

Review of: "[Mini Review] Global Burden and Evolving Understanding of Hepatitis E Virus"

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Potential competing interests: No potential competing interests to declare.

Abstract is well-written. One thing that needs to be mentioned in the abstract is the disease burden of hepatitis E virus on pregnant mothers and newborns since 15-20% mortality has been documented in pregnant women with HEV. Zoonotic transmission is another focus point for creating public awareness.

Introduction, Background, and Epidemiology are nicely stated. However, under Mode of Transmission, zoonotic transmission needs to be clarified in detail, e.g., ingestion of uncooked/undercooked animal meat, including infected animal liver, in particular, pork liver.

Under Geographic Distribution (Endemic Region), the author can add that the most recent HEV outbreak in Chattogram, Bangladesh, occurred between May and July 2018, coinciding with the rainy season of Bangladesh, and HEV affected approximately 2800 people in the Chattogram city area [Ref. Trop Med Infect Dis. 2022 Aug; 7(8): 170].

Geographical Distribution in Developed Countries- Few more pieces of information may enrich the article.

In Mechanism of HEV Persistence in Immunocompromised Individuals, authors may enrich the article by adding the significant role of CD4+ T cells in viral clearance that is not possible in an immunocompromised individual with a lower CD4 count. Another reason for HEV persistence is overexpression of IFN-stimulated genes (ISGs) in chronic HEV infection. A little bit of description of these factors is assumed to improve the quality of the present mini-review.

In Clinical Presentation (Acute Form): Addition of a few important and common clinical manifestations (e.g., low-grade fever, nausea, anorexia, metallic taste, upper abdominal tenderness, yellow-colored sclera, urine, and often generalized itching) will enrich the article. In Fulminant Form, some explanation can be given in favor of fulminant hepatic failure (FHF) as - a clinical syndrome of coagulopathy and encephalopathy resulting from massive necrosis of hepatocytes that leads to severe impairment of liver function. Since the encephalopathy develops within 8 weeks of the first symptoms in the absence of pre-existing liver disease, FHF is considered a severe form of acute hepatitis. More common in pregnant women who are HEV-infected in their third trimester.

The rest of the clinical presentation is assumed to be alright.

Under Virological Diagnosis (Indirect Virological Diagnosis), a little bit of modification of a few sentences may be done. The detection of anti-HEV IgG antibodies alone cannot confirm the presence of active disease but indicates previous exposure to the virus. However, the coexistence of both anti-HEV IgM and anti-HEV IgG is strongly suggestive of acute

hepatitis E infection. In direct diagnosis, detection of viral copy number by real-time qRT-PCR is still considered the gold standard. Identification of HEV1 and HEV 4 capsid proteins by detecting viral antigen is not encouraged recently due to the narrow detection window as well as intermittent excretion. In immunocompetent individuals, the detection of anti-HEV IgM antibodies is enough for the diagnosis of acute hepatitis E. Because of low sensitivity, serological diagnosis is not advised for immunocompromised individuals; detection of viral RNA in plasma or stool can be considered an appropriate method for the diagnosis of HEV in this group of people.

The treatment and management of chronic hepatitis E, prevention of hepatitis E, and HEV239 (Hecolin) vaccine - construction of a few sentences needs to be developed. Otherwise, well-written.

My recommendation - the mini-review, 'Global Burden and Evolving Understanding of Hepatitis E Virus,' is well written and can be accepted after a few modifications as stated above.