Changing Epidemiology of Hepatitis A and Hepatitis E in Hong Kong

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Hepatitis A virus (HAV) and hepatitis E virus (HEV) are both transmitted by faecal-oral route. More local data on hepatitis A relative to hepatitis E was available over the last decades. Hong Kong is of intermediate endemicity for HAV [1]. Since 1988 with the breakdown of reported hepatitis according to aetiologic agents, the largest epidemic of hepatitis A occurred in 1992, with over 3,500 cases reported to the Department of Health (DH). This represents a notification rate of 63 per 100,000 population and since then, a gradual declining trend in HAV incidence has been observed. Since 2005, the annual number of notifications was below 100 and the respective numbers in the last 5 years were: 68 (2007), 71 (2008), 64 (2009), 65 (2010) and 46 (2011). Overall, case fatality rates from hepatitis A had been low and ranged between 0 and 0.7%. A seasonal pattern of acute hepatitis A is present, with cases more commonly reported between January and May each year. Over the years, there is an overall increase in age, with decrease in proportion of 15-24 age group people but increase in those >25 years old. The discernible decline in hepatitis A led to a parallel declining trend in overall reported viral hepatitis since 2002.

An analysis was made by the Surveillance and Epidemiology Branch (SEB) of Centre for Health Protection (CHP), DH on the 227 HAV cases notified between 2003 and 2004. The incidence rates were 1.57 per 100,000 in 2003 and 1.78 per 100,000 in 2004, which were lower than the rates in Mainland China (7.4 per 100,000 in 2003 and 6.9 per 100,000 in 2004). The male to female ratio was 1.83 to 1. There were five clusters of hepatitis A infection involving 2 persons in each cluster. No large single source outbreak was identified. During that period, 17 cases were classified as imported cases, with 8 from Mainland China, and the remaining from Asian and South-east Asian countries such as Indonesia, Pakistan and Thailand. One hundred and thirty-three (58.6%) required hospitalization. Patients were hospitalized for an average of 5.5 days, with a range of 1 to 25 days and a median stay of 5 days. Out of the 227 cases, 154 (67.8%) were in the working population. The majority of those affected was plant and machine operators and assemblers (34%) or were working in elementary occupations (26%). One hundred forty-two cases (63%) had history of consumption of marine products, of which 128 had eaten shellfish.

From the available data, prevalence of hepatitis A infection has been falling in Hong Kong, which echoes the finding of a higher median age in reported HAV cases that reflects the increased susceptibility of the adult population. In a local household study conducted in 2001, (Community Research Project for Viral Hepatitis 2001, CRPVH), anti-HAV positivity was less frequent ($P<0.001$) across all age groups among subjects >21 years [2] than subjects in the same age groups of another study conducted in late 1980s [3]. HAV prevalence has only increased insignificantly in every 10-year age groups of people aged 21-50 [2] when compared with their corresponding 10-year younger age groups [3], signifying an aging cohort effect with no major infections in the last 10 years [2]. Similar conclusions can be drawn when

comparing the late 1980s findings with those of a late 1970s study on local HAV seroprevalence [4]. Overall, these 3 studies suggest that age-specific prevalence of HAV has right-shifted locally in the last two decades. As of 2001, anti-HAV was present in about 20% of adults below 30 years old while it was over 80% in people aged >=40 years in the general Chinese population. Data from a serosurvey in 2010 on 691 subjects with blood collected for conditions unrelated to hepatitis [unpublished data of DH] found that anti-HAV was present in more than 60% of adults aged over 40 years. Besides an increasing prevalence with higher age, people born outside Hong Kong were more likely to test positive for anti-HAV whereas the reverse was true for people of non-labour work [2]. From the telephone interview part of the CRPVH 2001, some 11% of 4,564 subjects reported a history of HAV vaccination, with about 80% of which completed the course. More people less than 40 years old had received the vaccination. Over 98% had the cost paid by them or covered by their employers.

Cross-sectional surveys of anti-HAV at Kowloon Bay Integrated Treatment Centre (ITC) have been started since 2007. The subjects consisted of all new HIV/AIDS patients who first attended ITC between Jul 2007 and 2010 and convenient samples of all active HIV/AIDS patients who first attended ITC before Jul 2007. It appeared that the prevalence of anti-HAV increased with age of HIV/AIDS patients. The overall positivity rate among HIV/AIDS patients tested between 2007 and 2010 appeared to be comparable with that of the 2010 serosurvey data. Confounding factors, such as different levels of past infection, immunodeficiency in HIV patients, history of HAV vaccination and difference in years of testing, may have affected the results. As compared with patients infected HIV via other routes, those infected via homosexual or bisexual routes were at the highest risk of hepatitis A infection, as reflected by the lowest level of anti-HAV prevalence in this group of patients. Though this could be partially explained by the larger proportion of younger patients aged <40 years infected HIV via homosexual or bisexual routes, this finding may shed light on the clinical management regarding recommendation on hepatitis A vaccination in HIV/AIDS patients.

