

Viral Hepatitis C in Hong Kong

Nancy Leung^a Carol M.C. Chu^b John S. Tam^c

^aAlice Ho Miu Ling Nethersole Hospital, ^bPostgraduate Medical School, and ^cDepartment of Microbiology, Chinese University of Hong Kong, Hong Kong, SAR, China

Key Words

Chronic hepatitis · Epidemiology · Genotype · Hepatitis B virus · Hepatitis C virus · Hepatocellular carcinoma

Abstract

Objective: Hepatitis C virus (HCV) infection can lead to serious liver disease. Its medico-socio-economic burden on society can be immense. This study investigates the epidemiology of HCV infection in Hong Kong. **Methods:** Data from the Department of Health, relevant publications from Medline search and data from two acute hospitals were reviewed. **Results:** The prevalence of anti-HCV among voluntary blood donors is stable, remaining at approximately 0.035–0.099% over the past 10 years, and is higher in the older age group. Among the high-risk groups, the anti-HCV prevalence is as follows: (1) hospital patients 0.8%, (2) intravenous drug users 46.0%, (3) patients infected with HIV 7.9%, (4) children with transfusion-dependent hematologic disease 16.3%, (5) patients on continuous ambulatory peritoneal dialysis 1.8%, patients on hemodialysis 16.4%, recipients of kidney transplants 6.2% and (6) patients with hepatocellular carcinoma 7.3%. Among blood donors, 58.8% were infected with HCV genotype 1b and 27.0% with genotype 6a. Genotype 6a is particularly common among intravenous drug users. **Conclusion:** Hong Kong has a low prevalence of HCV infection. Patients are mostly infected through transfusion with blood or products prior to the introduction of anti-HCV screening to the blood transfusion ser-

vice. Illicit drug use constitutes another significant risk. Since 1997, there has been a great increase in population movement between China and Hong Kong which might affect the epidemiology of HCV infection.

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Introduction

Hong Kong is a region endemic for hepatitis A virus and hepatitis B virus (HBV), where viral hepatitis A accounts for most acute hepatitis, while viral hepatitis B accounts for the majority of chronic liver disease. Around 10% of the adult population are seropositive for hepatitis B surface antigen (HBsAg). In the early 1980s, posttransfusion non-A, non-B (NANB) hepatitis was recognized. With the identification of hepatitis C virus (HCV) in 1989 and the development of serological tests that followed, most of the posttransfusion NANB hepatitis was found to be HCV-related. The epidemiology of HCV infection is gradually emerging as studies were conducted. With highly sensitive and specific methodologies becoming more widely available, the clinical impact of HCV is increasingly coming to the fore. Although there is no region-wide population-based survey of HCV infection in Hong Kong, data from various studies on population subgroups are useful in identifying possible routes of HCV transmission. Public education and an improved healthcare system in Hong Kong have helped identify asymptomatic patients during medical check-ups. Hong Kong is a dy-

namic cosmopolitan city hosting millions of visitors and tourists. Furthermore, after 1997, there has been a great increase in population movement between Hong Kong and the Mainland China. This is likely to have certain effects on the epidemiology of infectious diseases including HCV infection. Strategies for prevention and control of HCV infection should be planned accordingly.

Acute Hepatitis C

Acute viral hepatitis is a notifiable disease in Hong Kong. Most cases of acute hepatitis are acute hepatitis A, with occasional acute hepatitis B. Each year, a few cases fall into the category of NANB hepatitis which might include cases of acute hepatitis C. However, there is a technical difficulty in diagnosing acute hepatitis C in Hong Kong, since an assay for serum HCV RNA is not readily available in most healthcare settings. Clinicians can attend patients who are in the window period when anti-HCV antibody is not yet detectable, thus missing the diagnosis.

Clinical Impact of HCV Infection – Prevalence of Anti-HCV among Patients with Chronic Liver Disease and Hepatocellular Carcinoma

