Epidemiology of hepatitis E infection in Hong Kong

DPC Chan *, KCK Lee, SS Lee

KEY MESSAGES

1. The overall anti–hepatitis E virus (HEV) seropositivity was 32.0%. It increased with age from 9.4% in individuals aged <30 years to 45.1% in those aged >59 years.
2. Independent risk factors associated with HEV seropositivity were age >35 years (odds ratio [OR]=3.25), no hand-washing practice after handling shellfish (OR=1.63), and higher education level (OR=0.57).
3. Anti-HEV seropositivity was more prevalent in patients with chronic liver disease (44.0%) and individuals aged >54 years (44.0%).
4. In a subgroup of frequent food handlers, the incidence of HEV infection was 0.8% during a 12-month period.

Hong Kong Med J 2017;23(Suppl 5):S31-5
RFCID project number: 11100202

DPC Chan, KCK Lee, SS Lee

Stanley Ho Centre for Emerging Infectious Diseases, The Chinese University of Hong Kong

* Principal applicant and corresponding author: denisechan@cuhk.edu.hk

Introduction

Hepatitis E virus (HEV) is the most common cause of enterically transmitted hepatitis worldwide and can manifest as an epidemic, particularly in Asia, Africa, and Latin America where sanitation is suboptimal. HEV infection is a major public health problem in developing countries where over 50% of acute viral hepatitis cases occur.[1] The mode of HEV transmission is mainly through the faecal-oral route, usually through contaminated food or drinking water. Although HEV infection is less common in developed countries, autochthonous HEV infection is increasingly recognised in Japan, France, the United Kingdom, and the United States, with a possible link to zoonotic transmission. Zoonotic transmission from pigs has been documented in Europe, and consumption of raw or undercooked meat from wild boar and deer has been identified as a source of zoonotic transmission of HEV in Japan.[2] Although HEV infection is often asymptomatic and self-limiting, mortality can occur particularly during pregnancy and in patients with chronic liver disease and fulminant liver failure.

The prevalence of HEV seropositivity varies between populations. In developed countries, 4% to 6% of the general population are positive for anti-HEV antibodies. Recently, higher prevalences have been reported: 16% in the United Kingdom, 21% in the United States, 29% in Germany, and 52% in southwest France. In Hong Kong, the number of HEV cases notified increased from 34 in 2006 to 150 in 2012.[3]

The burden of HEV infection in the at-risk subpopulations and the associated risk factors remain undefined. The present study aimed to assess the prevalence and risk factors of HEV infection in five subpopulations at varying risk of acquiring HEV, and to estimate the incidence of infection in the subgroup of frequent food handlers.

Methods

This cross-sectional seroepidemiological study was conducted between February 2012 and May 2014. Participants were eligible if they were aged >18 years. The study subpopulations consisted of healthy adults, pregnant women, patients with chronic liver disease, elderly people (age ≥55 years), and frequent food handlers. Pregnant women and patients with chronic liver disease were recruited from the antenatal and gastroenterology outpatient clinics, respectively. Frequent food handlers (food handling >4 days per week) included housewives, home helpers, and butchers at the wet markers.

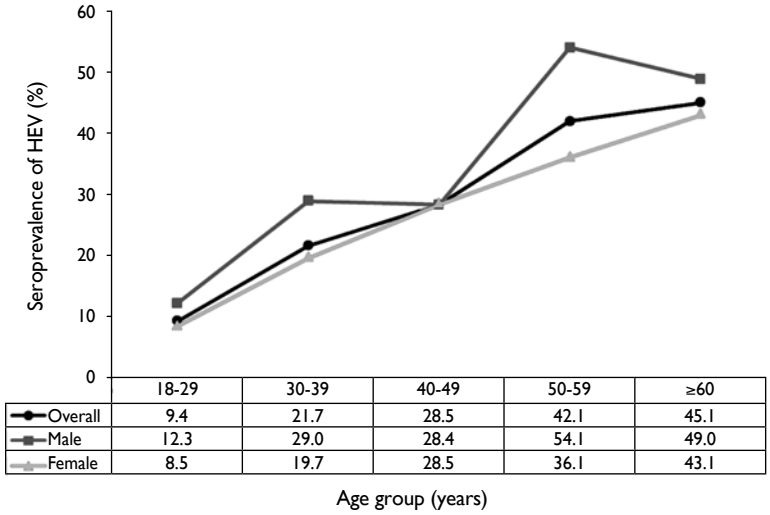
A blood sample was collected for anti-HEV serological testing. Anti-HEV immunoglobulin (Ig) M and G were determined using commercially available enzyme-linked immunosorbent assay; positive results were confirmed by repeated serological testing. In the subpopulation of frequent food handlers, follow-up serological tests were conducted to estimate the incidence of HEV over the 12-month follow-up period. A questionnaire was used to obtain participants' sociodemographics, eating habits, food-handling practices, and knowledge and awareness of HEV infection.

