

Original Article

Prevalence of sexually acquired hepatitis C virus (HCV) infection in sexually transmitted infection (STI) patients

性病患者中經性接觸感染丙型肝炎病毒的盛行率

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Objectives: Hepatitis C virus (HCV) is commonly contracted through parenteral exposures such as needle-sharing in injection drug users (IDU) and transfusion of contaminated blood. As the significance of sexual transmission of HCV remains controversial, this study was designed to examine its prevalence in sexually transmitted infections (STI) patients, the latter considered as a surrogate of sexually active individuals who have engaged in unsafe sex. **Methods:** A cross-sectional study was conducted in Hong Kong at the Social Hygiene Service which operates STI clinics in the public sector. Over a 3-month period, all adult patients attending two major clinics were invited to have a blood test for HCV antibody (anti-HCV). Positive results were investigated afterwards by RNA testing, genotyping and phylogenetic analysis, coupled with their correlation with clinical histories. **Results:** Totally 959 STI clinic attendees were screened. Six were anti-HCV positive, giving an overall HCV prevalence of 0.6%. Four were ex-IDU with HCV genotype 6a, the same molecular identity of virus in IDU in Hong Kong. One RNA negative patient had probably contracted the virus via tattooing. An HIV co-infected patient with secondary syphilis had HCV genotype 3a that clustered with those of HIV-infected men who have sex with men (MSM) in Hong Kong. **Conclusion:** The risk of HCV transmission through sexual contacts in the community remains low. Its occurrence in MSM and the setting of HIV co-infection is however a cause for concern.

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目的：丙型肝炎病毒主要通過非消化道接觸而感染，例如靜脈注射濫藥者共用的針頭和輸注受污染的血液。由於經性接觸傳播丙型肝炎病毒的重要性仍存在爭議，本研究旨在檢查其在性病患者中的盛行率，此群組一般被認定是不安全性行為的性活躍個體的代表。方法：在香港的社會衛生科進行了一個橫斷面研究，該服務營運著本地的公共性病診所。在三個月內，邀請了兩間主要診所的所有成年就診者進行丙型肝炎病毒抗體的血液檢查。當中陽性樣本會再進行核糖核酸測試、基因分型和系統發生分析，從而比對臨床病歷的相關性。結果：總共篩選了959名性病診所就診者。發現六例丙型肝炎病毒抗體陽性個案，總體盛行率為0.6%。四個是具有丙型肝炎病毒六甲基因型的前靜脈注射濫藥者，與香港靜脈注射濫藥者群組中發現的病毒分子身份相同。一名核糖核酸呈陰性的患者有可能是通過紋身感染了此病毒。另一名人類免疫力缺乏病毒並第二期梅毒感染患者的丙型肝炎病毒為三甲基因型，歸入香港男男性接觸者中的人類免疫力缺乏病毒患者的丙肝感染群組。結論：社區中通過性接觸傳播丙型肝炎病毒的風險仍然甚低。然而，它在男男性接觸者族群的傳播和人類免疫力缺乏病毒的合併感染情況，實令人擔憂。

Keywords: Hepatitis C virus (HCV), men who have sex with men (MSM), sexually transmitted infection (STI)

關鍵詞：丙型肝炎病毒、男男性接觸者、性傳播感染

Introduction

With an estimated global prevalence of around 2-3%, hepatitis C virus (HCV) is long known to be commonly contracted through parenteral exposure.¹ Notably needle-sharing among injection drug users (IDU) constitutes the main route of HCV transmission in most countries.^{1,2} In Hong Kong, for example, the anti-HCV seroprevalence in IDU was above 80%.³ Transfusion is another major route for HCV spread,⁴ the risk of which is strongly associated with the volume of contaminated blood transfused.⁴ The epidemiological importance of HCV transmission through sexual contacts remains controversial although such occurrence has been reported. Some studies consider HCV as a much less efficiently transmitted pathogen compared to other sexually transmitted viruses like hepatitis B virus (HBV) and human immunodeficiency virus (HIV).^{5,6} In recent years, however, outbreaks of HCV have been reported in men who have sex with men (MSM) especially those co-infected with HIV.⁶ It is important, therefore, to investigate the prevalence of sexual transmission of HCV in the community so that tailored interventions can be developed.

