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Brief Communication

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# Fulminant hepatic failure from hepatitis E in a non-pregnant female traveller

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## Abstract

A non-pregnant Canadian woman returning from India presented with a 1-week history of jaundice and malaise. Subsequently, she developed fulminant hepatic failure caused by hepatitis E virus (HEV). HEV can cause fulminant hepatic failure, most commonly in pregnant women and those with chronic liver disease; however, all travellers are at risk.

**Key words**: Hepatitis E, infectious diseases, travel medicine

## Introduction

Hepatitis E virus (HEV) is a single-stranded RNA virus of the Herpeviridae family causing acute viral hepatitis.[1] Infection with HEV is the most common causative agent of acute viral hepatitis in tropical and subtropical developing countries of Asia, Africa and the Middle East.[2] It is estimated that >20 million cases of HEV infection occur worldwide each year, resulting in 70 000 deaths.[1] HEV is a cause of sporadic cases of viral hepatitis in the developed world. Unlike hepatitis B and C, HEV does not progress to a chronic state.

HEV is a water-borne pathogen with fecal-oral transmission; infection results from drinking contaminated water.[2] The incubation period has been estimated to be 15–64 days with a mean of 6 weeks.[3] Although Hepatitis E is usually a benign condition, it can cause severe disease most notably in pregnant women, patients with chronic liver disease or the elderly. Clinically overt disease occurs most often in the 15–40-year age group. Symptoms of HEV typically last 1–2 weeks and include anorexia, dark urine, nausea and vomiting, abdominal pain and eventually icterus.[1] Laboratory findings include elevated alanine aminotransferase, aspartate aminotransferase and bilirubin. Hepatitis caused by HEV is clinically indistinguishable from hepatitis A. As this case illustrates, infection with HEV poses a significant risk for acute viral hepatitis to travellers in endemic areas.[4]

## Case presentation

A 33-year-old previously healthy woman presented to the emergency department of the North York General Hospital, Toronto, Canada on 9 April 2015 with a 1-week history of jaundice and malaise. The patient was a tourist in Rajasthan, India for one month returning 3 March 2015. Her travels took her to both rural and urban areas.

Two weeks after arrival in India she developed a significant diarrheal illness with nausea, vomiting and fever for 24 h that improved after receipt of an unknown antibiotic. Upon returning to Canada the patient developed recurrent diarrhea. On 13 March, her family doctor initiated treatment with metronidazole, at which point her symptoms began to improve. Stool for parasite examination was positive for *Giardia intestinalis*.

On admission, the patient reported no relevant past medical or surgical history, medication use or allergies. For a previous trip in 2009, she received yellow fever vaccine, along with immunizations for hepatitis A and B, typhoidand Japanese Encephalitis. The patient drank only commercially bottled beverages but ate salads and food from street venders while in India.

Physical examination was unremarkable. The patient had no evidence of hepatic encephalopathy such as asterixis or confusion. She continued to deteriorate over the next few days with multiple intermittent bouts of nausea and vomiting. Her liver enzymes reflected her worsening condition. The results of the

**Table 1.** The patient's biochemical tests

| | Results | | | Normal range of values |
|---|---|---|---|---|
| | 9 April 2015 | 14 April 2015 | 29 April 2015 | |
| AST (U/L) | 1577 | 2598 | 76 | 18–40 |
| ALT (U/L) | 962 | 1625 | 34 | 17–63 |
| Total bilirubin (umol/l) | 419 | 855 | 657 | <26 |
| INR | 1.55 | 6.13 | 1.10 | 0.9–1.2 |
| PT (s) | | 55.1 | 14.8 | 28–36 |

ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, international normalized ratio; PT, prothrombin time.

biochemical tests are summarized in Table 1. An abdominal ultrasound on admission was consistent with hepatitis and splenomegaly. A liver biopsy performed 10 April suggested viral hepatitis (A or E) but could not exclude a drug related etiology. Markers for acute Hepatitis B and C virus, Epstein-Barr virus, and cytomegalovirus were negative. The patient tested positive for specific anti- HEV IgM and IgG by enzyme-linked immunosorbent assay on 14 April.