Lok et al. [1] reported high prevalence of anti-HCV among patients with posttransfusion NANB hepatitis and hepatocellular carcinoma (HCC), 87 and 37.3%, respectively, using the first-generation enzyme immunoassays on stored serum samples. On retesting with the second-generation enzyme immunoassays and neutralization assays, only 70 and 56% were confirmed positive. Another retrospective study using the first-generation recombinant assay verified by the second-generation assay also detected anti-HCV in 70% of posttransfusion NANB hepatitis, 20% of cryptogenic cirrhosis, 3% of alcoholic liver disease and 20% of autoimmune chronic active hepatitis. Only 1 of the 157 (0.6%) controls was positive for anti-HCV [2]. Among 424 consecutive patients with HCC attending the Hepatoma Clinic in a single center, 80% tested positive for HBsAg and 7.3% for anti-HCV, of whom 3.8% were positive for anti-HCV alone and 3.5% both for HBsAg and anti-HCV. The mean age of patients with anti-HCV was older than that of patients with HBsAg at 60 and 53 years, respectively [3]. Among 155 liver transplantations performed in Hong Kong, 7 (4.5%) were due to cirrhosis related to hepatitis C [4].

Coinfection with HCV and HBV

In Hong Kong, 10% of the adult population is seropositive for HBsAg. Most of them were infected at birth through mother-to-child transmission or horizontal transmission in early childhood. There has been a declining trend in HBsAg prevalence during the past two decades. Although the frequency of HCV infection in the general population remains low, 3.5% of HCC patients in Hong Kong had serological evidence for coinfection with HBV and HCV [3]. Coinfection with HBV and HCV has been shown to increase the risk of HCC. In a separate study on 571 patients with chronic hepatitis B, 4 (0.7%) were found to be anti-HCV positive; all 4 were positive for serum HCV RNA. Liver histology revealed lymphoid aggregates and bile duct changes in 3 of them. None had detectable HBV core antigen and HBV DNA was negative, while 3 had HCV RNA detected by *in situ* reverse transcription polymerase chain reaction (RT-PCR). Therefore, it appears that coinfection with HBV and HCV is uncommon in Hong Kong; there was no active replication of HBV in the few coinfecting cases [5].

Blood Donors

Posttransfusion hepatitis C accounts for a significant proportion of chronic hepatitis C in Hong Kong. In 1991, the Hong Kong Red Cross Blood Transfusion Service introduced anti-HCV testing for all blood donors. Prior to this, HBsAg and serum alanine aminotransferase levels were screened to minimize posttransfusion viral hepatitis. Blood donation has been on voluntary basis. Potential donors are requested to complete a very comprehensive Blood Donation Registration Form to ensure his/her suitability. Inquiry includes immediate and past health (history of parenteral exposures such as surgical interventions, blood or organ transplantation, tattoo, acupuncture, body piercing and needlestick injury) and lifestyle issues (sexual activities and history of drug abuse). In an update report from the Department of Health published in December 2003, entitled 'Surveillance of viral hepatitis in Hong Kong' [6], the prevalence of anti-HCV among an average of 4,000 donors each year has remained at 0.035–0.099% since 1991; most blood donors are young adults. In the age group of 16–19 years, the prevalence of anti-HCV is 0.01–0.02%, increases to 0.1–0.2% in those aged 20–40 years and remains 0.1–0.3% in the age group over 40 years. Men tend to have a higher anti-HCV prevalence than women (table 1). The route of transmission

Table 1. Prevalence of anti-HCV in Hong Kong

Population subgroups	Anti-HCV positive	
	men	women
Blood donors ^a :		
All	21/20,563 (0.10)	13/21,750 (0.06)
Age groups		
16–19 years	2/12,856 (0.02)	1/13,483 (0.01)
20–29 years	7/4,901 (0.14)	5/4,620 (0.11)
30–39 years	5/1,716 (0.29)	3/2,115 (0.14)
40–49 years	4/841 (0.48)	3/1,213 (0.25)
>49 years	3/249 (1.20)	1/319 (0.31)
Patients on peritoneal dialysis		(1.8)
Patients on hemodialysis		(16.4)
IDUs ^a	97/210 (46.2)	
Patients with HIV/AIDS ^a	11/140 (7.9)	
Selected hospital-based patients	1,848/23,729 (7.8)	
Patients with chronic hepatitis B	4/571 (0.7)	
Patients with HCC	31/424 (7.1)	

Figures in parentheses are percentages.

^a Data during 2002 from the Department of Health, Hong Kong.

among these anti-HCV-positive blood donors deserves further detailed studies.

In 1998, a review program for viral hepatitis C was launched by the Hong Kong Hospital Authority in collaboration with the Hong Kong Red Cross Blood Transfusion Service. Press releases have been made to promote checks for anti-HCV in order to identify individuals who might have been infected with HCV from a blood transfusion they received before anti-HCV screening of blood donors. Therapy was offered when indicated. This program instigated public awareness of HCV infection and encouraged individuals with a possible risk to come forward for anti-HCV testing.