The aim of this study was to assess the importance of sexual transmission of HCV in the

community through determining its prevalence in sexually transmitted infections (STI) patients in Hong Kong, an international city and Special Administrative Region in China. As a surrogate of sexually active individuals with engagement in unsafe sex, the HCV burden in STI patients could be treated as a marker of the efficiency of virus spread through sex in the community.

Methods

The study was conducted at the Social Hygiene Service of the Hong Kong Government Department of Health. The service is the exclusive provider of STI care in the public sector in the territory of Hong Kong. Over a 3-month period, all patients attending the service of one major male and one female STI clinic with or without microbiological diagnoses were invited to join the study. Other inclusion criteria were: understanding Chinese, provision of informed consent, age of 18 or above. Enrolled patients were asked to have 5 ml of their collected blood saved for the determination of HCV serology.

A commercial HCV ELISA kit (Murex Anti-HCV version 4 [DiaSorin]) was used for anti-HCV screening. Samples tested positive were retested by another ELISA (anti-HCV 3.0 Enhanced Save

[Ortho Clinical Diagnostics]). A positive anti-HCV test was defined as one with both ELISAs showing positive results. RNA extraction was performed on confirmed anti-HCV positive serum samples using QIAamp viral RNA kit (Qiagen, USA), followed by cDNA synthesis using the Superscript III first-strand synthesis system and random primers (Invitrogen, USA). Two segments of the HCV genome including the NS5B and Env regions were amplified by nested-PCR for HCV genotyping and then phylogenetic analysis, the latter in MEGA6. Patients positive for anti-HCV were interviewed by clinic doctors to establish the most probable route of HCV transmission. Approval was granted by Joint Chinese University of Hong Kong – New Territories East Cluster Clinical Research Ethics Committee and the Ethics Committee of Department of Health.

Results

Between May 2015 and July 2015, a total of 959 patients attending the two public STI clinics were screened for anti-HCV, who accounted for

some 37% of all patients seen during the study period. Of these, 766 (80%) were male and 193 (20%) were female. The age of the tested patients was 38.9 ± 14.8 years (male: 40.1 ± 15.3 ; female: 34.5 ± 11.9). Six were confirmed to be anti-HCV positive of which 5 were RNA positive, giving an overall HCV prevalence of 0.6%. All anti-HCV positive cases were male, with a median age of 46 (range from 29 to 78 years) (Table 1). Four of them had active STIs – gonococcal and chlamydial anterior urethritis (1 case); genital wart (1 case); late latent syphilis (1 case); HIV and secondary syphilis (1 case). One patient without active STIs gave previous history of genital herpes and treated late latent syphilis. The remaining patient did not reveal any active or past history of STIs, and he was HCV RNA negative. He attended the clinic after unprotected sex with commercial sex worker, without a subsequent clinical diagnosis of STI.

In the investigation of the possible route of HCV transmission, heterosexual contact was reported by all six anti-HCV positive cases. Other risk factors were previous history of injection drug use (4 cases) and tattooing (2 cases). Genotyping

Table 1. General characteristics of six anti-HCV positive STI patients

Patient number	Gender	Age (years)	STI		Non-sexual risk factors for HCV	HCV genotype
			Past history	Current diagnosis		
1	Male	69	GC	GC/CT	Ex-IDU	6a
2	Male	39	–	LLS	Ex-IDU	6a
3	Male	78	LLS/HG	–	Ex-IDU	6a
4	Male	53	GW NGU	GW	Ex-IDU, tattoo, ear piercing	6a
5	Male	32	–	–	Tattoo	NA (RNA negative)
6	Male	29	–	HIV/SS	–	3a