On 14 April, 5 days after admission, the patient was somnolent with a bilirubin of 855 micromol/l and an INR of 6.13. The diagnosis was fulminant hepatic failure with progression. She was transferred to a tertiary care hospital to be followed by the Liver Transplant team. Fulminant hepatic failure is defined by the presence of jaundice, coagulopathy and encephalopathy. The definition used by the acute liver failure study group (NIH) is, 'the presence of coagulopathy (prothrombin time >15 s or international normalized ratio ≥1.5) and any hepatic encephalopathy within 26 weeks of the first symptoms without previous underlying liver disease'.[5]

The patient was found to be an eligible candidate for a liver transplant and emergency surgery was scheduled. Listing for transplant is generally based on the King's College criteria for acute liver failure. For nonacetaminophen overdoses, these are INR > 6.5 OR 3 of the 5 following: age <11 or >40, serum bilirubin >300 μmol/l, time of jaundice to encephalopathy >7 days, INR > 3.5 and etiology is drug toxicity.

In hospital, treatment with oral cholestyramine (4 gm), IV ondansetron (4 mg every 8 h), oral ursodial (500 mg b.i.d.), oral pantoprazole sodium (40 mg daily) and lactulose were initiated. However, on 17 April she began to recover spontaneously.

The patient was discharged 29 April in good condition, returning to near baseline functional status (Table 1).

## Discussion

This case is unusual because in men and non-pregnant women, HEV is usually self-limited and has a low case-fatality rate (<0.1%).[6] However, in pregnant women, HEV infection leads to fulminant hepatic failure and death in up to 15–20% of cases and is associated with intrauterine fetal death, preterm delivery and stillbirths.[1,6] It is currently unclear why pregnant women are more vulnerable.

The first documented case of HEV in Canada was in 1995.[7] Subsequently, the majority of confirmed HEV infections in Canada arise in individuals returning from India, Pakistan and Bangladesh.[8] The risk of acquiring infection is significantly higher for visiting friends and relatives compared with Canadians travelling to the same countries as tourists. The incidence of HEV infection in Canada is not known as infections are mainly asymptomatic, rarely reported and the disease is not on the list of the Nationally Notifiable Diseases. One study conducted in the United States estimated the seroprevalence of HEV to be 21%.[9] Furthermore, in a study conducted of Israeli travellers 39% of the cases of acute hepatitis were due to hepatitis E, the most frequent hepatitis among Israeli travellers.[10]

Diagnosis can be confirmed through the detection of HEV in serum or stool by polymerase chain reaction or by the detection of IgM antibodies to HEV.[11] The detection of serum anti-HEV IgM indicates recent infection.[7] Anti-HEV IgG remains elevated following infection and is ineffective in differentiating acute from previous infection. The differential diagnosis of HEV includes other causes of viral hepatitis, drug-related hepatitis, as well as other infectious causes including leptospirosis, Q fever, malaria, and typhoid fever.[7] As illustrated by the severity of our case, HEV testing must be considered by physicians as part of the first-line diagnosis for acute hepatitis.

Fecally contaminated water is the primary source of exposure to HEV; therefore, travellers to endemic countries should follow strict food and water precautions.[12] Prophylactic measures against HEV include using bottled water for drinking, washing food and practicing good hand hygiene. There is no commercially available vaccine in North America.

HEV infection is often not well recognized but must be considered by physicians as part of the initial diagnosis for acute hepatitis, especially in returned travellers. Although rare, HEV can cause fulminant hepatic failure most frequently in pregnant women and those with chronic liver disease. However, as this case indicates, all travellers are at risk. Travellers to endemic areas must be educated about prevention of Hepatitis E.

**Conflict of interest:** None declared.

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