Community burden of hepatitis A infection and risk of transmission in Hong Kong

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KEY MESSAGES

1. The age/sex-adjusted prevalence of anti-hepatitis A virus antibodies was 39.25% among 2085 participants in a population survey in Hong Kong.
2. The estimated age at midpoint of population immunity for hepatitis A infection was 45 to 49 years, more than 30 years older than that estimated half a century ago.
3. Only 3% of participants gave a definitive history of previous hepatitis A vaccination.
4. Hepatitis A vaccine uptake was associated with employment in higher-risk occupations and frequent travel.
5. A household survey using building groups as sampling frame was a practical approach for developing epidemiologic analyses.

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Introduction

Hepatitis A virus (HAV) is transmitted through the oral-faecal route. Because of improvements in sanitation and access to clean water worldwide, the incidence of hepatitis A has fallen. However, the age-standardised incidence rates remain static, as revealed in the Global Burden of Disease Study in 2019.[1] Despite epidemiological improvements, there is a paradox: incidents of HAV foodborne outbreaks are increasing in high-income countries, whereas the transition from high to low endemicity in middle- and low-income countries is leading to increases in symptomatic diseases.[2] HAV vaccines, licensed in the 1990s, are highly immunogenic and can elicit long-lasting immunity. The susceptibility of a population to HAV infection depends on the interplay between the extent of natural infection and the effects of HAV vaccination. Vaccination coverage varies according to sociodemographic profile, local endemicity, and vaccination strategies.

In 2001, approximately 71% of Hong Kong adults in a population survey had detectable anti-HAV antibodies, largely because of natural infection.[3] Between 2001 and 2020, the yearly number of HAV cases reported to the Department of Health has steadily declined. In 2020, there were 28 reported HAV cases. In the past decade, there was a clear increase in the proportion of reported cases among people aged ≥45 years. However, major outbreaks have not occurred since the 1990s, despite the lack of public HAV vaccination programmes. Therefore, we conducted a seroprevalence study to evaluate the population risk of HAV and the role of vaccination in preventing HAV transmission in Hong Kong.

Methods

This study formed part of a prospective cross-sectional hepatitis A and B household survey, and the full protocol of which has been published.[4] Eligible members of spatially randomised households were invited to complete a questionnaire and provide blood samples for serological testing. The questionnaire covered demographics, medical history of hepatitis infection, exposure risk, and vaccination history. Serological analyses of anti-HAV IgG antibodies were performed by immunoassay.

The crude and age/sex-adjusted prevalences of anti-HAV antibodies were measured. The age at midpoint of population immunity (AMPI) was estimated,[5] which was defined as the youngest age at which ≥50% of the population had serologic evidence of prior HAV infection. A bivariable logistic regression model was used to compare participants who self-reported definitively or likely to have received the HAV vaccine with participants who self-reported definitively not or unlikely to have received the HAV vaccine. Multivariable logistic regression was conducted with age at survey year as a confounder. Complete case analyses were performed.

Results

Between September 2018 and October 2020, we sent 38 020 invitation letters by post, and respondents

TABLE 1. Characteristics of participants (n=2085)

Characteristic	Value*
Sex	
Female	1175 (56.4)
Male	910 (43.6)
Age, y (n=2085)	54 (39-63)
Ethnicity (n=2073)	
Non-Chinese	13 (0.6)
Chinese	2060 (99.4)
Permanent resident of Hong Kong (n=2072)	
No	41 (2.0)
Yes	2031 (98.0)
Born in Hong Kong (n=2084)	
No	598 (28.7)
Yes	1486 (71.3)
Marital status (n=1999)	
Never married	500 (25.0)
Widowed	104 (5.2)
Separated	7 (0.4)
Divorced	148 (7.4)
Married	1240 (62.0)
Education level (n=2078)	
Secondary and below	1192 (57.4)
Post-secondary	886 (42.6)
Currently employed (n=1997)	
No	844 (42.3)
Yes	1153 (57.7)
History of hepatitis or other liver disease	
Liver disease (n=2080)	
No	1948 (93.7)
Yes	132 (6.3)
Fatty liver	
No	1965 (94.2)
Yes	120 (5.8)
Cirrhosis	
No	2082 (99.9)
Yes	3 (0.1)
Liver cancer	
No	2081 (99.8)
Yes	4 (0.2)

* Data are presented as No. (%) of participants or median (interquartile range)