Patients with End-Stage Renal Disease

The prevalence of HCV infection among patients with end-stage renal disease (ESRD) is 1.8% among those on peritoneal dialysis, 16.4% among those on hemodialysis and 6.2% among kidney transplant recipients [1, 7]. The high prevalence may be due to transfusion requirements especially for more than 5 units and parenteral exposures to HCV in their clinical courses. However, this may be an overestimation, because in these studies, the first-generation assay was performed on stored sera. On the other hand, there might be patients not diagnosed with HCV infection, because those with ESRD may not have had raised detectable anti-HCV since they are immunocom-

promised. HCV RNA should also be checked for the accurate diagnosis of HCV infection.

Among the 51 patients undergoing hemodialysis, 8 (16%) were positive for anti-HCV and 1 (2%) for HCV RNA alone, giving an overall HCV infection rate of 18%. Follow-up for 19 months identified an incidence of HCV infection at 5% per patient-year [7]. Patients tolerated the standard interferon (IFN)- α_{2b} well, and 27% achieved sustained virological response. Special attention must be paid to prevent aggravation of anemia resistant to erythropoietin as well as malnutrition induced during IFN therapy [8].

Recipients of renal allografts from donors seropositive for HCV RNA may have HCV-related liver disease. However, histological examinations showed lower activity scores than nonimmunosuppressed subjects, but more severe disease than patients on dialysis [9, 10].

Patients with Hematological Disorders

The thalassemia gene is common among the ethnic Chinese. Despite genetic counseling and screening of potential parents, transfusion-dependent thalassemia is not uncommon among young children. Of the 57 thalassemic children aged from 2 to 16 years, 8 (14%) were positive for anti-HCV (unpublished observation). The clinical efficacy of combination therapy with IFN- α 3 million units/m² three times per week and oral ribavirin 16 mg/kg daily for 12 months was evaluated in 18 treatment-naive patients with thalassemia. The median age at baseline was 16 years (range 7–29). Of those, 14 were infected with HCV genotype 1b and 4 with genotype 6a. The sustained biochemical and virological response 6 months after treatment was high at 72%. Requirement for blood transfusion was temporarily increased by 30% due to hemolysis associated with ribavirin [11].

Intravenous Drug Users

Injection drug users (IDUs) in Hong Kong have been encouraged to undergo detoxification through government-run programs including methadone clinics. These clinics supervise oral methadone administration to wean off the intravenous drug addiction. There are also inpatient drug rehabilitation centers. Surveillance for makers of HBV and HCV infections indicates a declining trend in the prevalence of anti-HCV. Of the 134 samples tested, 74% were positive during 1991–1992. Ten years later, in

2000/2001, the prevalence dropped to 46% among the 210 samples tested. Genotyping of HCV showed a high prevalence of genotype 6a among drug users. Cross-infection due to sharing syringes is common and may explain this genotype profile [6].

HIV and AIDS Patients

Hong Kong has a relatively low prevalence of HIV infection. Since 1984, a total of 2,311 HIV-infected individuals and 676 AIDS patients have been reported [6]. About 70% are ethnic Chinese, 80% have been infected through sexual contacts, of whom 70% were heterosexuals; only 5% are IDUs. They are encouraged to attend the HIV specialist services of the Department of Health or the hospital authority. In the year 2001, 75 male and 26 female patients from the Integrated Treatment Center of the Department of Health were screened. The overall anti-HCV prevalence was 7.9% (9.3% in men and 3.8% in women). Similar results were observed in the following year.

Sex Workers

There are no published data or reports on this population subgroup.

Hospital-Based Patients

The Prince of Wales Hospital and the Alice Ho Miu Ling Nethersole Hospital are two district hospitals which serve a catchment area with around 2 million inhabitants. A survey for HCV infection was performed there. Between 1993 and 2002, 23,729 tests were performed for anti-HCV. The reasons for requests were hepatitis with abnormal liver function tests, hepatitis with history of blood transfusion, previously diagnosed NANB hepatitis or current/past IDU. Using the second- and third-generation immunoassays, 1,848 (7.8%) subjects were found positive for anti-HCV, of whom two thirds were men. Anti-HCV-positive rates were 5.1, 7.1, 8.5, 7.8 and 5.2% in age groups ≤ 20 , 21–40, 41–60, 61–80 and ≥ 81 years, respectively. The reason for HCV infection in 140 youngsters less than 20 years old is not entirely clear. It is postulated that they may have had blood transfusions repeatedly before the introduction of anti-HCV screening of blood donors, since most of them had suffered from he-

