Seroprevalence of hepatitis C in intravenous opioid users presenting in the early phase of injecting drug use in Singapore

Winslow M, Subramaniam M, Ng W L, Lee A, Song G, Chan Y H

ABSTRACT

Introduction: All over the world, Hepatitis C virus (HCV) accounts for an estimated 130 million chronic infections. Injection drug use has become one of the most important risk factors for HCV, and within the injection drug user population, the prevalence of HCV antibody ranges from 70 to 95 percent depending on an individual's length of use and the prevalence of infection in the community. This study was undertaken to determine the prevalence of and the risk factors for Hepatitis C antibodies in injecting drug users presenting to the Community Addictions Management Programme (CAMP) in Singapore.

Methods: Eligibility criteria for inclusion in this study were all intravenous buprenorphine users presenting to CAMP. 106 subjects, who consented to the study, completed an interviewer-administered questionnaire, and underwent a urine and blood analysis.

Results: The prevalence rate for HCV was 42.5 percent among the subjects included in our study. The odds of seroprevalence in those sharing needles were 5.6 times that of those who were not, and the odds of seroprevalence among those using with others (peers or partners) were 6.3 times, as compared to among those who were individual users. Racial differences were also seen, but these could be accounted for by the sharing of needles.

Conclusion: This study provides important local data at the onset of an early buprenorphine-injecting epidemic in Singapore. This data is useful for disease prevention and healthcare planning.

Keywords: drug abuse, hepatitis C virus, intravenous buprenorphine users, intravenous drug use, needle sharing

Singapore Med J 2007; 48(6):504–508

INTRODUCTION

All over the world, hepatitis C virus (HCV) accounts for an estimated 130 million chronic infections.[1] Preliminary results suggest that the prevalence of HCV infection is approximately 2.2% worldwide,[2] while the prevalence of HCV in the United States and western Europe ranges between 1% and 2.4%.[3,4] HCV infection is generally considered a public health problem of the Western countries, with Hepatitis B infection being more of a problem in the East. However, evidence is growing that prevalence of HCV in some countries like the Philippines, Thailand and China may be even higher than that in the United States.[5,6] A prevalence study of antibodies to HCV among a blood donor population in Singapore reported that 0.54% of donor samples were repeatedly reactive for anti-HCV.[7]

HCV is generally transmitted by the parenteral route. A well-known and common mode of transmission involves transfusion and/or parenteral contact with blood products.[8] Other modes of transmission include perinatal transmission, needle stick injury with contaminated needles and sexual transmission. Following the introduction of routine HCV antibody screening of blood products and the development of precautions across healthcare systems, these modes of transmission have shown a sharp decline. Injection drug use has since become the single most important risk factor for HCV in the United States.[9] Within the injection drug user population, prevalence of HCV antibody ranges from 70% to 95%, depending on an individuals' length of use and the prevalence of infection in the community.[10]

Although the acute phase of HCV infection is usually asymptomatic, 60%–85% of those infected develop chronic disease and serious symptoms like cirrhosis and hepatocellular carcinoma.[11,12] While risk reduction methods have successfully reduced the incidence and prevalence of human immunodeficiency virus (HIV)

Community Addictions Management Programme, Institute of Mental Health and Woodbridge Hospital, 10 Buangkok View, Singapore 539747

Winslow M, MBBS, MMed, FAMS
Senior Consultant and Chief

Subramaniam M, MBBS, MHSM
Research Manager

Ng WL, BA
Counselor

Lee A, MBBS, MMed, FAMS
Senior Consultant

Song G, PhD
Clinical Fellow

Faculty of Medicine, National University of Singapore, Blk MD11, #02-02 Clinical Research Centre, 10 Medical Drive, Singapore 117597

Chan YH, PhD
Biostatistician

Correspondence to:
Dr Mythily Subramaniam
Tel: (65) 6389 2381
Fax: (65) 6315 0548
Email: mythily@imh.com.sg

among drug users, there has been little or no effect on HCV transmission.[13,14] The spread of HCV is difficult to control due to the high-risk behaviour, social mixing of new and experienced drug users,[14] higher transmissibility of HCV as compared to HIV,[15] sharing of injection equipment by HCV positive abusers,[16] stronger tendency of HCV towards chronicity than other forms of viral hepatitis that generates a large reservoir of infected intravenous (IV) drug users.[17,18]