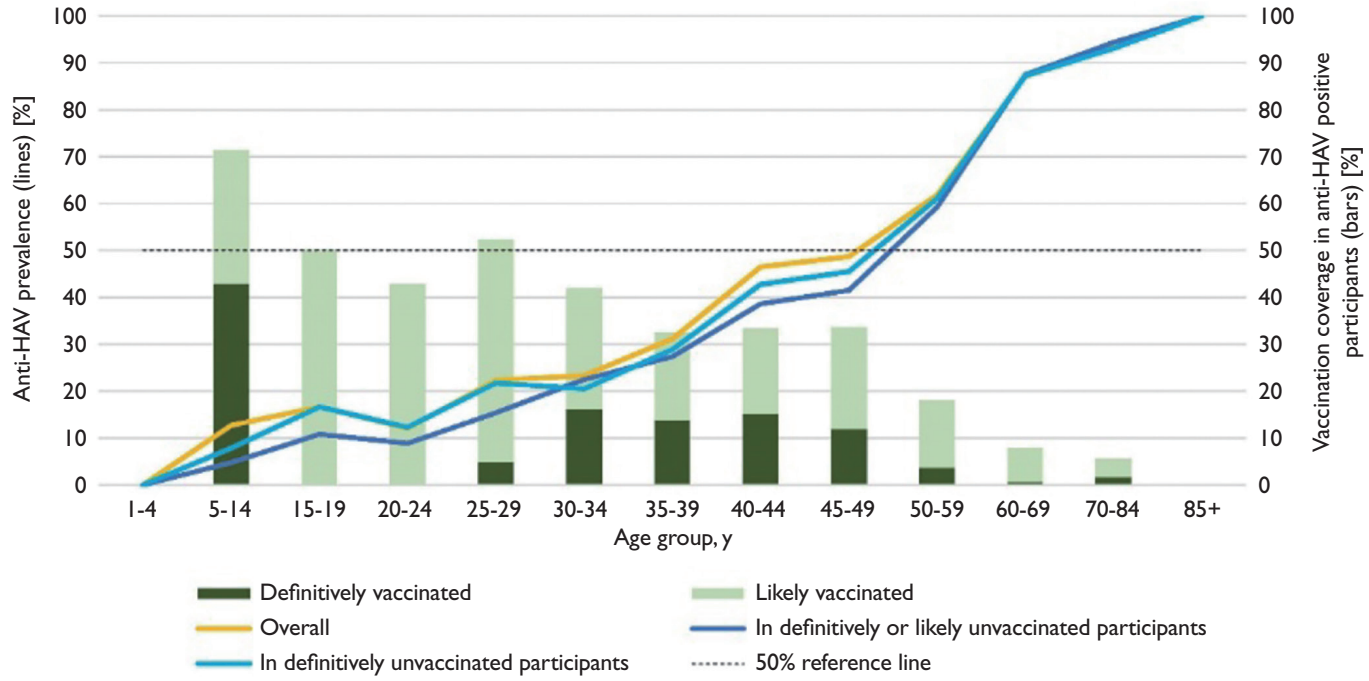

FIG. Hepatitis A virus (HAV) vaccination history and anti-HAV antibody prevalence in study population according to age

from 1497 (4%) households agreed to participate. Among 2085 participants, the median age was 54 years and the male-to-female ratio was 0.77; 99% of participants were Chinese and 71% of the participants were born in Hong Kong (Table 1). Compared with 2016 census, our participants had higher proportions of Chinese ethnicity, female, age ≥35 years, and post-secondary education. The distribution of recruited households among districts was within 2% of the distribution in residential building groups.

The crude prevalence of anti-HAV antibodies was 58.87% (1218/2069, 95% confidence interval [CI]=56.75%-60.99%), which became 39.25% (95% CI=37.14%-41.35%) after adjustments for age and sex. The anti-HAV antibody prevalence was positively associated with age (Fig). Approximately 89% of respondents aged ≥60 years were anti-HAV antibody-positive, compared with 14% of respondents aged <25 years. The estimated AMPI was 45-49 years.

