

Epidemiology of hepatitis E in China

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Introduction

Hepatitis E has been documented in China since 1982¹. The disease is most often seen in rural areas with poor sanitary conditions through contaminated drinking water or food in a form of outbreaks or epidemics. However, it may also occur in a sporadic form in endemic areas.

Incidence

To date, epidemics or outbreaks of Hepatitis E have been described in 6 of 30 provinces or autonomous regions in China, i.e. Jilin², Liaoning³, Hebei¹, Shandong⁴ Provinces and the Inner Mongolia⁵ and Xinjiang Uighur⁶⁻¹⁰ Autonomous Regions (**Figure 1**). Epidemics with similar epidemiological and clinical features were reported in Liaoning¹¹, Hebei¹² and Shandong¹³ Provinces in the 1960s. It is likely that the disease may have also occurred in other provinces or autonomous regions, but was not recognized.

Modes of Transmission

Waterborne transmission

To date, of 9 hepatitis E epidemics reported in China, 5 were associated with the contamination of drinking water⁷⁻¹⁰ (**Table 1**). The largest epidemic of hepatitis E has occurred in the south part of Xinjiang Uighur Autonomous Region from September 1986 to April 1988⁹. It involved

23 counties and towns, persisted for 20 months and underwent two epidemic periods. The total number of cases was 119,280, with an attack rate of 3.0%. The disease mainly affected Uighurs, with the attack rate of 7.1%, which was significantly higher than in Han, Hui and other ethnic groups (0.7%, 3.7% and 0, respectively). Almost all of the Uighur Tribe dwelling in rural areas of Xinjiang have a habit of drinking unboiled water from pools and canals, while the Han and Hui nations usually drink boiled or well water. The attack rate of the disease in the people using water from pools or canals was significantly higher than in the people with well water supply sources (7.7% vs 1.2%). In addition, the coliform reaction was present in all of the water samples collected from pools or canals during the epidemic, with coliform counts varying from 90 to 230/dl. The data showed gross fecal contamination of pool and canal water, and led us to believe that the epidemic was of a waterborne type with a common source of transmission.

Foodborne transmission

Recently four foodborne outbreaks of hepatitis E have been reported from China^{1-3,5}. In one outbreak² among 150 persons who had attended a wedding feast, nine came down with viral hepatitis successively within 45 days. The age of these patients ranged from 43 to 67 years. In the second outbreak³ of 112 people who had been at a dinner party for celebration of a national holiday, 24 de-

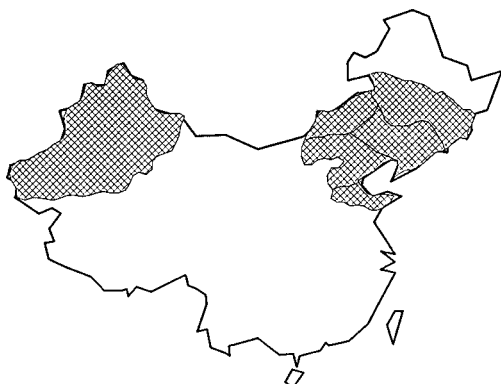


Fig. 1 Geographic distribution of hepatitis E in China.

Table 1 Epidemics of hepatitis E in China

Year	Place	Cases/Population (%)	Type of Epidemic
1982	Tiajing	10/63 (15.9)	Foodborne
1982	Xinjiang	35/221 (15.8)	Waterborne
1983	Xinjiang	459/17,261 (2.7)	Waterborne
1983	Inner Mongolia	61/341 (17.9)	Foodborne
1985	Jiling	9/150 (6.0)	Foodborne
1986	Shenyang	24/112 (21.4)	Foodborne
1986	Shandong	6/668 (0.9)	Waterborne
1986	Xinjiang	76/623 (12.2)	Waterborne
1986-1988	Xinjiang	119,280/4,028,577 (3.0)	Waterborne

veloped acute viral hepatitis from 15 to 36 days after the party. The third outbreak⁵ occurred in a technical secondary school, with a total of 61 cases of hepatitis among 249 students, 85 teachers and 7 kitchen staff. All the 61 patients were boarding at the school and contracted the disease within 46 days. Three of them were kitchen staff of the school. The attack rate of the illness in the students, teachers and kitchen staff were 23% (58/249), 0 (0/85) and 42.9% (3/7), respectively, with an overall attack rate of 19.8%. It is interesting to note that none of 85 teachers, living outside the school and having meals at home, developed hepatitis during this outbreak. The fourth epidemic occurred in the troops stationed in Tiajing from February to March, 1982. The first case reported during the epidemic was a cook of the troops. Then 10 cases were observed among 63

soldiers. The serum samples collected from all the patients of these four epidemics at the acute phase of the disease were negative for anti-HAV Ig M, HBsAg, anti-HBs IgM, anti-CMV Ig M and anti-EBV Ig M were also not detected in all these patients. The data indicate that these four foodborne epidemics were not associated with HAV, HBV, CMV and EBV.

Person-to-person transmission

Evidence of person-to-person transmission has been well documented even in common-source waterborne epidemics of hepatitis E^{7,9,10}. A case-control study conducted during the Xinjiang epidemic of 1986-1988 has indicated that the relative risk for the persons who had close contact with hepatitis E patients was 18 times higher than for those without contact history. A study on the distribution of 538 cases with hepatitis E by family demonstrated that 19.5% of secondary cases among household members developed hepatitis E at an interval of more than 60 days after the primary cases. The data suggest that the disease can be transmitted by intrafamily spread, although the secondary attack rate within families is relatively low, as compared with hepatitis A.

