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HIV/HCV Coinfection in Taiwan

Ching-Sheng Hsu[1] and Jia-Horng Kao[2]

[1]Division of Gastroenterology, Department of Internal Medicine, Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Taipei; School of Medicine and School of Post-Baccalaureate Chinese Medicine, Tzu Chi University, Hualien; [2]Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine, Taipei; Department of Internal Medicine; Department of Medical Research; Hepatitis Research Center, National Taiwan University Hospital, Taipei. Taiwan

Abstract

Both human immunodeficiency virus (HIV) and hepatitis C virus (HCV) infection are important global public health problems with shared transmission routes. Although HIV/HCV coinfection is not uncommon, the prevalence rates vary significantly across different studies and regions. In Taiwan, injection drug users have become the major contributors to the HIV/AIDS epidemic since 2005. Because the prevalence of HCV infection is high in injection drug users, this HIV epidemic is also associated with a significant increase of HIV/HCV coinfection in Taiwan. To control Taiwan's HIV epidemic, Taiwan Centers for Disease Control (CDC) launched a harm-reduction program in 2006. The HIV epidemic, the percentage attributed to injection drug users, and the prevalence of HIV/HCV coinfection gradually declined thereafter. In this article, we aimed to thoroughly examine the current literatures of HIV/HCV coinfection in Taiwan and hope to provide a better understanding of the needs for the management of this coinfection. We conducted a narrative review and searched for literature from PubMed, Ovid MEDLINE, and the Cochrane Library database untill August 2015. Studies relevant to the epidemiology and associated risk factors of HIV/HCV coinfection in Taiwan were examined and discussed. **(AIDS Rev. 2016;18:193-7)**

Corresponding author: Jia-Horng Kao, kaojh@ntu.edu.tw

Key words

HIV infection. Hepatitis C. Coinfection. Epidemic. Taiwan.

Background

Under the widely available care, support, and antiretroviral treatment for patients with HIV infection globally, HIV-infected patients may now live longer than ever. However, this increase in lifespan in HIV-infected patients is also associated with an increased risk of opportunistic infections and other related illnesses that may jeopardize their health. Particularly, as HCV and HIV share common transmission routes, coinfection of HCV and HIV is not uncommon and has become a growing threat in patients with HIV infection.

Taiwan has one of the highest HCV prevalence rates in East Asia. Although Taiwan's national reporting system has not reported the statistics of HCV infection in the literature, several screening programs funded by individual sponsors reported an estimated prevalence of HCV infection with a range of 2.9-17.0% in Taiwan[1]. On the other hand, according to the data extracted from the national reporting system of Taiwan Centers for Disease Control (CDC), the national reported cases of HIV/AIDS is 30,422 on 2015-5-15. Because injection drug

Correspondence to:
Jia-Horng Kao
Graduate Institute of Clinical Medicine
National Taiwan University College of Medicine
7 Chung-Shan South Road
Taipei 10002, Taiwan
E-mail: kaojh@ntu.edu.tw

users (IDU) have become the major contributor to the HIV/AIDS epidemic in Taiwan since 2005, and the prevalence of HCV infection is high in IDUs, Taiwan's HIV epidemic also contributed to a high HIV/HCV coinfection prevalence. Fortunately, the Taiwan CDC launched a harm-reduction program that included syringe exchange services, methadone clinics, and methadone therapy to control Taiwan's HIV epidemic since 2006. Therefore, Taiwan's HIV epidemic as well as the percentage attributed to IDUs has gradually declined in recent years.

Of note, although Taiwan's HIV/HCV coinfection prevalence is estimated to be high, no official report for the statistics of HIV/HCV coinfection exists. Moreover, even fewer studies examined the epidemiology of Taiwan's HIV/HCV coinfection, and no published studies addressed the management as well as treatment of this coinfection. Therefore, thoroughly examining the current literature of HIV/HCV coinfection in Taiwan may provide a better understanding of the needs for the management of this coinfection. To this end, we conducted a narrative review and searched for literatures from PubMed, Ovid MEDLINE, and the Cochrane Library database up to August 2015. Studies relevant to the epidemiology and associated risk factors of HIV/HCV coinfection in Taiwan were examined and further discussed.

Methods

Data sources and searches

We performed computer-based searches of the PubMed, Ovid MEDLINE, and the Cochrane Library database for articles between January 1947 and August 2015. We searched by using the combinations of following terms: "Hepatitis C", "HCV", "chronic hepatitis C", "human immunodeficiency virus", "HIV" and "Taiwan" in the title or abstract fields or key words. We screened each abstract resulting from these searches for eligibility. We also examined reference lists of each selected original article that might meet our eligibility requirements.

