



## CLINICAL CASE

# Fulminant hepatitis E in a pregnant woman

Mónica Velosa<sup>a,b,\*</sup>, António Figueiredo<sup>c</sup>, Helena Glória<sup>b</sup>, Ana Morbey<sup>b</sup>,  
Elia Mateus<sup>b</sup>, Zélia Neves<sup>d</sup>, Ana Araújo<sup>d</sup>, Ana Carvalho<sup>c</sup>,  
Judite Oliveira<sup>d</sup>, Eduardo Barroso<sup>b</sup>

<sup>a</sup> Serviço de Gastrenterologia, Hospital Central do Funchal, Funchal, Portugal

<sup>b</sup> Unidade de Transplantação, Hospital Lisboa Central – Curry Cabral, Lisboa, Portugal

<sup>c</sup> Serviço de Anatomia Patológica, Hospital Lisboa Central – Curry Cabral, Lisboa, Portugal

<sup>d</sup> Unidade de Cuidados Intensivos, Hospital Lisboa Central – Curry Cabral, Lisboa, Portugal

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### KEYWORDS

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**Abstract** Hepatitis E is an inflammatory liver disease caused by hepatitis E virus (HEV) infection, which is endemic in China, India, Nepal, and in several Asian and African countries, where the prevalence can be as high as 50%. In non-endemic countries, an increasing number of non-travel associated HEV has been reported in recent years, particularly in Europe.

The authors describe the clinical case of a puerperal 24-year-old woman from Pakistan admitted to our Tertiary Care Medical Center with acute hepatic failure developed during the third trimester of her pregnancy. She was icteric with grade III encephalopathy and hypothermia. Laboratory values showed significant AST, ALT and LDH elevations of twelve times the upper normal limit, and total bilirubin was significantly elevated (41.20 mg/dL). Prothrombin time was prolonged (4s) and factor V activity was diminished (15.1%). Extracorporeal albumin dialysis was initiated, but clinical deterioration occurred within 48 h, so she underwent OLT at day 4 post-admission.

Severe forms of HEV are known to be more pronounced in pregnant women. Even though most of the described cases of acute hepatic failure associated to HEV during pregnancy had a favorable clinical course, some cases of fulminant liver failure and death are described. It is unknown whether liver transplant outcomes in this setting are different from other causes of acute liver failure. To our knowledge, this is the first case report in Portugal from a pregnant woman who developed hepatic failure due to fulminant hepatitis E that underwent successful liver transplantation.

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\* Corresponding author.

E-mail address: [mo.velosa@gmail.com](mailto:mo.velosa@gmail.com) (M. Velosa).

**PALAVRAS-CHAVE**

Vírus da hepatite E;  
Transplante hepático;  
Hepatite Fulminante;  
Gravidez

**Hepatite E fulminante numa mulher grávida**

**Resumo** A Hepatite E é uma doença inflamatória do fígado causada pelo Vírus da Hepatite E (VHE). Este vírus é endêmico na China, Nepal, Índia e em vários países Africanos e Asiáticos, onde a sua prevalência pode atingir os 50%. Em países não endêmicos, particularmente na Europa, tem-se verificado um aumento da prevalência de VHE não associada a viagens.

Os autores descrevem o caso de uma doente de 24 anos, puérpera, natural do Paquistão, admitida no nosso Centro Terciário com insuficiência hepática aguda, com início no terceiro trimestre da gravidez. A doente encontrava-se icterica, com encefalopatia hepática grau III e hipotermia. Os valores laboratoriais mostraram elevação significativa de 12 vezes o limite superior do normal das aminotransferases (AST e ALT) e da LDH, com bilirrubina total elevada (41.2 mg/dL), prolongamento do tempo de protrombina (4 seg) e actividade do factor v diminuída (15.1%). A doente iniciou diálise de albumina extra-corporal, contudo verificou-se rápida deterioração, tendo sido submetida a transplante hepático no 4º dia após a admissão.