Singapore is a multiracial and multicultural city-state located just north of the equator at the southern tip of the Malay Peninsula. The latest data from 2005 indicate that the racial breakdown is Chinese (76%), Malays (13.7%), Indians (8.4%) and others (1.8%). The literacy rate is over 95% and the total resident population is just over 3.5 million people. Since the 1970s, Singapore has adopted a multi-pronged approach in its fight against drugs. This approach involves tough legislation, vigorous enforcement and a high-profile drug prevention programme aimed at sustaining a national consensus towards zero tolerance for drug abuse. In 2002, buprenorphine became available as an office-based treatment for opioid dependence. Its use took off rapidly and by 2004, we were seeing numerous reports of injecting drug use (IDU) of buprenorphine. This IDU was a new phenomenon, as the primary mode of heroin use in Singapore was by the inhalant method, or "chasing the dragon". This study was undertaken to determine the prevalence of, and risk factors for, Hepatitis C antibodies in injecting drug users presented to the Community Addictions Management Programme (CAMP) in Singapore.

METHODS

CAMP was started by the Ministry of Health as a five-year pilot-programme in 2001, to treat eligible patients suffering from addiction problems. CAMP is currently the major provider of basic addiction care in Singapore, with added emphasis on training, prevention and public education initiatives. This study is part of a larger study meant to profile buprenorphine abusers in Singapore during the early stage of an injecting drug epidemic. The study was approved by the institutional review board and written informed consent was taken from all the patients who expressed their willingness to participate in the study. Recruitment for this cross-sectional study was done from February 2005 to January 2006. All patients abusing buprenorphine, who met the DSM-IV-TR criteria for opioid dependence, and who were attending CAMP's inpatient and outpatient treatment clinics, were invited to join the study. Patients were informed of the procedures and that HIV is a notifiable infection in Singapore. 106 of the 124 patients invited to participate in the study agreed to take part, giving a response rate of 85.5%.

Subjects eligible for the study were all intravenous buprenorphine users fulfilling the diagnostic criteria for opioid dependence. Those with a serious medical illness requiring prescription of buprenorphine for analgesic purposes were excluded from the study. Each of the subjects who consented to the study completed an interviewer-administered questionnaire, and underwent a urine analysis and blood-draw. The questionnaire comprised mainly close-ended questions covering demographic characteristics, drug use history, drug use trends, criminal justice records and health behaviour.

Blood specimens collected for HCV antibody screening were sent immediately to the hospital's laboratory. They were then sent to the National Referral Laboratory on dry ice. Samples were analysed for HCV seropositivity, using a third-generation CA (VITROS Eci; Ortho Clinical Diagnostics, New Jersey, USA). Western blot confirmation was done for all positive and intermediate results. HIV antibodies were detected using AXSYM HIV 1/2 gO (Abbott, Wiesbaden, Germany) a microparticle enzyme immunoassay. Standard descriptive statistics were used to analyse the characteristics of participants. Chi-square test and Mann-Whitney U test were used to test for significant differences between groups in categorical and continuous variables, respectively. A logistic regression was performed using HCV seroprevalence as the dependent variable and age, gender, ethnic group, years of IV drug use, years spent in drug rehabilitation centres (DRCs), needle reuse and needle sharing as the covariates.

RESULTS

The age of the 106 subjects ranged from 20 to 64 years, with a mean age of 39.5 (SD 7.9) years. The majority of the participants were male (90.6%); 49.1% were Chinese, 28.3% were Malays, 12.3% were Indians and 10.4% belonged to other ethnicities. This is consistent with national opioid dependence rates that show higher rates among the non-dominant races. The prevalence rate for HCV was 42.5% among the subjects included in our study. The sample characteristics of this group are presented in Table I.

