

Hepatitis E

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Background

Introduction

Hepatitis E Virus (HEV) was first isolated at the beginning of the 1990s (1) and is endemic in many developing countries where it occurs both in sporadic form and in outbreaks. In African and Asian countries it is responsible for acute hepatitis outbreaks due to the contamination of the water distribution system. In industrialized countries, HEV is now recognised as an emerging disease where an increasing number of locally acquired (autochthonous) infections has been noticed (2). Its severity varies from asymptomatic or self limited disease to a fulminant or fatal disease. Mortality rates associated with HEV are low but can rise up to 20% in pregnant women in whom the disease is more severe. Chronic infection may appear in immune-suppressed patients e.g. organ transplant recipients.

HEV is a non-enveloped single strand RNA virus which belongs to the *Hepeviridae* family. The virus causing the disease in humans has four genotypes (2). Most autochthonous cases occurring in industrialized countries are due to the genotype 3. The incubation period ranges between 14 and 60 days (mean 30-40 days). Transmission of the virus is primarily through faecally contaminated food or water especially in developing countries. Person to person secondary transmission seems to be rare (1 to 2% secondary attack rate) but can occur via faecal-oral routes.

Locally acquired HEV in industrialized countries

In non-endemic settings, the reservoir of the disease is still unknown. The virus has been found in both domestic and wild animals. Recent studies suggest that HEV may in fact be a zoonotic infection. Phylogenetic analyses revealed some similarities between human strains and strains from pigs in the same area in the United States (3), Taiwan (4), the United Kingdom (5), Spain (6) and the Netherlands (7). Occupational exposure to pigs was significantly associated with higher levels of IgG anti-HEV in Moldova (8). In some studies, links were made between HEV and the consumption of uncooked deer (9) and shellfish (10). Significant epidemiological associations were found between HEV cases and consumption of boar (11-13) and offal (11). In addition, the virus is present in sheep, cattle and rodents (14). The virus was also found in sewage in Barcelona (Spain), Washington (USA) and Nancy (France) (6).

The demographic features of patients who acquired HEV infection in developed countries differ from those in developing countries. According to descriptive studies in England and Wales, France and the Netherlands, most of the patients were male, Caucasian and aged over 55 years (10;15-17). This is in contrast to developing countries where cases are usually reported in all age groups and in both sexes (18-20)

Serological Diagnosis

Serological diagnosis of acute infection is based on enzyme immunoassay (EIA) tests. IgM anti-HEV is usually detectable at the onset of symptoms (and maximum three months after), with abnormal liver function. IgG reaches a peak shortly after and can persist for years. The virus can be detected in serum and stools immediately before the onset of symptoms and until a few days after (longer in stools).

Control

No vaccine is currently available. Some clinical trials are ongoing.

Surveillance in Europe

A number of European countries have recently begun to investigate locally acquired HEV.

Hepatitis E virus is notifiable in Germany where a total of 75 cases were notified in 2007 (including travel related cases). In 2006, a case control study was launched to determine the risk factors for autochthonous HEV (11). The study included 45 cases and 135 controls. Offal and wild boar meat were found to be significantly associated with HEV infection.

In the United Kingdom, the disease is not notifiable, but a HEV enhanced surveillance programme covers all patients tested for HEV and cases confirmed as HEV positive by the two reference laboratories (Birmingham and Centre for Infection, Colindale, London). The objective is to ascertain and investigate non-travel associated cases of HEV in the UK and to identify potential risk factors. Descriptive results were published on 28 autochthonous cases interviewed, out of 329 hepatitis E notified in 2005 (16). Most of the cases were Caucasian males over 55 years old who reported a high consumption of pork.

In France, a voluntary surveillance system using reference laboratories for HEV was set up in 2008. Enhanced surveillance of cases and a nested case control study among reported cases has been initiated in order to determine risk factors associated with local infection.

The disease is not notifiable in the Netherlands. However, a retrospective descriptive study including case finding through the different microbiological laboratories was performed in 2004-2006. A total of 19 cases were included in this study. Most of them were male (n=17/19), the median age of cases was 50 years, sixteen reported eating pork and six owned dogs (15).

Epidemiology of Hepatitis E in Ireland

The disease is not notifiable in Ireland and few data concerning the epidemiology of hepatitis E in Ireland are readily available.

A survey published in 1994 tested 45 haemodialysis patients for HEV infection. These patients were from different regions of Ireland. None of them were positive (21).

A second serological survey published in 1995 tested 600 samples for HEV. These samples were tested in a laboratory which covered about 500,000 people in the southern part of Ireland. Five hundred samples were antenatal samples, the others were consecutive samples sent to the laboratory for serological diagnosis of hepatitis. Only six samples were found to be positive: two among 500 antenatal samples (0.4%) and four among the 100 other samples (4%), which indicated a low prevalence of HEV in Ireland (22).

The National Virus Reference Laboratory performs hepatitis E serology when it is specifically requested by clinicians. The test used is a Biokit hepatitis E IgM assay (Bioelisa HEV IgM; BLOKIT, Barcelona, Spain).

Between January 2004 and December 2008, HEV testing was requested in the NVRL on 309 patients; 17(5.5%) were positive for HEV IgM. The number of requests increased from 26 in 2004 to 105 in 2008. Most of the cases were diagnosed in 2007 (8/17). Nine cases were male (53%) and the median age of the cases was 18 years (range: 2-48 years). Most of the cases (9/17) came from the Eastern Region. No information was available regarding travel history.

Discussion

Hepatitis E infection is increasingly recognised as a cause of liver dysfunction in developed countries where it appears to be a zoonotic infection. The number of people tested positive for hepatitis E in Ireland was very low during the last few years. Although the incidence of the disease is unclear in developed countries, health professionals here should be aware of the risk of autochthonous hepatitis E infection and should consider hepatitis E in the differential diagnosis of non travel associated hepatitis, regardless of the age and the sex of the patient.

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