Formas mais graves de hepatite associada a VEH têm sido descritas durante a gravidez. Geralmente, mesmo as formas mais graves têm uma evolução tendencialmente favorável, com apenas alguns casos descritos de morte e de hepatite fulminante. Desconhece-se para já qual o resultado a longo prazo dos doentes transplantados por hepatite E fulminante, quando comparados com outras populações. Este caso representa o primeiro caso descrito em Portugal de uma doente grávida com hepatite fulminante causada por VHE, submetida com sucesso a transplante hepático.

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**Introduction**

Hepatitis E is an inflammatory liver disease caused by hepatitis E virus (HEV) infection, which is a single-stranded, non-enveloped RNA virus and the only virus within the genus *Hepevirus* and the family *Hepeviridae*.<sup>1,2</sup> The first described cases of acute liver disease caused by an enteric infectious agent that differed from hepatitis A and hepatitis B viruses were reported in India in the 1970s.<sup>2</sup> HEV is endemic in China, India, Nepal, as well as in several Asian and African countries, where the prevalence of HEV IgG antibody can be as high as 50%.<sup>3</sup> It has been recently estimated that its infection causes more than 3 million symptomatic cases of acute hepatitis E each year, resulting in approximately 70,000 deaths worldwide.<sup>4</sup> In non-endemic countries, an increasing number of non-travel associated HEV cases have been reported in recent years, particularly in Europe.<sup>5,6</sup> In Portugal, sporadic cases have been reported, and a study on 237 individuals, from which 152 were patients from a Gastroenterology Department, showed that 4.2% of the population enrolled was seropositive for anti-HEV. Furthermore, in the seropositive group, only 20% had a history of traveling to endemic countries.<sup>7</sup>

Testing for hepatitis E should be done in the diagnostic analysis of all patients with acute or chronic hepatitis that cannot be explained by other causes. Acute HEV infection is diagnosed in immunocompetent individuals based on the detection of anti-HEV IgM. Immunocompromised individuals should always be tested for HEV RNA, if there is suspicion that they are infected, because seroconversion can be delayed in these patients.<sup>8,9</sup>

Most infections have a clinically silent course. In symptomatic cases, the incubation period ranges from 2 to 8 weeks, with a mean of 40 days.<sup>1</sup> Initial symptoms of acute hepatitis E are typically unspecific and include flu-like myalgia, arthralgia, weakness and vomiting. However, more

severe forms of acute liver disease can occur in pregnant women or patients with underlying chronic liver diseases, sometimes progressing to fulminant hepatic failure.<sup>10</sup> In immunocompetent patients, HEV is mainly self-limited and causes no chronic evolution. In fact, in these individuals, acute hepatitis E does not usually require therapy.<sup>11</sup> Nevertheless, in immunocompromised patients, HEV can pursue a chronic course. Persistent HEV infection was first reported in 2008 in 8 French solid organ transplant recipients on immunosuppression. Furthermore, one kidney-transplant patient had cirrhosis attributed to chronic HEV infection.<sup>2</sup> HEV-associated liver cirrhosis or hepatocellular carcinoma in the immunocompetent patient has not been reported, so far; however, acute HEV infection is known to be a cause of decompensated liver cirrhosis.<sup>12</sup>

**Case report**

A 24-year-old puerperal woman was admitted to our Tertiary Care Medical Center with acute hepatic failure. She was a Pakistani woman living in Portugal for 3 years that had recently traveled to Pakistan while pregnant, for a total stay of 3 months. She returned to Portugal during the third trimester of her pregnancy, 3 weeks before admission in our Hospital. During her time in Pakistan, she was observed by an Obstetrician and did a fetal ultrasound that she reported as being normal. She denied having any symptoms while in Pakistan, contact with sick people and/or previous history of hepatitis in her relatives. Her background was unremarkable, she was married and mother of a 2-year-old healthy child, with a regular pregnancy and an eutocic delivery and a history of 2 previous spontaneous abortions. She denied current medication and toxic or alcohol consumption.

During pregnancy week 32, the patient reported nausea, vomiting, asthenia and myalgia. She went to an outpatient Obstetrics Consult in another Institution and in the

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