Subjects with hepatitis C antibodies had similar demographical characteristics to the group that was not tested positive for HCV antibodies. There were no significant differences in the age, age of onset of illicit drug use, age of onset of IV drug use, or the duration of IV use, between the two groups. There were significant differences in the ethnic composition of the two groups ($p = 0.003$, $\chi^2 = 18.0$) and in their injecting characteristics. Those who shared syringes with others were more likely to have a reactive test than those who did not share syringes (56% vs 44%, $p = 0.008$, $\chi^2 = 7.1$). Those who used drugs with peers or partners were more likely to have hepatitis C antibodies as compared to individual

Table I. Sample characteristics of the survey group.

Variable description	HCV +ve Mean (SD)	HCV –ve Mean (SD)	Unadjusted OR	95% CI	Adjusted OR	95% CI
Age (years)	39.6 (6.9)	39.5 (8.8)	1.0	0.9–1.0	0.9	0.8–1.1
Age of onset of illicit drug use (years)	16 (3.7)	17.3 (5.6)	0.9	0.9–1.0	1.1	0.8–1.5
Age of onset of IV drug use (years)	31.9 (9.9)	30.6 (10.8)	1.0	0.9–1.0	1.0	0.9–1.1
Length of IV drug use (months)	1.0 (1.7)	2.3 (4.8)	1.0	0.9–1.0	1.0	0.8–1.1
Number of years spent in DRC*	7.0 (4.4)	5.1 (4.2)	1.1	1.1–1.2	1.1	0.8–1.6
Number of times in DRC*	4.3 (1.7)	3.5 (1.7)	1.3	1.1–1.7	1.2	0.4–3.5
Number of years spent in prison	3.5 (2.7)	4.0 (3.9)	0.9	0.9–1.0	1.0	0.9–1.3
Number of times in prison	3.0 (1.9)	2.6 (1.3)	1.2	0.9–1.5	1.2	0.7–2.0
	HCV +ve No. (%)	HCV –ve No. (%)				
Gender						
Male	39 (40.6)	57 (59.4)				
Female	6 (60.0)	4 (40.0)	2.1	0.6–8.2	21.5	0.5–1114.0
Ethnicity**						
Chinese	13 (25.0)	39 (75.0)				
Malay	20 (66.7)	10 (33.3)	6.0	2.2–16.0	5.9	0.9–39.0
Indian	7 (53.8)	6 (46.2)	3.5	1.0–12.3	13.5	1.1–164.2
Others	5 (45.5)	6 (54.5)	2.5	0.6–9.6	27.7	1.7–451.8
Employment status						
Employed	21 (38.9)	33 (61.1)				
Unemployed	24 (46.2)	28 (53.8)	1.3	0.6–2.9	1.4	0.3–6.3
Marital status						
Never married	23 (38.3)	37 (61.7)	0.7	0.3–1.5	0.9	0.2–4.8
Ever married	22 (47.8)	24 (52.2)				
Living situation						
Living alone	6 (40)	9 (60)	0.9	0.3–2.7	3.0	0.3–30.2
Living with others	39 (42.9)	52 (57.1)				
Ever been to prison						
No	6 (26.1)	17 (73.9)				
Yes	39 (47)	44 (53)	2.5	0.9–7.0	–	
Ever been to DRC						
No	2 (16.7)	10 (83.3)			–	
Yes	43 (45.7)	51 (54.3)	4.2	0.9–20.1		
Ever injected with previously-used needles/syringes						
No	4 (36.4)	7 (63.6)	0.8	0.2–2.7	–	
Yes	41 (43.2)	54 (56.8)				
Ever shared syringes with anyone*						
No	17 (30.4)	39 (69.6)				
Yes	28 (56.0)	22 (44.0)	2.9	1.3–6.5	5.6	1.0–31.5
Description of usage*						
Used alone	28 (35.4)	51(64.6)				
Used with others	10 (66.7)	5 (33.3)	3.3	0.1–0.8	6.3	1.0–39.5
Ever used more than one drug while injecting (polysubstance use)						
No	5 (25)	15 (75)	0.3	0.1–1.1	0.2	0.01–2.0
Yes	40 (46.5)	46 (53.5)				
Ever used booting (mix blood and drug inside the syringe)						
No	12 (31.6)	26 (68.4)	–		0.7	0.2–3.4
Yes	33 (48.5)	35 (51.5)				

