

Hepatitis E and Pregnancy

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ABSTRACT

HEV generally causes mild, self-limiting hepatitis E that may lead to acute or fulminant liver failure, chronicity and cirrhosis in some individuals. Pregnancy can further exacerbate hepatitis E, affecting both mother and child with significant morbidity and mortality rates. The mechanisms leading to acute or fulminant liver failure in pregnant patients still remain elusive. Compared to developing countries, industrialized nations have very few reported cases of HEV infection during pregnancy. Immediate hospitalization is recommended for suspected cases, and liver transplantation is the only option for who develop acute or fulminant liver failure. Ribavirin is the only drug of choice that is however, contraindicated during pregnancy because of severe side-effects and the risk of teratogenicity.

Key words: Hepatitis E; HEV; Pregnancy; Fulminant liver failure; Ribavirin

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INTRODUCTION

Hepatitis E virus (HEV) is a hepatotropic RNA virus that typically causes mild, self-limiting illness similar to acute hepatitis A or B in the general population. HEV is responsible for about 20 million new infections and over 55,000 deaths annually, worldwide^[1]. Of the known seven genotypes of HEV (HEV1-7) belonging to a single serotype, four (HEV1-4) are pathogenic to humans^[2]. A unique characteristic of HEV is its differential epidemiological and pathophysiological manifestations among its different genotypes. While HEV1 and HEV2 are waterborne (fecal-oral) and associated with large outbreaks in developing countries, autochthonous cases of zoonotic (swine and wild boar) HEV3 and 4 infections in industrialized nations have increased in recent years^[3]. Though acute hepatitis E is commonly self-limiting, some patients may also develop acute or fulminant liver failure, cholestatic jaundice or neuromuscular symptoms^[4,5]. In European and North American countries, the most virulent HEV3 is responsible for chronic infections and liver cirrhosis in immunosuppressed transplant recipients and transfusion patients^[3,6].

HEPATITIS E IN PREGNANCY

Viral hepatitis in general, affects mother and child, and pregnancy can further exacerbate hepatitis E. Pregnant women with acute hepatitis E are at higher risk of morbidity and death than those with chronic hepatitis E. HEV can be transmitted vertically from infected mothers to their fetuses^[4,7]. During pregnancy, unlike the mild self-constraining infection, HEV can result in fulminant hepatic failure, membrane rupture, low birth weight, spontaneous abortions, and stillbirths^[8]. Studies from developing countries have shown a high incidence of hepatitis E in pregnancy with a significant proportion of third-trimester women progressing to fulminant hepatitis with a fatality rate of up to 30%^[8]. The cascade of molecular events preceding

the liver failure in this population is hitherto not well understood but one possible explanation may be increased estrogen levels.

Nonetheless, very recently in pregnant women with acute hepatitis E, signature microRNA (miRNA) molecules are identified that preferentially target the gene expression profiles of neutrophils, eosinophils, monocytes, macrophages, T and B lymphocytes, natural killer cells and plasmacytoid dendritic cells^[9].

Compared to HEV1, there are very few reported cases of HEV3 infection during pregnancy in industrialized countries^[6,10-13]. Very recently, cases of HEV3 infection in French pregnant women who neither travelled to endemic region nor eaten undercooked pork are reported^[11-13]. Although chronic hepatitis E has not been reported in patients treated with infliximab or azathioprine, it is observed in a chronic case of a pregnant woman who received infliximab and azathioprine, and spontaneously resolved after delivery^[14].

RISK FACTORS AND CONTROL

Pregnant women, especially in third trimester are the high-risk population, including travelers to endemic regions, pork consumers, patients with acute hepatitis or underlying liver disease, and immunocompromised transplant recipients and transfusion patients. Though HEV has been detected in breast milk with comparable seropositivity, there is insufficient data on HEV transmission via breast milk^[15]. There is an approved vaccine (HEV239 or Hecolin) in China that is however, not available in other countries^[16]. The most important measure to prevent HEV infection is good sanitation and protecting potable water from fecal or slurry contamination. Travelers to endemic regions must take precautions while drinking water. Pregnant women should avoid unnecessary travel to endemic areas and avoid consumption of undercooked pork or other products. Further, managing hepatitis E in pregnancy requires assessing the risk of transmission to the baby, determining the gestational age at the time of infection and the mother's risk of decompensation.

DIAGNOSIS AND TREATMENT

Hepatitis E can be diagnosed by ELISA based detection of anti-HEV antibodies (IgMab) that however, vastly relies on the assay specificity and sensitivity^[17]. The RT-PCR based molecular detection of HEV RNA in the blood or stool is the most reliable confirmation. Furthermore, cases of acute hepatitis E are often under/misdiagnosed due the co-circulation of other hepatotropic viruses with similar clinical presentations^[18]. Acute hepatitis E is generally resolved within one week that may take up to 6 weeks in some cases, requiring only supportive care. Immediate hospitalization should be considered for suspected cases of pregnant women. Patients who develop acute or fulminant liver failure need liver transplantation.

Ribavirin alone or in combination with pegylated-Interferon α is the only treatment of choice in chronic cases of HEV3 infection^[19]. Although ribavirin effectively clears HEV and induces a sustained virological response, emergence of viral polymerase gene mutants lead to non-response or failure to therapy^[19,20]. Notably, in pregnant women, use of ribavirin needs a proper understanding of its side-effects (eg, anemia, dyspnea, insomnia and irritability), and is further contraindicated because of the risk of teratogenicity^[20].

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