Categorical variables were compared using Pearson's Chi squared test or Fisher's exact test. Association between potential risk factors and HEV

seropositivity (defined as positive for anti-HEV IgG and/or IgM) was assessed using univariate analysis. Variables with a P value of <0.2 were included in a multiple logistic regression model using the stepwise backward method. A P value of <0.05 was considered statistically significant.

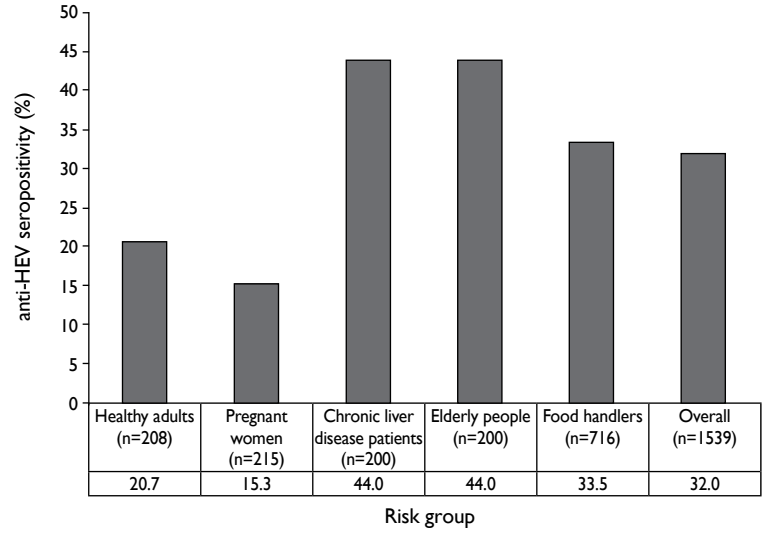
Results

A total of 1539 participants, including 208 healthy adults, 215 pregnant women, 200 chronic liver disease patients, 200 elderly people, and 716 frequent food handlers were recruited. The overall HEV seropositivity was 32.0% (95% confidence interval [CI]=29.6-34.3%). The prevalence of anti-HEV increased with age (9.4% in individuals aged <30 years and 45.1% in those aged >59 years, P<0.001) and was higher in males than females (39.4% vs. 28.7%, P<0.001) [Fig 1]. In the subgroup analysis, the seroprevalence was higher among patients with chronic liver disease (44.0%, 95% CI=37.1-50.9%) and elderly people (44.0%, 95% CI=37.1-50.9%), followed by food handlers (33.5%, 95% CI=30.1-37.0%), healthy adults (20.7%, 95% CI=15.1-26.2%), and pregnant women (15.3%, 95% CI=10.5-20.2%) [Fig 2]. During the 12-month follow-up of food handlers, three cases of HEV seroconversion were identified and the incidence of HEV infection was 0.8%.



	18-29	30-39	40-49	50-59	≥60
Overall	9.4	21.7	28.5	42.1	45.1
Male	12.3	29.0	28.4	54.1	49.0
Female	8.5	19.7	28.5	36.1	43.1

FIG 1. Seroprevalence of hepatitis E virus (HEV) infection in Hong Kong by age group and gender



Healthy adults (n=208)	Pregnant women (n=215)	Chronic liver disease patients (n=200)	Elderly people (n=200)	Food handlers (n=716)	Overall (n=1539)
20.7	15.3	44.0	44.0	33.5	32.0

FIG 2. Seroprevalence of hepatitis E virus (HEV) infection in Hong Kong by risk group