* $p < 0.05$; ** $p < 0.005$

users ($p = 0.01$, $\chi^2 = 6.2$). No significant differences were found in the family history of drug use between the two groups. Significant differences were found between the two groups in the number of years spent in DRCs ($p = 0.04$) and the number of times they had been in DRCs ($p = 0.03$). Those with hepatitis C antibodies had been to the DRCs more frequently and had spent more years serving term in the criminal justice system.

On performing a stepwise logistic regression using HCV seroprevalence as the dependent variable, the significant predictors were ethnicity, syringe sharing and the pattern of usage. The odds of Malays, Indians and other ethnicities being seropositive were 5.9, 13.5 and 27.7 times, respectively, as compared to those of Chinese ethnicity. The odds of seroprevalence in those sharing needles were 5.6 times that of those who were not, and the odds of seroprevalence among those using with others (peers or partners) were 6.3 times, as compared to individual users. The subjects were also tested for hepatitis B antigen and HIV antibodies. Nine of the subjects (8.5%) tested positive for hepatitis B antigen, which is above the national average of 4%; none tested positive for HIV. Of those positive for hepatitis B antigen, 3 (33.3%) were also positive for hepatitis C antibodies.

DISCUSSION

Our study shows that there is a high prevalence of HCV antibodies (42.5%) among the IV drug users sampled as compared to the population of Singapore as a whole. Studies have reported varying rates of prevalence among IV drug users: 53% in New Zealand,[19] 59% in New York[20] and 76.7% in another study.[21] In the late 1990s, a small cross-sectional study among IV drug users in Kuala Lumpur, Malaysia, found the rate of hepatitis C antibodies to be 100%.[22] An earlier study in Malaysia found the prevalence of hepatitis C among IV drug users to be 85%.[23] Our results indicate that the epidemic of IDU is still in its early stages, and that prevention messages and health education would have an impact on the rate of increase of HCV.

A higher proportion of those who were not Chinese, shared syringes, injected with peers or partners and had undergone rehabilitation, were more likely to be seropositive for HCV. Ethnicity, syringe sharing and using with peers were also strongly associated with HCV positivity. The Chinese have the lowest prevalence rates of HCV, while the Malays, Indians and other races all have significantly higher odds of being HCV antibody positive. This would tend to correlate well with the patterns of drug taking in the different ethnic populations.[24] The Chinese tend to be the least communal when it comes to abusing substances, and share drugs much less frequently than the other ethnicities. Subjects with more chronic opioid use and polysubstance abuse often have a history of being in involuntary and custodial DRCs. This is reflected in the higher prevalence of HCV in this population, which is in turn reflective of the chronicity and severity of drug use. Duration of injecting, together with frequency of injection, are commonly reported as risk factors[25,26] and reflect the cumulative exposure to infective needles and paraphernalia. There was no significant difference in HCV rates detected by looking at length of IDU. This is likely to be because we are at the early stages of this IDU epidemic.

Many of those who tested positive for HCV were adamant that they had not shared needles, although they did admit to generally using the same syringe more than once, as they had to inject themselves 3–4 times a day. Further questioning revealed that although IV drug users were aware that sharing syringes could lead to infectious diseases, they nevertheless shared the "hot water" purchased at neighbourhood coffee shops for dissolving their medications prior to injecting. The parenteral transmission of HCV is more efficient than that of HIV and has more sources of exposure in the injecting settings like cookers and cotton.[27] Some other studies, however, failed to find an association between HCV prevalence and sharing of needles, syringes and other paraphernalia.[28] It has been suggested that the nature of injecting is an intimate act and involves such subtle processes that the individuals involved may not actually realise that the sharing of injectable equipment/solutions, etc. is occurring.[29] Rhodes et al suggest that sharing may be under-reported especially in quantitative studies. Their study also revealed that injectors tended to make sense of HCV risk in relation to HIV. Most view HCV prevalence as high and HCV transmission as an inevitable consequence of injecting, and HCV risk was perceived as ubiquitous and unavoidable.[30] One of the factors that may have kept the rate relatively low in this study population is that most people were cognizant of the fact that sharing needles could spread diseases. There is also an abundance of relatively inexpensive and accessible disposable needles and syringes found at traditional medicine shops and pharmacies in Singapore. These, meant mainly for diabetic patients, have been widely used by our IV drug user population. It is therefore important that prevention messages emphasise not only the risk of transmission via syringe sharing, but also the risks from sharing of cookers, cotton and water.[31]