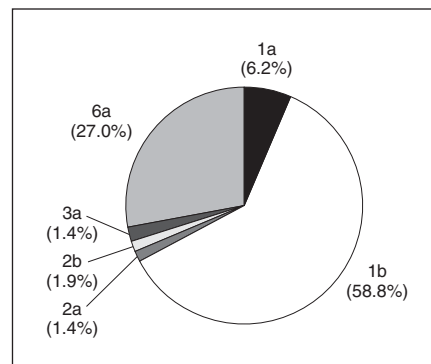


Fig. 1. Genotypes of HCV among blood donors in Hong Kong [data adapted from ref. 12].

matological disorder or oncological disease. The review on case notes of 401 patients revealed a median age of 42 years (range 3–78) with a male-to-female ratio of 7:3. The possible route of transmission was IDU (44.9%), followed by history of blood transfusion including ESRD requiring dialysis and/or blood transfusion (19.5%), surgical or dental intervention (7.5%) and renal transplantation (3.7%). The possible route of transmission in the remaining 24% of the patients was not documented in the case note, although 2 might have been infected through acupuncture. Despite the HCV lookback program in 1998 to promote check-ups for anti-HCV in those with a history of blood transfusion, many patients still present with a late complication of cirrhosis [unpubl. observations].

HCV Genotypes

Among 212 blood donors, 58.5% were infected with HCV genotype 1b and 27.0% with genotype 6a. Other genotypes included 1a (6.2%), 2a (1.4%), 2b (1.4%) and 3a (1.9%) (fig. 1) [12]. In the hospital-based study at the Prince of Wales Hospital and the Alice Ho Miu Ling Nethersole Hospital, 82.4% of all patients with anti-HCV were positive for HCV RNA by PCR. In these 294 HCV RNA-positive samples, the genotype profile was similar to 1b (60.6%), 6a (28.6%) and 2a/2b/3a (10.8%) [unpubl. observations]. Among IDUs, 70% were PCR-positive for HCV RNA, and a high prevalence of genotype 6a was confirmed with 1b (33.9%), 2a/3a (7.2%) and 6a (58.9%). The rate of therapeutic response among the Chinese has not been formally assessed or compared with that in the Caucasians. Pilot studies have shown that genotype 6 be-

haves much the same as non-1 genotypes in the therapeutic response [pers. commun.].

Discussion

Hong Kong has a relatively low prevalence of anti-HCV in the general population. Chronic HCV infection is mainly the result of transfusion with unscreened blood or blood products in the past. The introduction of a detailed questionnaire and screening of potential blood donors for anti-HCV should have minimized the risk of infection to a negligible level; Hong Kong does not accept paid blood donation and the majority of donors are young volunteers. The fact that 0.01–0.2% of those aged between 16 and 19 years were anti-HCV-positive needs to be further investigated.

Hong Kong is undergoing great sociopolitical changes, including for example a relatively free movement of populations across the border separating Hong Kong and China. Certain regions in China have an exceedingly high prevalence of HBV, as well as HCV and HIV, largely due to failure in stemming out paid blood and organ donations. This may affect profiles of disease epidemiology in Hong Kong, including that of HCV infection.

IDU is not a major problem in Hong Kong. Young people tend to use oral drugs for recreational activities. However, for IDUs, there is no syringe change program to minimize cross-infection among the inmates. The methadone clinics were often abused by IDUs as a trafficking point. Concerted effort by the government and police department to stem out drug trafficking across the border and in the community is important. Many non-governmental organizations also provide support for IDUs to rehabilitate them in the society.

Body piercing and tattoos are back in fashion. Nail manicure is also popular. The hygienic standard of facilities providing these services is variable. Acupuncture has been and still is popular among Chinese for diverse ailments. Disposable acupuncture needles are available and acupuncturists must promote their usage. In the hospital-based study, 23.9% of the patients with anti-HCV were found to have no documented risk factors. This may be due to poor documentation or some other risk factors yet to be identified.

Therapy for chronic hepatitis C is expensive. The main focus of the healthcare system should be on the prevention of HCV infection. Public education is vital in the prevention of viral hepatitis. The awareness of risks and ways to avoid them must be promulgated.

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