In univariate analysis, anti-HEV seropositivity was associated with older age in individuals aged >35 years (odds ratio [OR]=4.38, 95% CI=3.20-6.00, P<0.001), male gender (OR=1.61, 95% CI=1.29-2.03, P<0.001), never heard of HEV infection (OR=1.35, 95% CI=1.02-1.80, P=0.038), not knowing the animal sources of HEV infection (OR=2.23, 95% CI=1.32-3.75, P=0.003), report of no hand-washing practice after handling shellfish (OR=1.54, 95% CI=1.10-2.16, P=0.012), travel to China (OR=1.44, 95% CI=1.42-1.83, P=0.002), frequent food handling (OR=1.94, 95% CI=1.34-2.80, P<0.001), and chronic liver disease (OR=3.02, 95% CI=1.95-4.67, P<0.001) [Table]. Predictors associated with decreased OR of HEV infection were observed in individuals with a higher education level (OR=0.37, 95% CI=0.29-0.48, P<0.001) and monthly income (OR=0.67, 95% CI=0.49-0.91, P=0.011).

In multivariate analysis, age >35 years (OR=3.25, 95% CI=1.96-5.40, P<0.001), report of no hand-washing practice after handling shellfish (OR=1.63, 95% CI=1.07-2.48, P=0.023), and education level (OR=0.57, 95% CI=0.37-0.87, P=0.009) were independently associated with anti-HEV seropositivity (Table).

Discussion

In Hong Kong, the number of HEV infection cases has increased more than threefold since 2006, with 90 cases reported to the Centre for Health Protection in 2013. The epidemiology of HEV has changed over the past years, and all age groups are susceptible to HEV infection. In 2008-2009, the prevalence of anti-HEV seropositivity in Hong Kong was 28.7%.[4] The increased prevalence observed in our study suggests that exposure to HEV is common in our local populations, unlike that to hepatitis A infection.

In a community-based HEV surveillance study in a rural population in China, the risk of HEV seropositivity was higher in hepatitis B virus carriers than in the general population.[5] In our subpopulation of those with chronic liver disease, the prevalence of HEV seropositivity was 44.0%. HEV infection in the

TABLE. Predicators associated with hepatitis E virus (HEV) seropositivity in Hong Kong (n=492)

Variable	HEV seropositivity				
	No. (%) of subjects	Crude OR (95% CI)	P value	Adjusted OR (95% CI)*	P value
Demographics					
Age (years)			<0.001		<0.001
≤35	52 (10.6)	1		1	
>35	440 (89.4)	4.38 (3.20-6.00)		3.25 (1.96-5.40)	
Gender			<0.001		0.061
Female	309 (62.8)	1		1	
Male	183 (37.2)	1.61 (1.29-2.03)		1.59 (0.98-2.58)	
Level of education			<0.001		0.009
High school or less	401 (82.3)	1		1	
Above high school	86 (17.7)	0.37 (0.29-0.48)		0.57 (0.37-0.87)	
Monthly income (HK$)			0.011		0.853
≤20 000	420 (86.8)	1		1	
>20 001	64 (13.2)	0.67 (0.49-0.91)		0.947 (0.53-1.69)	
Knowledge and risk perception of HEV infection					
Ever heard of HEV infection			0.038		0.284
Yes	81 (20.6)	1		1	
No	313 (79.4)	1.35 (1.02-1.80)		1.27 (0.82-1.98)	
Vaccines are available for HEV prevention			0.172		-
Yes	41 (12.7)	1		-	
No	282 (87.3)	1.30 (0.89-1.90)			
Could identify the transmission route of HEV infection			0.696		-
Yes	3 (0.7)	1		-	
No	401 (99.3)	1.30 (0.35-4.82)			
Could identify the animal sources of HEV infection			0.003		0.909
Yes	18 (4.5)	1		1	
No	386 (95.5)	2.23 (1.32-3.75)		1.04 (0.55-1.98)	
Could identify symptoms of HEV infection			0.137		-
Yes	7 (1.7)	1		-	
No	397 (98.3)	1.88 (0.82-4.31)			
Perceived risk of HEV infection			0.795		-
High chance	276 (86.8)	1		-	
Low chance	42 (13.2)	0.95 (0.65-1.39)			
Eating habits					
Consumption of pork and pig offal			0.266		-
No	12 (2.8)	1		-	
Yes	420 (97.2)	1.45 (0.75-2.80)			
Consumption of undercooked pork and pig offal			0.710		-
No	386 (90.4)	1		-	
Yes	41 (9.6)	1.08 (0.73-1.59)			
Consumption of game meat and offal			0.766		-
No	443 (91.2)	1		-	
Yes	43 (8.8)	1.06 (0.72-1.56)			

* Adjusted for age, gender, education level, monthly income, knowledge of HEV infection, hand washing after handling shellfish, travel to China, and risk exposure groups