This study done in Singapore provides the first local data in this significant group, and can be used for disease prevention and health planning. Over the past four years, the pattern of drug consumption in Singapore has changed dramatically; it has shifted from mainly inhalant or oral consumption of illicit drugs like heroin or morphine, to more IV drug use with combinations of prescriptive drugs, especially buprenorphine and the benzodiazepines.

The high prevalence of HCV (42.5%), and the fact that those infected are likely to be chronic carriers, suggest that reducing HCV prevalence will take considerable time and effort. In our country, we have the advantage of being relatively small, and therefore have access to most of those misusing illicit or prescription drugs. Medical practitioners, counsellors and other healthcare workers, who have contact with this population of IV drug users must deliver to them targeted prevention messages that strongly encourage cessation of IDU in order to minimise the risk of this special population from acquiring and transmitting all blood-borne infections.

Events in Singapore, since this study was conducted, will be especially revealing. Singapore has continued with its policy of zero-tolerance for drug addiction by making buprenorphine a schedule A controlled drug in the same category as heroin and opium on August 14, 2006. Additional legislation also allows for added punishment for those with drug antecedents caught with needles and syringes or assorted paraphernalia. This is likely to rapidly halt and cause a decline in IDU. We recommend further studies on the group of opioid dependent patients, who used buprenorphine intravenously, to monitor the status of the major blood-borne viruses.

ACKNOWLEDGEMENT

This project was supported by an institutional block grant received from the National Medical Research Council, Singapore