Study selection

Because there was no literature addressing the management or treatment of HIV/HCV coinfection in Taiwan, we included papers on epidemiology of patients with HCV and HIV coinfection. Outcomes were incidence, prevalence, and risk factors of HIV/HCV coinfection.

We restricted the inclusion to English-language articles, and excluded: (i) review articles, (ii) editorials; (iii) letters to the editor (iv) research protocols; (v) duplicated records.

Data abstraction

The following data were extracted from each report: year and type of publication (original article or conference abstract); number and characteristics of the study population (age, gender, characteristics, and transmission route, including incarcerated, sexual behavior, or drug injection); epidemiological parameters (prevalence, incidence of coinfection); and risk factors of coinfection.

Results

The flow chart of the narrative review is shown in figure 1. Our initial search yielded 179 articles. Ultimately, 21 articles were chosen for review, including 21 investigating the prevalence of HIV/HCV coinfection, and 11 examining the risk factors of HIV/HCV coinfection in Taiwan.

Prevalence and incidence of HIV/HCV coinfection in Taiwan

A few studies reported the prevalence of HCV infection among different populations with HIV infection in Taiwan[2-4] (Supplementary Table 1).

Although HIV and HCV may transmit through parenteral, sexual, and vertical exposure, the transmission efficiency differs among these routes. Therefore, the prevalence of HIV/HCV coinfection varies in populations with different transmission routes. In Taiwan, after an extensive outbreak of HIV infection occurred among IDUs in 2004, injection drug use has become the most frequent risk factor for incident HIV infection, from 1.7% in 2002, to 41.3% in 2004, and 68.6% in 2006[5].

Except for one report that enrolled patients from the Taipei methadone maintenance treatment program (MMTP)[6], the reported prevalence of HIV/HCV coinfection among HIV-infected IDUs was high (65.5-100%)[7-11], compatible with western reports[12,13]. It increased from 65.5% before 2002 to 98.6% in 2006[8]. The increase in prevalence was compatible with the rapid increase of newly reported HIV-positive cases from 860 to 3,381, and the markedly increased percentage attributed to IDUs from 2.1 to 72.4% during the period between 2003 and 2005[14].

The reported prevalence of HIV/HCV coinfection among other HIV-infected populations in Taiwan was as follows: 13% in HIV-infected adolescents[15], 5.3-10.9% among adults with sexually transmitted HIV infection[16,17] (compatible with western reports[18]), 39.1% in patients with isolated anti-HBc[19], and 23.5-100% among heroin users[20-23].