HCV=hepatitis C virus; STI=sexually transmitted infections; GC=gonococcal urethritis; CT=chlamydial urethritis; LLS=late latent syphilis; HG=herpes genitalis; GW=genital warts; NGU=non-gonococcal urethritis; SS=secondary syphilis; HIV=human immunodeficiency virus; IDU=injection drug users; NA = not available

showed that all 4 IDUs (cases 1-4 in Table 1) were infected with HCV type 6a. One non-IDU gave a history of tattooing (case 5) in the past but no RNA could be extracted for further molecular analysis. Phylogenetic analysis suggested that the HCV 6a sequences of the ex-IDU were similar to those of other HCV infected IDUs in Hong Kong, though clustering was not observed (Figure 1). Case 6 (co-infected with HIV and secondary syphilis) did not have any previous history of drug injection, surgery or transfusion. His HCV belonged to genotype 3a, the sequence of which clustered with those of HIV infected MSM diagnosed in Hong Kong in the past two years (Figure 1).⁷ He however denied ever having sex with men.

Discussion

In this study, we set out to determine the HCV prevalence of STI clinic attendees in Hong Kong, a metropolitan city in Asia where the main mode of HCV spread was through IDU. An anti-HCV prevalence of 0.6% was derived, a rate similar to the result (0.3%) obtained in a population based survey conducted in 2001 but somewhat higher than the <0.1% in new blood donors in Hong Kong.⁸ The differences could be explained by the much younger age of eligible blood donors compared to adults in the general population, and the specific deferral of IDUs from the donor pools. Our results did not support a higher rate of HCV infection in STI patients. Of all STI patients tested positive for HCV infection, previous exposure through injection drug use was probably the most important route of virus transmission. They were generally older in age compared to STI patients attending the clinics. Their detection in STI patients could in fact be just be incidental. This phenomenon was evidenced not just by the demonstration of IDU-related risks in anti-HCV positive STI patients, but also their genotypic identity with HCV infected IDU. Previous studies in Hong Kong have repeatedly shown that genotype 6a is significantly more prevalent in local IDU in

Hong Kong, paralleling the molecular pattern in south East Asia.^{9,10} The anti-HCV positive non-IDU patient with history of tattooing (case 5) might have been infected by contaminated equipment in the distant past. On interviewing, the patient recalled that the tattooing was performed over 20 years ago in a setting with suspected suboptimal infection control. In the absence of virus sequence, we were unable to establish the lineage of the virus in this specific case.

In reviewing all anti-HCV positive STI cases in our series, only one patient (case 6) had not experienced any parenteral exposure commonly reported by HCV-infected individuals. While this patient denied having man-to-man sex, the virus genotype (3a) and the molecular clustering suggested that he could in fact be an MSM, but the social stigma might have discouraged him from disclosing his sexual orientation. Alternatively he might have acquired the virus from an infected female who had previously contracted the virus from a bisexual MSM. Studies have however shown that adults in a stable heterosexual relationship with HCV-infected partners were not associated with any increase in virus transmission risk.⁵ The rarity of heterosexual transmission of HCV also argued against such pathway of virus transmission for case 6. Conversely, the high rate of sexual transmission of HCV in MSM, especially those with HIV co-infection is probably due to the sexual practices involving mucosal trauma and presence of genital ulcerative disease.^{5,6} As case 6 did in fact have HIV co-infection and secondary syphilis, it remains speculative that virus transmission has come directly from another MSM.

We acknowledge that our study had certain limitations: the small number of patients enrolled in selected clinics does not allow us to extrapolate the results to all STI patients in Hong Kong. In view of the very low anti-HCV prevalence in the study population, it was not feasible to make