REFERENCES

1. Alter MJ. Epidemiology of viral hepatitis and HIV co-infection. J Hepatol 2006; 44 (1 suppl):S6-9.
2. The Global Burden of Hepatitis C Working Group. Global burden of disease (GBD) for hepatitis C. J Clin Pharmacol 2004; 44:20-9.
3. Heintges T, Wands JR. Hepatitis C virus: epidemiology and transmission. Hepatology 1997; 26:521-6. Comment in: Hepatology 1999; 29:299-300.
4. Williams I. Epidemiology of hepatitis C in the United States. Am J Med 1999; 107:2S-9S.
5. Songsivilai S, Jinathongthai S, Wongsena W, Tiangpitayakorn C, Dharakul T. High prevalence of hepatitis C infection among blood donors in northeastern Thailand. Am J Trop Med Hyg 1997; 57:66-9.
6. Li L, He J, Zhao L. [Epidemiologic features of viral hepatitis in Fujian]. Zhonghua Liu Xing Bing Xue Za Zhi 1998; 19:89-92. Chinese.
7. Kuperan P, Choon AT, Ding SH, Lee G. Prevalence of antibodies to hepatitis C virus in relation to surrogate markers in a blood donor population of Singapore. Southeast Asian J Trop Med Public Health 1993; 24 suppl 1:127-9.
8. Heintges T, Mohr L, Niederau C. [Epidemiology and clinical features of chronic viral hepatitis]. Dtsch Med Wochenschr 1994; 119:1365-70. German.
9. Alter MJ, Mast EE. The epidemiology of viral hepatitis in the United States. Gastroenterol Clin North Am 1994; 23:437-55.
10. Lorvick J, Kral AH, Seal K, Gee L, Edlin BR. Prevalence and duration of hepatitis C among injection drug users in San Francisco, Calif. Am J Public Health 2001; 91:46-7.
11. Lauer GM, Walker BD. Hepatitis C virus infection. N Engl J Med 2001; 345:41-52. Comment in: N Engl J Med 2001; 345:1425-6; author reply 1427-8.
12. Jauncey M, Micallef JM, Gilmour S, Amin J, et al. Clearance of hepatitis C virus after newly acquired infection in injection drug users. J Infect Dis 2004; 190:1270-4.
13. Miller CL, Johnston C, Spittal PM, et al. Opportunities for prevention: hepatitis C prevalence and incidence in a cohort of young injection drug users. Hepatology 2002; 36:737-42.
14. Miller M, Mella I, Moi H, Eskild A. HIV and hepatitis C virus risk in new and longer-term injecting drug users in Oslo, Norway. J Acquir Immune Defic Syndr 2003; 33:373-9.
15. MacDonald M, Crofts N, Kaldor J. Transmission of hepatitis C virus: rates, routes, and cofactors. Epidemiol Rev 1996; 18:137-48.
16. Vidal-Trecan G, Coste J, Varescon-Pousson I, Christoforov B, Boissonnas A. HCV status knowledge and risk behaviours amongst intravenous drug users. Eur J Epidemiol 2000; 16:439-45.
17. Thomas DL, Astemborski J, Rai RM, et al. The natural history of hepatitis C virus infection: host, viral, and environmental factors. JAMA 2000; 284:450-6. Comment in: JAMA 2000; 284:2592-3.
18. Esteban JI, Lopez-Talavera JC, Genesca J, et al. High rate of infectivity and liver disease in blood donors with antibodies to hepatitis C virus. Ann Intern Med 1991; 115:443-9. Comment in: Ann Intern Med 1992; 116:427.
19. Kemp R. Injecting drug users have high rates of hepatitis C, but HIV infection remains uncommon. New Zealand Public Health Report 1999; 6:17-9.
20. Des Jarlais DC, Perlis T, Arasteh K, et al. Reductions in hepatitis C virus and HIV infections among injecting drug users in New York City, 1990-2001. AIDS 2005; 19 suppl 3:S20-5.
21. Abraham HD, Degli-Esposti S, Marino L. Seroprevalence of hepatitis C in a sample of middle class substance abusers. J Addict Dis 1999; 18:77-87.
22. Yoong KY, Cheong I. A study of Malaysian drug addicts with human immunodeficiency virus infection. Int J STD AIDS 1997; 8:118-23.
23. Sinniah M, Ooi BG. Hepatitis C – the Malaysian story. Singapore Med J 1993; 34:132-4.
24. Teo SH, Chee KT, Tan CT, Ng BC. Heroin abuse in Singapore--a profile and characteristics study. Singapore Med J 1978; 19:65-70.
25. Hahn JA, Page-Shafer K, Lum PJ, Ochoa K, Moss AR. Hepatitis C virus infection and needle exchange use among young injection drug users in San Francisco. Hepatology 2001; 34:180-7.
26. Thorpe LE, Ouellet LJ, Levy JR, Williams IT, Monterroso ER. Hepatitis C virus infection: prevalence, risk factors, and prevention opportunities among young injection drug users in Chicago, 1997-1999. J Infect Dis 2000; 182:1588-94.
27. Hagan H, Thiede H, Weiss NS, et al. Sharing of drug preparation equipment as a risk factor for hepatitis C. Am J Public Health 2001; 91:42-6.
28. Judd A, Hutchinson S, Wadd S, et al. Prevalence of, and risk factors for, hepatitis C virus infection among recent initiates to injecting in London and Glasgow: cross sectional analysis. J Viral Hepat 2005; 12:655-62.
29. Taylor A, Fleming A, Rutherford J, Goldberg D. Examining the injecting practices of injecting drug users in Scotland. Edinburg: Effective Interventions Unit, 2004.
30. Rhodes T, Davis M, Judd A. Hepatitis C and its risk management among drug injectors in London: renewing harm reduction in the context of uncertainty. Addiction 2004; 99:621-33.
31. Centres for Disease Control and Prevention. HIV prevention bulletin: medical advice for persons who inject illicit drugs. Atlanta, GA: Centres for Disease Control and Prevention, 1997.