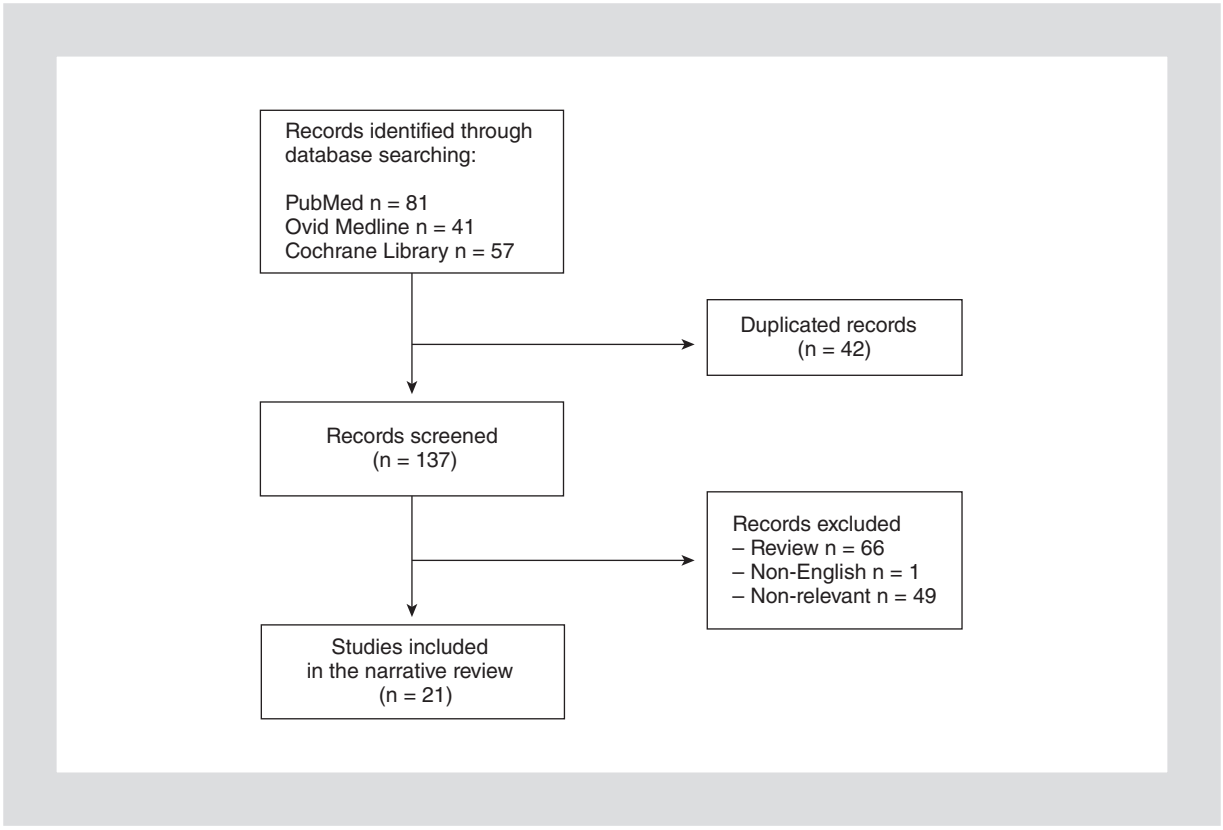

Figure 1. *Summary of evidence search and selection.*

Notably, Sun, et al. examined the incidence of HIV/HCV coinfection in a cohort with HIV infection that included 892 HIV-infected patients (731 men who have sex with men [MSM] and 161 heterosexuals] who were not IDUs and with a total follow-up duration of 4,270 person-years (PY). Among these HIV-infected patients, 30 (3.36%) had HCV seroconversion, with an overall incidence rate of 7.03 per 1,000 PY. The rate increased from 0 in 1994-2000 and 2.29 in 2001-2005 to 10.13 per 1,000 PY in 2006-2010 ($p < 0.05$)[24].

Risk factors of HIV/HCV coinfection in Taiwan

A few studies examined the risk factors of HIV/HCV coinfection in Taiwan. Older age, injection drug use[25], higher aminotransferase levels, CD4 ≥ 200 cells/μl, and recent syphilis[24] were associated with a higher risk of HIV/HCV coinfection in Taiwan. A longer duration of injection drug use ≥ 3.0 years and a travel history to China or Southeast Asia were significantly associated with infection of HCV genotypes 1a, 3, and 6[8]. Among patients from the MMTP, syringe sharing within six months before MMTP enrollment (adjusted odds ratio [AOR]: 27.72; 95% confidence interval [CI]: 13.30-57.76), number of MMTP enrollments (AOR: 2.28; 95% CI: 1.33-3.90) or incarceration (AOR: 2.01, 95% CI: 1.71-2.37) were positively associated with HIV/HCV coinfection, whereas smoking amphetamine within six months before MMTP enrollment was inversely associated with HIV/HCV coinfection (AOR: 0.44; 95% CI: 0.25-0.76)[6]. In addition, MMTP patients with HIV/HCV coinfection had a higher plasma level of IP-10 and tumor necrosis factor-α than those with HCV infection only, or those without any infection[20]. Of note, among IDUs positive for anti-HCV, HCV viremia (detectable serum HCV RNA level) after HCV exposure was strongly associated with HIV infection (OR: 6.262; 95% CI: 1.515-18.28), but negatively associated with HBsAg seropositivity (OR: 0.161; 95% CI: 0.082-0.317)[10].

HCV genotype of HIV/HCV coinfection in Taiwan

Among 990 HIV-infected IDUs recruited from four hospitals, the main circulating HCV genotypes were 1a (accounting for 29.2% of samples), 6a (23.5%), and 3a (20.2%), whereas 1b, the most predominant genotype

circulating in the general population in Taiwan, accounted for only 13.2% of samples[8]. Another study examining 180 blood samples of IDU with HIV-1 infection from prisons or detention centers, 80% of them had a single infection, 12% had double infections, and two had triple infections. Among those with single infection, HCV genotype 1b was the most common subtype (24%). Phylogenetic analyses found that the distribution of HCV genotypes among IDUs was distinct from those of the general population, and seemed originated geographically in association with the transmission of IDUs and HIV infection in Taiwan[8,9]. For example, the HCV genotype 3a, 6a, and 6n strains were clustered with strains present in Thailand and China[9].

Antiretroviral therapy and HIV/HCV coinfection

In a retrospective study, 215 patients with HIV/HCV coinfection (71 HAART experienced) were analyzed, and the overall prevalence rate of transaminase elevation, defined as aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ≥ 1.25 times the upper limits of normal (ULN) in patients with normal plasma transaminase at baseline, or ≥ 1.25-fold increase from baseline in patients with abnormal plasma transaminase at baseline was 16%, and the incidence was 1.38 cases/100 patient-months. Patients who initiated HAART during the study period or had CD4 cell count < 350 cells/mm^3 had a higher likelihood of transaminase elevation. In addition, the subgroup analysis showed that HAART might improve liver fibrosis status in patients who had advanced liver fibrosis at baseline ($p = 0.033$)[26].

