Vaccine 34 (2016) 3715–3718

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Brief report

A hepatitis E outbreak by genotype 4 virus in Shandong province, China

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ARTICLE INFO

Article history:
Received 22 November 2015
Received in revised form 23 May 2016
Accepted 1 June 2016
Available online 16 June 2016

Keywords:
Hepatitis E
Outbreak
Vaccination
China

ABSTRACT

Hepatitis E vaccine was available in China in 2012, but the priority population for immunization is not clear. In 2013, a hepatitis E outbreak occurred in a company of Shandong province, China where most employees moved from other provinces and dined at the company's cafeteria. A total of fourteen (19%, 14/73) case-patients were identified, and three of them had symptomatic infection with one death. The proportion of symptomatic infection was much higher among those aged ⩾50 years than those aged <50 years (2/2 vs. 1/12, $P = 0.03$), and higher in males than females (3/8 vs. 0/6, $P = 0.21$). Food in the company's cafeteria might be the possible source of the outbreak. The findings from this outbreak investigation indicate that individuals aged ⩾50 years, particularly males, might be the population of top priority for hepatitis E vaccination in China.

1. Introduction

Hepatitis E virus (HEV) is an enterically transmitted virus, and outbreaks from HEV was first verified and confirmed in 1990 s [1] and is responsible for about 50% of acute viral hepatitis cases in the endemic countries [2,3]. HEV is endemic in China and the seroprevalence among the general population was around 23% [4]. Hepatitis E cases are required to report to the National Notifiable Reporting System (NNDRS) in China since 1997, and the number of reported cases increased from 16,444 in 2004 to 19,202 in 2011[5]. In 2012, hepatitis E vaccine became available in China, and offered an effective way to prevent HEV infection [6]; but the vaccination coverage is still very low.

Between December 2013 and January 2014, a hepatitis E outbreak occurred in a company in Donggang District, Rizhao Prefecture of Shandong province, China. We reported the HEV outbreak, and examined risk factors associated with HEV infection, and explored the implications for hepatitis E prevention.

2. Methods

2.1. General information of the company

Donggang District of Rizhao Prefecture was located in the east of China, having a population of 78,000. The company where the outbreak occurred was established in Rizhao city in December 2011. There were 73 employees in the company, including 69 employees moved from other provinces of China during December 2011 and October 2012 and four local employees (two cooks and two janitors). All migrant employees lived in the apartments near the company. Free bottled water from dispensers was available in apartments and the offices. The company had a cafeteria which opened all day long for three meals.

2.2. Active case-finding

To identify all persons infected with HEV in the company, blood and stool samples were collected from all employees and were tested for HEV IgM and HEV IgG. The IgM-positive employees who developed signs and symptoms compatible with hepatitis were reported to NNDRS. Face-to-face interviews were conducted for all local employees and their family members on whether they had developed signs and symptoms indicative for hepatitis in the past two months. If any family had any sign/symptom for hepatitis, blood and stool samples would be collected and tested for HEV infection.

2.3. Case investigation

A face-to-face interview was conducted among HEV IgM-positive employees. Information on demographics information and the potential risk factors during the potential exposure period (from October 1, 2013 to November 15, 2013, 15–60 days prior to the disease onset of the index case) was collected, including the

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http://dx.doi.org/10.1016/j.vaccine.2016.06.010
0264-410X/

Table 1
The prevalence of HEV IgM and HEV IgG among the employees by age, gender and employee types.

	No. tested	HEV IgM positive *n* (%)	HEV IgG positive *n* (%)	Symptomatic hepatitis[a] *n* (%[b])
Total	73	14 (19)	14 (19)	3 (21)
Age (years)				
20–49	67	12 (18)	12 (18)	1 (8)
⩾50	6	2 (33)	2 (33)	2 (100)
Gender				
Male	45	8 (18)	8 (18)	3 (38)
Female	28	6 (21)	6 (21)	0 (0)
Employee types				
Local employee	4	1 (25)	1 (25)	0 (0)
No-local employee	69	13 (19)	13 (19)	3 (23)

[a] Defined as HEV IgM+ with signs and symptoms for hepatitis.
[b] The denominator was the number of the employees who were HEV IgM+.

histories of diet, drinking water, travel, contact with other persons infected with HEV, transplantation and transfusion and the clinical information including the date of disease onset, the symptoms and signs. The medical records were checked for those who were hospitalized to verify their clinical information. Verbal informed consents were obtained from all employees before interview and sample collection.