Hepatitis E appeared to run an opposite trend to hepatitis A over the last decade. The annual notification of hepatitis E infection jumped from 11 in 1996 to a record high of 119 in 2011, becoming the most common viral hepatitis reported to Department of Health. The last few years number of notifications were 65 (2007), 90 (2008), 73 (2009), and 118 (2010). Seasonal pattern was observed with the peak season in March to April, indicating that the infection was more common during winter and spring seasons. Of 575 cases reported from 1996 to 2010, 397 (70%) were male, giving male to female ratio of 2.2:1. The majority were adults, with the highest notification rate at 45-54 years age group, followed by 55-64 years old. The death rate could be as high as 0.44 per million population.

Similar rising trend of hepatitis E infection was observed in neighbouring areas including mainland China, Singapore and Japan. According to the Ministry of Health of mainland China, the number of cases of hepatitis E infection increased from 15,965 in 2004 to 20,854 in 2009. Similarly in Singapore, the Ministry of Health recorded 90 cases in 2009, compared to the 5-year median number of 30 cases between 2004 and 2008. In Japan, the Infectious Disease Surveillance Centre reported 56 cases of hepatitis E in 2007, compared with 3 cases in 2000 [5].

The Centre for Health Protection reviewed all Hepatitis E cases recorded between 2001 to 2010 [6]. Of the 524 cases, the commonest presentations were tea-coloured urine, jaundice,

anorexia, fever, myalgia and nausea. 78.2% were hospitalized with a median stay of 7 days. A total of 12 cases were fatal (9 males and 3 females), age ranged from 53 to 82 (median age 67.5 years). The case fatality rate was 2.3%, which was comparable with reported figures from other countries. None of the fatal cases were pregnant. Most cases (99.4%) were sporadic infection and 87.4% acquired the disease locally. A small family cluster involving 2 males (aged 15 and 44 years) was identified. The 2 victims had shared multiple high-risk food items at home during the incubation period. It proved difficult to determine the exact source of infection of individual sporadic cases as hepatitis E has a long incubation period of 15-64 days. Nonetheless, epidemiological investigation has not identified any outbreak linked to a particular food premises.

In the CRPVH study conducted in 2001, 19% of adult subjects were found to have serologic evidence of HEV infection. People in the 40-49 years age group had the highest positivity rate of 24%. Unlike HAV infection, a pattern of right shift in HEV seroprevalence was not as prominent when temporal change was analysed. Both the overall and age-specific HEV prevalence were lower in 2001, when compared with the findings of a study done in late 1980s [7], which could have been contributed by the use of different laboratory assays.

Another published study identified differences in epidemiology and clinical features between sporadic hepatitis E and hepatitis A cases. Of 105 acute hepatitis A and 24 hepatitis E patients seen at Princess Margaret Hospital (PMH) in 2002, HAV patients were significantly younger (median age of 27 years) and had recent history of shellfish consumption while HEV patients were older (median age = 53 year) and most had a recent travel history [8]. Moreover, whereas hepatitis A was milder and recovery was uneventful, hepatitis E was more severe, associated with significant mortality and frequently complicated by protracted coagulopathy and cholestasis [8]. Liver transplantation may be warranted in patient complicated by acute liver failure. [9]

A local study examined the genotype of 57 patients with acute HEV infection who were admitted to Prince of Wales Hospital [10]. Fifty-six patients (98%) were Chinese. All cases were sporadic. No fulminant hepatitis was recorded and all patients recovered. Phylogenetic analyses of the open reading frame ORF2 fragments from 46 patients and ORF1 fragments from 33 patients showed complete agreement, with most (n= 45 [98%]) belonging to genotype 4. The remaining isolate was genotype 3 obtained from a woman who had no history of travel. Most of the Hong Kong isolates clustered closely with a swine isolate reported from Guangxi Province, China.