Another study on 786 HIV-infected patients who received HIV care at a referral hospital from 1999 to 2006 found that IDUs who were HCV-seropositive and infected with CRF07_BC (a recombinant form of HIV) were associated with a lower risk for infection with antiretroviral drug resistant viruses[27].

Summary

Because Taiwan is an epidemic area for HCV infection, HIV/HCV coinfection is indeed an important public health threat. Therefore, the government has to enhance the general awareness and provide effective solutions. However, existing data on the extent of HIV/HCV coinfection and practical methods to manage this coinfection in Taiwan remain scarce.

After an extensive outbreak of HIV infection among IDUs in 2004, IDUs remain a major contributor to HIV/HCV coinfection in Taiwan. Although the percentage attributed to IDUs for incident HIV infection has declined since the harm-reduction program in 2006, according to Taiwan CDC's update report on July 2, 2015, IDUs are ranked as the second exposure (22.97%) in HIV infection. Therefore, IDUs are still an important attributor of HIV/HCV coinfection in Taiwan.

Notably, according to the press release from AIDS Virtual Museum of Taiwan CDC on Dec 1, 2010, the proportion of HIV-infected youth aged 15-24 years was increasing from 14% (272 cases) in 2007 to 20% (351 cases) in 2008, and 28% (413 cases) in 2009, and most (90%) of them acquired HIV infection through sexual behavior, especially high-risk sexual behavior[15,28]. Therefore, high-risk sexual behavior among youth may create a potential epidemic of HIV and other sexually transmitted diseases, such as HCV infection, in Taiwan. Therefore, although the sexual route is less efficient than parenteral route, considering the increasing number of HIV-infected youth in Taiwan and their high-risk sexual behavior, sexual transmission will become the major transmission route of HIV/HCV coinfection in Taiwan in the near future, which needs much attention from experts and health authorities.

Because Taiwan is also hyperendemic for HBV infection, several studies have examined the effect of HBV on HIV/HCV-coinfected patients[10,11,19]. Although HIV/HCV-coinfected IDUs are more likely to transmit HCV, and HCV viremia after HCV exposure was strongly related to HIV infection (OR: 6.262; 95% CI: 1.515-18.28), HCV viremia was negatively correlated to HBsAg seropositivity (OR: 0.161; 95% CI: 0.082-0.317)[10]. This fact suggests an inhibitory effect of HBV on HCV transmission in HIV-infected patients; however, further studies are required to address this important and interesting issue.

Unresolved issues and unmet needs in Taiwan

- In Taiwan, some studies have examined the antiretroviral treatment for HIV in coinfected patients, but there remains no published study addressing the antiviral treatment of HCV for coinfected patients. Our unpublished data revealed satisfactory sustained viral response rates (83% for acute and 72% for chronic HCV infection) in HIV-infected Taiwanese patients receiving peginterferon plus ribavirin therapy. Future studies to improve the understanding of natural history, indications of treatment, and treatment outcomes of patients with HIV/HCV coinfection, particular those who already received direct-acting antiviral agents for HCV infection are urgently needed.

- Development and assessment of non-invasive markers for the evaluation of natural history, the severity of liver disease, for the follow-up of treated and untreated HIV/HCV-coinfected patients, and prediction of therapeutic responses.
- Assessment of the efficacy, long-term safety, and resistance to antiviral agents (such as direct-acting antiviral agents) for HCV infection in Taiwanese patients with HIV/HCV coinfection.
- Assessment of long-term impact of therapy on the prevention of liver disease progression, cirrhosis and its complications, as well as hepatocellular carcinoma in patients with HIV/HCV coinfection.
- Development of strategies for the prevention of HCV coinfection in HIV-infected patients with different risk factors (transmission routes).
- Development of effective and optimized treatment for HCV/HIV coinfection.

Supplementary Data

Supplementary data is available at AIDS Reviews journal online (http://www.aidsreviews.com).

This data is provided by the author and published online to benefit the reader. The contents of all supplementary data are the sole responsibility of the authors.

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Declaration of interest

Ching-Sheng Hsu stated nothing to declare. Jia-Horng Kao: Consultant for Bristol-Myers Squibb, Gilead Sciences, and Novartis; on speaker's bureau for Roche, Bristol-Myers Squibb, Gilead Sciences, Merck Sharp & Dohme, and Novartis.

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