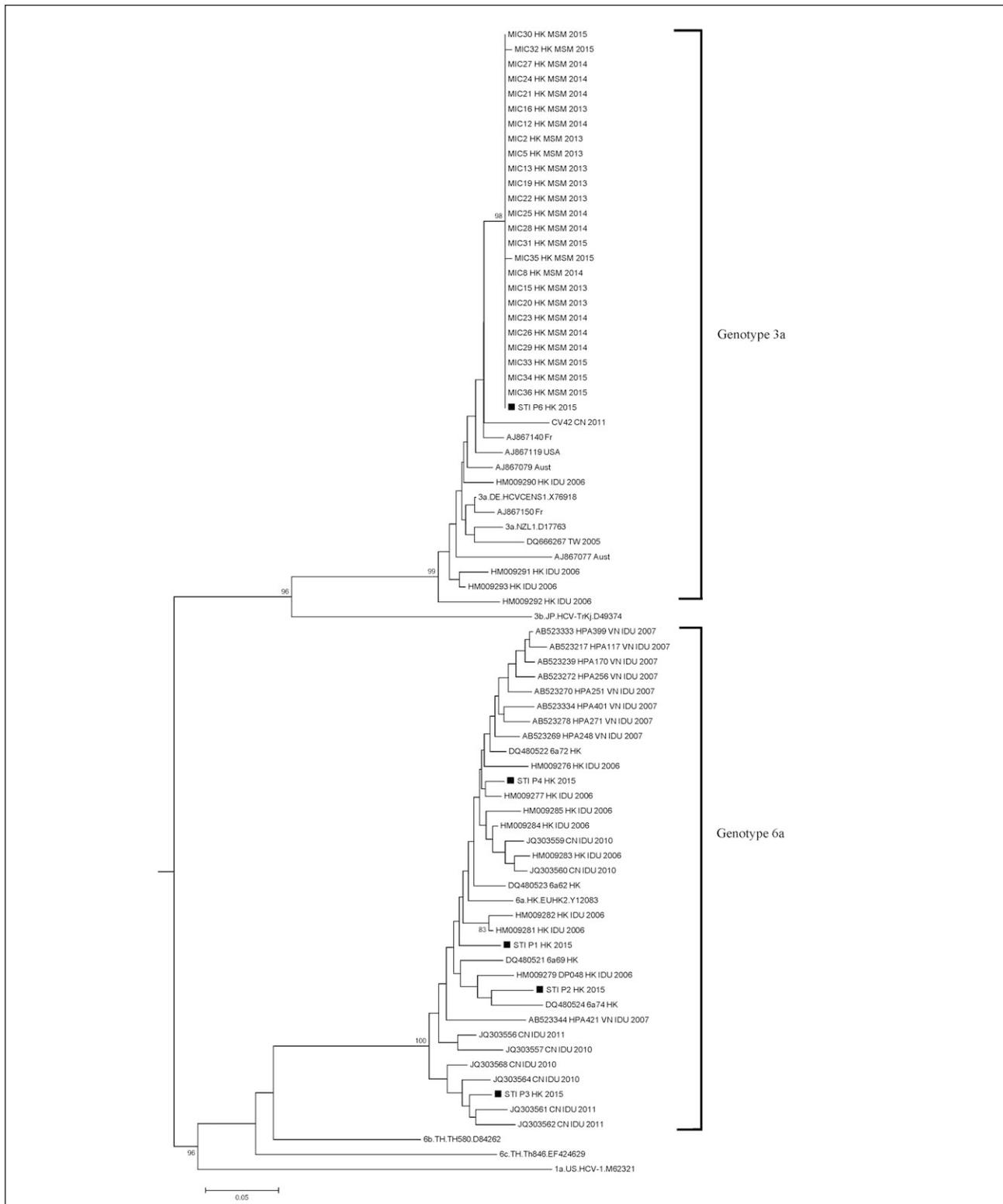


Figure 1. Neighbour-joining tree of partial HCV NS5B sequences isolated in STI clinic attendees in Hong Kong. Phylogenetic tree (1,000 bootstrap replicates) was constructed by the neighbour-joining method, implemented in MEGA6 software. Reference sequences from subtypes 1a, 3a, 3b, 6a, 6b, and 6c are marked by place of origin and GenBank accession number. Black squares indicate HCV strains isolated in this study. The numbers at nodes represent bootstrap values (>70%). Scale bar indicates the nucleotide substitutions per site.

a cohort comparison between HCV positive and negative patients. As a descriptive epidemiological study, caution with interpretation of the results is recommended. Despite these drawbacks, our study results support a conclusion of a low risk of HCV transmission through sexual contacts in the community except in the case of MSM and the setting of HIV co-infection.

Competing interests

The authors declare that they have no competing interests.

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