Only 64 (3%) of participants gave a definitive history of HAV vaccination. Among anti-HAV antibody-positive participants, the percentage of participants with a definitive history of vaccination was highest among people aged 5 to 14 years (43%), followed by people aged 30 to 49 years (16%) [Fig]. Vaccination history (definitive or likely) was associated with younger age (odds ratio [OR]=0.97, 95% CI=0.96-0.98), higher education level (adjusted OR [aOR]=2.40, 95% CI=1.87-3.07), and being employed (aOR=1.69, 95% CI=1.29-2.23). People working in higher-risk occupations (eg, laboratory workers, sewage workers, food handlers, zookeepers, veterinarians, and researchers in contact with non-human primates) were more likely to have received the HAV vaccine (aOR=2.05, 95% CI=1.23-3.39). Frequent travellers who had more than one trip per year were more likely to be vaccinated, compared with travellers who had one trip every year (aOR=0.67, 95% CI=0.51-0.89) and travellers who had one trip every 2 to 3 years (aOR=0.52, 95% CI=0.36-0.77). A history of travel to HAV-endemic areas (aOR=1.34, 95% CI=1.03-1.74) or Southeast Asia (aOR=1.64, 95% CI=1.17-2.28) was also associated with vaccine uptake (Table 2).

Discussion

Considering its age/sex-adjusted anti-HAV antibody prevalence of <40%, Hong Kong is transitioning from high to low endemicity. We estimated AMPI, an index of HAV endemicity,[2] to assess epidemiologic burden. High-income countries with low endemicity typically have an AMPI of ≥50 years, in contrast to the AMPI of <5 years in low-income countries with high endemicity. In Hong Kong, the estimated AMPI was 11 to 20 years in the late 1970s, 21 to 30 years in the late 1980s, and 30 to 39 years in 2001,[3] compared

TABLE 2. Factors associated with self-reported hepatitis A virus vaccination (n=2081)

	Self-reported hepatitis A vaccination history		Odds ratio (95% confidence interval)	Adjusted odds ratio (95% confidence interval)
	No (n=1731)*	Yes (n=350)*		
Sex				
Female	981 (56.7)	192 (54.9)	Reference	Reference
Male	750 (43.3)	158 (45.1)	1.08 (0.85-1.36)	1.06 (0.83-1.34)
Age, y	56 (42-64)	44 (31-55)	0.97 (0.96-0.98)†	-
Age group, y				
<20	87 (5.0)	24 (6.9)	2.37 (1.46-3.86)†	-
20-29	113 (6.5)	44 (12.6)	3.35 (2.26-4.96)†	
30-39	187 (10.8)	85 (24.3)	3.91 (2.85-5.36)†	
40-49	261 (15.1)	71 (20.3)	2.34 (1.70-3.22)†	
≥50	1083 (62.6)	126 (36.0)	Reference	
Ethnicity (n=2069)				
Non-Chinese	9 (0.5)	4 (1.2)	Reference	Reference
Chinese	1713 (99.5)	343 (98.8)	0.45 (0.14-1.47)	0.51 (0.15-1.74)
Permanent resident of Hong Kong (n=2068)				
No	34 (2.0)	7 (2.0)	Reference	Reference
Yes	1687 (98.0)	340 (98.0)	0.98 (0.43-2.23)	1.37 (0.59-3.17)
Born in Hong Kong (n=2080)				
No	515 (29.8)	83 (23.8)	Reference	Reference
Yes	1216 (70.2)	266 (76.2)	1.36 (1.04-1.77)†	1.12 (0.85-1.48)
Ever married (n=1997)				
No	388 (23.3)	112 (33.8)	Reference	Reference
Yes	1278 (76.7)	219 (66.2)	0.59 (0.46-0.77)†	1.36 (0.99-1.87)
Education level (n=2074)				
Secondary and below	1065 (61.8)	124 (35.4)	Reference	Reference
Post-secondary	659 (38.2)	226 (64.6)	2.95 (2.32-3.74)†	2.40 (1.87-3.07)†
Currently employed (n=1995)				
No	755 (45.4)	88 (26.4)	Reference	Reference
Yes	907 (54.6)	245 (73.6)	2.32 (1.78-3.01)†	1.69 (1.29-2.23)†
Healthcare worker (n=1987)				
No	1577 (95.2)	311 (94.2)	Reference	Reference
Yes	80 (4.8)	19 (5.8)	1.20 (0.72-2.02)	1.10 (0.65-1.87)
Higher-risk occupations (n=1989)			Reference	Reference
No	1596 (96.4)	309 (92.8)	2.07 (1.27-3.37)†	2.05 (1.23-3.39)†
Yes	60 (3.6)	24 (7.2)		
Anti-hepatitis A virus antibody result (n=2065)				
Negative	704 (41.0)	144 (41.5)	Reference	Reference
Positive	1014 (59.0)	203 (58.5)	0.98 (0.77-1.24)	2.22 (1.66-2.97)†
Any liver disease (n=2077)				
No	1614 (93.5)	331 (94.6)	Reference	Reference
Yes	113 (6.5)	19 (5.4)	0.82 (0.50-1.35)	1.07 (0.64-1.77)