Age and Sex Distribution

Hepatitis E most frequently affects young adults, with fewer cases in children and the elderly^{14,15}. In the xinjiang epidemic of 1986-1988²¹, 77.3% of the patients were 15-49 years of age. The attack rate of the disease was 0.9% in children <14 years of age, 5.1% in young adults 15-49 years of age, and 0.2% in the population >50 years of age.

The distribution by sex of hepatitis E demonstrates a relative male excess of cases, with a male-to-female ratio of 1.3:1~3:1^{14,15}. The male predominance of the disease is presumably associated with the greater exposure to HEV in men. However, the fatality rate in female patients with hepatitis E is significantly higher than in male. We have followed up 379 pregnant cases with hepatitis E. The fatality rates in those of the first, second and third trimester were 1.5%, 8.5% and 21.0%, respectively. The data suggest that hepa-

Table 2 Viral shedding in feces of patients with hepatitis E detected by IEM

Time of feces collection (days)	No. tested	No. positive	%
Before onset of illness			
1-4	3	3	100.0
After onset of illness			
1-3	10	7	70.0
4-6	10	4	40.0
7-9	8	2	25.0
10-12	7	1	14.3
13-24	22	0	0.0
Total	60	17	28.3

titis E is more severe in pregnant women, especially in the third trimester. Analysis of 155 deaths of patients with hepatitis E demonstrated that main causes of deaths were cerebral edema (33.5%), liver-kidney syndrome (24.5%), postpartum hemorrhage (18.1%), hernia cerebri (12.3%), and hemorrhage of upper alimentary tract (11.6%)¹⁶.

Seasonal Distribution

Most waterborne epidemics of hepatitis E have been observed during rainy seasons or after flooding^{4,7-10}, while foodborne outbreaks of the disease may occur in all months. A distinctive autumn seasonality of hepatitis E has been described in Xinjiang, with a regular peak in October or November, which is also associated with rains and flooding⁷⁻¹⁰.

Viral Shedding

A total of 60 serial fecal specimens collected from 6 patients with hepatitis E during epidemic were tested by immune electron microscopy (IEM)^{9,17,18}. Virus particles in a diameter of 27-32 nm were found in feces in 83.3% (5/6) of patients, and in 28.3% (17/60) of fecal specimens collected. Also 100% of stool samples obtained 1-4 days before onset of disease were positive for the virus. The positive rates of the virus in feces collected 1-3, 4-6, 7-9, 10-12 days after onset of illness were 70% (7/10), 40% (4/10), 25% (2/8)

Table 3 Prophylactic efficacy of serum immunoglobulin (SIG) for the contacts of hepatitis E patients

Group	No. of studied	No. of cases	Attack rate (%)
SIG	78	7	8.97
Placebo	63	5	7.94

T=0.29 P>0.05

and 14.3% (1/7), respectively. However, no virus was detected in 22 stools obtained 13-24 days after the illness (**Table 2**). It was demonstrated that a high proportion of patients with hepatitis E shed the virus in feces during the late incubation period and early acute phase, and viral shedding had been decreasing before the levels of serum alanine aminotransferase (ALT) reached their peaks^{9,18}.

Incubation Period

Studies on three common source epidemics of hepatitis E from China^{2,3,9} revealed that the incubation period of the disease ranged from 15 to 75 days, with a mean of 36 days, which is similar to that reported by other investigators²⁰⁻²⁴.

Immunoprophylaxis

A randomized double-blind and controlled study²⁵ was carried out in an epidemic of hepatitis E, using a single dose of human immune serum globulin (ISG) for protecting contacts from the disease. A total of 141 contacts were randomly divided into two groups. Group I was given 3 ml of 10% solution of ISG produced in Beijing, while group II was injected with 3 ml normal saline as a placebo. Both groups were followed up for 2.5 months. Of 78 contacts who received ISG, 7 developed acute hepatitis, with an attack rate of 9.0%. A total of 66 contacts from the control group were followed up and 5 of them had the disease. The difference between these two groups was not statistically significant (**Table 3**). These data suggest that ISG had no prophylactic effects on hepatitis E.

The elimination of hepatitis E will ultimately

rely on a protective strategy utilizing active immunization by an effective HEV vaccine. Recently, HEV has been molecularly cloned^{26,27}. The progress of molecular cloning of virus genome provides the possibility of HEV vaccine production.

Summary

A total of 9 hepatitis E epidemics have been documented in China since 1982. Five of them were waterborne and four foodborne, and they occurred in 6 of 30 provinces or autonomous regions in the country. The disease most frequently affects young adults, with fewer cases in children and the elderly. A relative male excess of cases has been observed. However, the fatality rate in female patients with hepatitis E is significantly higher than in males. The disease has a distinctive autumn seasonality in endemic areas. A peak of fecal excretion of hepatitis E virus is found at the late incubation period and early acute phase. The incubation period of the disease ranges from 15 to 75 days, with a mean of 36 days. A randomized double-blind and controlled study showed that human immune serum globulin had no prophylactic effects on hepatitis E.

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