2.4. Laboratory testing

The blood samples were tested for HEV IgM and IgG using Wantai ELISA kit (Wantai Biological, Beijing, China) according to the manufactory's instructions. The sera and the stool samples from HEV IgM-positive employees were analyzed for HEV RNA by reverse transcription-nested PCR with primers designed within 644-bp region of open reading frame (ORF) 2 [7]. Phylogenetic analysis with 594 nt sequences of the ORF2 was performed to determine the HEV genotype using Mega 4.0 and the nucleotide similarity among the HEV isolations in the outbreak and other

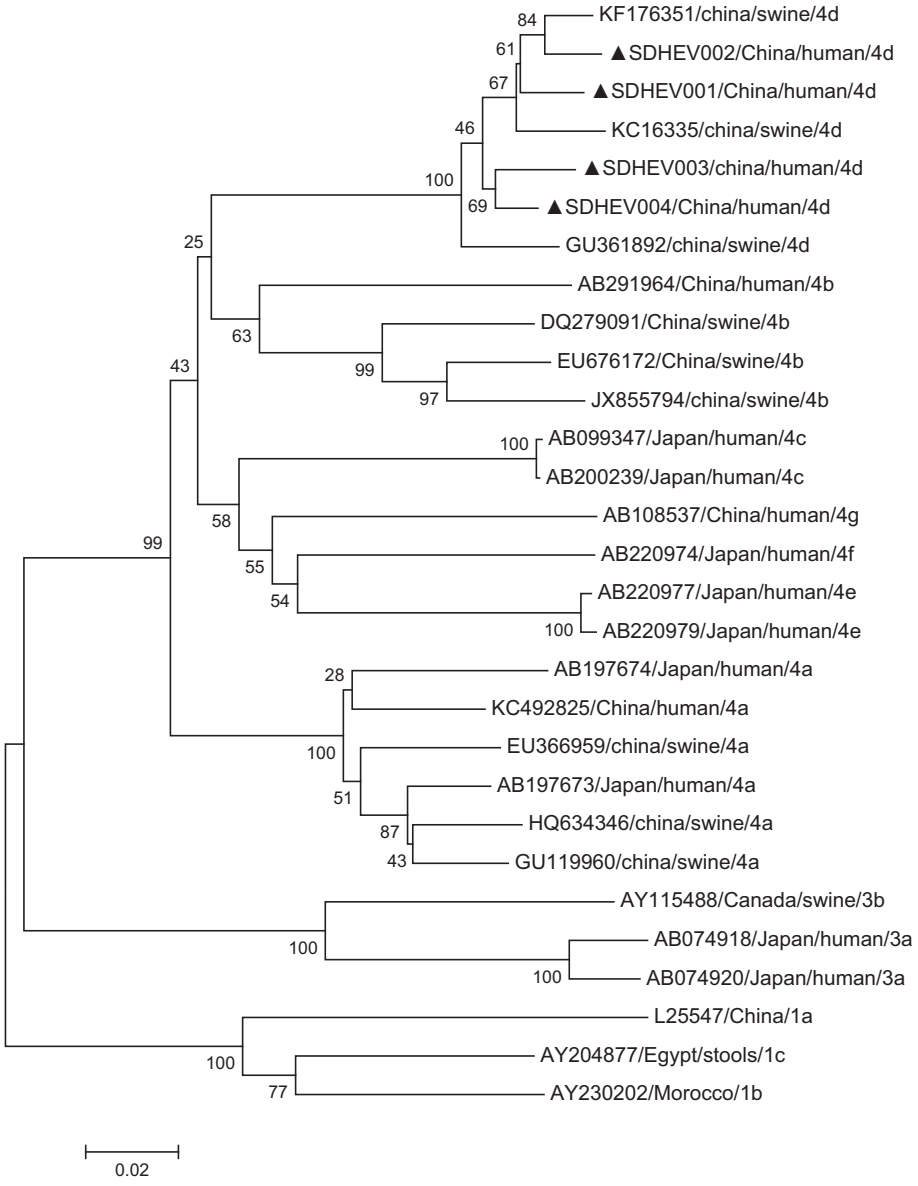

Fig. 1. Phylogenetic tree based on partial open reading frame (ORF) sequences of the hepatitis E virus monophyletic strain in Rizhao city of Shandong province, China. Using the neighbor joining method. Genetic distances were calculated using the Kimura two-parameter method.