* Data are presented as No. (%) of participants or median (interquartile range)
† P<0.05

TABLE 2. (cont'd)

	Self-reported hepatitis A vaccination history		Odds ratio (95% confidence interval)	Adjusted odds ratio (95% confidence interval)
	No (n=1731)*	Yes (n=350)*		
Self-reported history of hepatitis A diagnosis (n=2078)				
No	1680 (97.2)	343 (98.0)	Reference	Reference
Yes	48 (2.8)	7 (2.0)	0.71 (0.32-1.59)	0.98 (0.44-2.21)
Travel to high endemic areas (n=2058)				
Never	1254 (73.3)	246 (70.9)	Reference	Reference
Ever	457 (26.7)	101 (29.1)	1.13 (0.87-1.45)	1.34 (1.03-1.74)†
Travel to Mainland China, Macau SAR, and/or Taiwan (n=2076)				
Never	5 (0.3)	2 (0.6)	Reference	Reference
Ever	1722 (99.7)	347 (99.4)	0.50 (0.10-2.61)	0.46 (0.08-2.57)
Travel to Southeast Asia (n=2076)				
Never	328 (19.0)	50 (14.3)	Reference	Reference
Ever	1399 (81.0)	299 (85.7)	1.40 (1.02-1.94)†	1.64 (1.17-2.28)†
Travel frequency in the past 10 years (n=2076)				
None	46 (2.7)	3 (0.9)	0.25 (0.08-0.82)†	0.36 (0.11-1.19)
Every >3 years	188 (10.9)	29 (8.3)	0.60 (0.39-0.92)†	0.67 (0.43-1.03)
Every 2-3 years	283 (16.4)	39 (11.2)	0.54 (0.37-0.78)†	0.52 (0.36-0.77)†
Every year	526 (30.5)	102 (29.2)	0.75 (0.58-0.99)†	0.67 (0.51-0.89)†
<1 year	684 (39.6)	176 (50.4)	Reference	Reference

with 45 to 49 years in the current study. The AMPI has increased by about 10 years per decade. Because of the increasing AMPI, young and middle-aged adults now have a higher risk of symptomatic HAV diseases, compared with half a century ago.

In Hong Kong, our study estimated that only 3% of the population have HAV vaccination. Natural infection continues to be the main factor for population immunity development. Although the anti-HAV antibody prevalence in unvaccinated people increased with age, the susceptibility to infection (indicated by the percentage of anti-HAV antibody-negative people) decreased with age. The low vaccination coverage (especially in young people) and the decrease in HAV disease incidence may lead to episodic outbreaks. In 2017, an unusual increase in HAV infection among men who have sex with men (MSM) occurred because of oral-anal sex in an unvaccinated young population. Worldwide, transmission clusters have occasionally occurred after consumption of contaminated produce and seafood imported from endemic countries. This highlights the effects of globalisation and international food trade.[2]

Participants with a higher risk of HAV transmission were more likely to have received the HAV vaccine. However, the overall rate of vaccination remained low. In the United States, routine vaccination is recommended for children aged 12 to 23 months and catch-up vaccination for children aged 2 to 18 years who have not previously vaccinated, as well as vaccination for adults with a risk of HAV infection or severe disease. In the absence of a universal vaccination programme, targeted strategies for increasing HAV vaccination coverage in selected vulnerable populations are needed to minimise the risk of outbreaks and the community burden of symptomatic disease.

The present study had limitations. First, the response rate was low (around 4%), and the recruitment was slowed by the COVID-19 pandemic. Second, there may have been self-selection bias because some individuals might have already known their infection status. Third, self-reported vaccination history could not be validated; some participants might have confused hepatitis B virus and HAV. Nevertheless, this study showed that the use of socially homogenous groups is robust for population survey for epidemiological analyses in Hong Kong.

Funding

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