† Univariate logistic regression comparing with healthy adults as controls

TABLE. (cont'd)

Variable	HEV seropositivity				
	No. (%) of subjects	Crude OR (95% CI)	P value	Adjusted OR (95% CI)*	P value
Having hotpot			0.131		-
Sometimes	301 (70.3)	1		-	
Frequently	127 (29.7)	0.83 (0.65-1.06)			
Consumption of shellfish			0.085		-
No	103 (29.9)	1		-	
Yes	241 (70.1)	0.78 (0.59-1.03)			
Consumption of undercooked shellfish			0.478		-
No	264 (89.2)	1		-	
Yes	32 (10.8)	1.17 (0.76-1.82)			
Wash hands before eating			0.506		-
Yes	250 (57.9)	1		-	
No	182 (42.1)	1.08 (0.86-1.36)			
Food-handling practice					
Frequency of handling pork			0.149		-
Never	28 (7.6)	1		-	
Frequently	339 (92.4)	1.39 (0.89-2.17)			
Wash hands after handling pork			0.397		-
Yes	275 (70.3)	1		-	
No	116 (29.7)	1.12 (0.86-1.47)			
Frequency of handling shellfish			0.078		-
Never	131 (36.2)	1		-	
Frequently	231 (63.8)	0.79 (0.61-1.03)			
Wash hands after handling shellfish			0.012		0.023
Yes	155 (67.4)	1		1	
No	75 (32.6)	1.54 (1.10-2.16)		1.63 (1.07-2.48)	
Store perishable food in refrigerator and well covered			0.603		-
Yes	378 (88.5)	1		-	
No	49 (11.5)	0.911 (0.64-1.30)			
Separate raw and cooked food to prevent cross contamination			0.728		-
Frequently	332 (68.6)	1		-	
Never	152 (31.4)	0.96 (0.76-1.21)			
Risk/exposure characteristics					
Travel to HEV endemic area (China)			0.002		0.077
Never	332 (67.5)	1		1	
Frequently	160 (32.5)	1.44 (1.42-1.83)		1.49 (0.96-2.30)	
Frequent food handlers (food handling >4 days per week)†			<0.001		0.239
No	43 (15.2)	1		1	
Yes	240 (84.8)	1.94 (1.34-2.80)		0.69 (0.38-1.28)	
Pregnancy†			0.155		-
No	43 (56.6)	1		-	
Yes	33 (43.4)	0.69 (0.42-1.15)			
Chronic liver disease†			<0.001		0.240
No	43 (32.8)	1		1	
Yes	88 (67.2)	3.02 (1.95-4.67)		1.47 (0.77-2.79)	

context of liver disease carries a poor prognosis and increases the severity of the disease.

In our population, eating habits (including the consumption of pork, pig offal, and hotpot) were not associated with increased OR of HEV seropositivity. Nonetheless, multivariate analysis indicated that hand-washing practice after handling shellfish was independently associated with anti-HEV positivity, suggesting that shellfish is a potential source of foodborne HEV transmission. Further studies are needed to determine the prevalence of HEV in the food chain and to provide advice about processing of shellfish to reduce the risk of HEV infection.

Conclusion

The rising prevalence of HEV infection highlights the need to strengthen preventive measures and education to reduce the disease burden and improve public awareness of HEV infection.

Acknowledgement

This study was supported by the Research Fund for the Control of Infectious Diseases, Food and Health Bureau, Hong Kong SAR Government (#11100202).

References

1. Myint KS, Gibbons RV. Hepatitis E: a neglected threat. Trans R Soc Trop Med Hyg 2008;102:211-2.
2. Takahashi K, Kitajima N, Abe N, Mishiro S. Complete or near-complete nucleotide sequences of hepatitis E virus genome recovered from a wild boar, a deer, and four patients who ate the deer. Virology 2004;330:501-5.
3. Leung A. Update on hepatitis E infection in Hong Kong. Communicable Dis Watch 2012;9:17-8.
4. Chiu DM, Chan MC, Yeung AC, Ngai KL, Chan PK. Seroprevalence of hepatitis E virus in Hong Kong, 2008-2009. J Med Virol 2013;85:459-61.
5. Zhu FC, Huang SJ, Wu T, et al. Epidemiology of zoonotic hepatitis E: a community-based surveillance study in a rural population in China. PLoS One 2014;9:e87154.