Similar to hepatitis A, hepatitis E is mainly transmitted through consumption of contaminated water or food. While people may take hepatitis A vaccination for personal protection, good personal and food hygiene practices is essential to prevent both hepatitis A and E infections. Most importantly, food, especially shellfish and animal offal, should be cooked thoroughly before consumption [9]. There is evidence suggesting a zoonotic source for HEV in overseas studies, and that pigs may be an important reservoir. In light of these observations, the Centre for Food Safety conducted a risk assessment study titled " Hepatitis E Virus in Fresh Pig Livers" [11] to determine the HEV prevalence in fresh pig liver samples obtained in local markets. One hundred fresh pig liver samples were collected from pigs slaughtered between mid-January to May. Sixteen (31%) out of 51 roaster pig (around four months old) liver samples were positive for HEV, while none of the 49 porker pig (around six months old) liver samples tested positive. Partial sequences of some HEV isolates from roaster pigs were

identical to those from 7 among 48 local human cases with date of onset from January to July 2009, as well as local cases recorded in the past. The findings suggest the possibility of roaster pigs as one of the sources of local human hepatitis E infections.

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Test paper - Changing Epidemiology of Hepatitis A and Hepatitis E in Hong Kong

Expiration Date: 26 April 2013

CME point: 1 / CNE point: 1 / PEM point:1(NOT direct Midwifery related)

- Please indicate one answer to each question.

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1. In what year was a major hepatitis A outbreak last occurred in Hong Kong?
   (a) 1991
   (b) 1992
   (c) 1993
   (d) 1994
   (e) 1995

2. Which of the following is not true about hepatitis A prevalence in Hong Kong community?
   (a) anti-HAV positivity generally increases with increasing age
   (b) there is evidence of aging cohort effect from serial studies over 2 to 3 decades
   (c) anti-HAV positivity may be contributed by hepatitis A vaccination
   (d) the falling community prevalence of anti-HAV suggests increased susceptibility to HAV infection
   (e) none of the above

3. Which of the following is not true in comparing HAV and HEV epidemiology in Hong Kong?
   (a) hepatitis E has taken over hepatitis A as the commonest notified viral hepatitis
   (b) unlike HAV, there is no discernible right shift in hepatitis E prevalence when temporal change was analysed
   (c) the increase in HEV prevalence with older age is not as prominent as in hepatitis A
   (d) more clusters were found for notified hepatitis E cases
   (e) more imported cases were found for notified hepatitis A cases

4. Which of the following is true regarding clinical course of acute hepatitis E?
   (a) the commonest clinical presentations are tea-colour urine, jaundice, anorexia, fever, myalgia etc.
   (b) case fatality rate was about 2%
   (c) liver transplantation may be required if complicated by acute liver failure
   (d) clinical course is more severe in pregnant women
   (e) all of the above

5. Which of the following is not true in comparing the clinical disease of acute hepatitis A and E?
   (a) hepatitis A cases are milder
   (b) hepatitis E cases are more often with complications such as prolonged coagulopathy and cholestasis
   (c) case fatality rate is higher for hepatitis A
   (d) duration of hospitalization is longer for hepatitis E
   (e) none of the above

6. Which of the following is not true concerning HEV epidemiology in Hong Kong?
   (a) there are more sporadic cases for hepatitis E than hepatitis A
   (b) hepatitis E cases tend to be older than hepatitis A cases
   (c) HEV cases are less common in winter and spring seasons
   (d) rising trend of hepatitis E was also observed in neighbouring areas including Mainland China, Singapore and Japan
   (e) vaccination is unlikely to impact on the epidemiology at present

7. Which of the following is not true about anti-HAV data in HIV/AIDS patients locally?
   (a) similar to general population, anti-HAV positivity increases with age
   (b) homosexual and bisexual patients are at highest risk of contracting HAV
   (c) there is no obvious temporal change overall from 2007 to 2010
   (d) besides past infection, hepatitis A vaccination and degree of immunodeficiency could have affected the anti-HAV positivity
   (e) none of the above

8. Which of the following is not true regarding the source of infection for hepatitis A and hepatitis E cases?
   (a) both HAV and HEV are transmitted via intake of contaminated water or food
   (b) source of infection is more difficult to be identified in HEV cases due to its longer incubation period
   (c) there is evidence of zoonotic source for hepatitis E but not hepatitis A
   (d) in one study of hospitalized patients, a history of shellfish consumption was significantly more in hepatitis E than A cases
   (e) HEV was identified in liver of young roaster pig liver in a local risk assessment study

9. Which of the following can help prevention of HAV and HEV infection?
   (a) good personal and food hygiene
   (b) thoroughly cook food before consumption, especially for those high risk items
   (c) do not eat raw food
   (d) HAV vaccination for personal protection
   (e) All of the above

10. Which of the following is not true from a local study on HEV molecular epidemiology?
   (a) genotype 4 was the commonest
   (b) all cases were sporadic
   (c) genotype 1 was also found
   (d) genotype 4 cases were closely clustered to a swine isolate from China from sequence analysis
   (e) none of the above