acute HEV infection as a cause of decompensation in patients with advanced HCV fibrosis (4). Furthermore, investigators from Paris, France recently reported that only 3 of their 84 (3.5%) hospitalized patients with severe alcoholic hepatitis had evidence of acute HEV infection but 2 of the 3 anti-HEV IgM (+) patients had detectable HEV genotype 3 by PCR. The difference in results across studies could, in part, relate to the variable sensitivity and specificity of the serological assays used. The Beijing Wantai test is believed to have the best performance characteristics amongst the available assays but additional validation studies using a World Health Organization reference sample and carefully constructed test panels are needed.

We congratulate Renou et al on their important work regarding the potential role of unsuspected HEV infection in hospitalized patients with decompensated alcoholic liver disease. However, additional studies from well-characterized cohorts of western patients with acute on chronic liver failure are still needed to improve our understanding of the potential routes of transmission, pathogenesis, and clinical outcomes of previously unsuspected autochthonous HEV infection.

Words=492

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