

HCV and HIV prevalences strongly correlated in Asian communities with reservoirs of HIV in high-risk groups

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Abstract

Background: In some Asian communities, HIV epidemics initially concentrated in high-risk groups develop into generalized epidemics, while in others HIV epidemics remain confined to high-risk groups. We examined whether blood exposures in a community, as indicated by hepatitis C virus (HCV) prevalence, can account for the variability in HIV prevalence in Asia.

Methodology: We searched the published literature for temporally comparable HCV and HIV prevalence estimates for pregnant women and other “low-risk” population segments in Asian communities with established HIV epidemics in injection drug users or prostitute women. We assessed the correlation between HCV and HIV prevalences in these communities.

Results: HCV and HIV prevalences were strongly correlated ($r = .97$, $p < .001$).

Conclusion: This finding suggests that blood-borne transmission drives generalized HIV epidemics in Asia and highlights the need for appropriately designed investigations of transmission modes.

Key words: hepatitis C virus (HCV), human immunodeficiency virus (HIV), prevalence, iatrogenic disease

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Introduction

Asian countries vary considerably in the scope and intensity of their HIV epidemics [1]. Despite decades of epidemiologic research on HIV transmission, it remains unclear whether a concentrated epidemic in high-risk groups, such as injection drug users (IDUs) or prostitute women, develops into a generalized epidemic affecting a significant share of the general population. Growing evidence, though, suggests that iatrogenic transmission may be an important component of HIV epidemics in much of Asia and Africa [2-4].

In Asia and throughout the world, hepatitis C virus (HCV) is transmitted primarily, if not overwhelmingly, by blood-to-blood contact [5-6]. Several investigators have proposed that if HIV and HCV share primary modes of transmission, then the two pathogens should have similar epidemiologic profiles and distributions [7-8]. HCV prevalence in the general population can indicate the extent of blood exposures in formal and informal health care, cosmetic care, rituals, and other contexts in a community.

We investigated the relationship between HCV and HIV prevalences for communities in Asia. We focused our analysis on communities in which HIV had been established in high-risk groups because it is meaningful to study factors related to the spread of an infectious disease only in those settings with a reservoir of infection [9].

Materials and methods

Literature search and inclusion criteria

We searched for relevant estimates of HCV and HIV prevalences in Asian communities in the scientific literature as indexed by PubMed, Google, and the regional indexes of Global Index Medicus that cover Asia (EMRO, SEARO, and WPRO, including the country-specific indexes for Indonesia [IMID], Myanmar [IMMM], Nepal [IMNP], and Thailand [IMTH]). In October 2008, we searched each resource with the following keyword combinations: 1) “HCV” (or “hepatitis C”) and [country name], and 2) “HIV” x [country name] for each country in Asia. We also conducted a search in Google Scholar with the same key words restricted to publications in 2007 and 2008. We reviewed all

records obtained in PubMed, Global Index Medicus, and at least the first 200 records returned by each Google and Google Scholar search, and then inspected relevant publications. In addition, we consulted relevant publications cited in publications identified in these searches.

We included communities in our analysis if several criteria were met. First, the necessary information in the source had to be reported in English.

Second, the community must have had an established HIV epidemic ($> 10\%$ prevalence) in a high-risk group (e.g. IDUs or prostitute women) conventionally thought to be a reservoir of infection that could spread into the general population.

Third, for a community to be included, there had to be prevalence estimates for HCV and HIV in unselected samples of the general population that were unlikely to include many IDUs, prostitute women, or men who have sex with men. Such unselected samples included pregnant women receiving antenatal care, women receiving family planning services, post-secondary students, healthy persons receiving routine medical checks, and household probability samples of community members. Samples from pregnant women receiving antenatal care, in particular, provide the least biased samples because men who have sex with men are excluded by definition, prostitute women would presumably be very uncommon in such samples, and females comprise very small fractions of IDUs in Asia (0-14% of IDUs in the areas included in our analysis were female [10-15]). We excluded prevalence estimates for samples that were likely to include a disproportionate number of IDUs (e.g. commercial or replacement blood donors), from persons seeking HIV testing because of self-perceived risk (e.g. voluntary blood donors in settings with limited free HIV testing), or from ill persons (e.g. medical patients seen for reasons other than routine screening/checkups).

Fourth, the HCV and HIV prevalence estimates must have been based on serological or nucleic acid assays. For both HCV and HIV, these assays were typically enzyme immunoassays. In many studies, positive HIV results were confirmed with a second enzyme immunoassay, particle agglutination test, or Western blot.

Fifth, the HCV and HIV prevalence estimates had to correspond to time points within ten years of each other. When multiple HIV prevalence estimates were available, we used the most recent data that

satisfied this criterion. HCV prevalence is likely to be fairly stable over periods of several years (barring dramatic changes in the underlying risk environment) because HCV-related mortality typically occurs decades after onset of infection [16-17]. When estimates for HCV and HIV prevalences were available for the same sample, we used both estimates for maximal comparability. Finally, the HIV prevalence estimate in the high-risk group had to be contemporaneous or prior to the HIV prevalence estimate for the general population.

Statistical analysis

We computed the Pearson correlation and simple bivariate linear regression between HCV and HIV prevalences in the communities identified in our literature search and displayed the relationship graphically with a scatter plot.

Results

We identified 12 communities that met our criteria, including New Delhi, India; Kathmandu, Nepal; Muse, Myanmar; Kawthaung, Myanmar; Pathumthan province, Thailand; Bangkok, Thailand; Central region, Thailand; seven provinces (four in Central region), Thailand; Takeo province, Cambodia; Thai Binh province, Vietnam; Ho Chi Minh City, Vietnam; and Bali, Indonesia (Table 1). The HCV and HIV prevalence estimates we used for each community were separated by a median of three years (range = 0-9). For these 12 communities, the HIV prevalence in high-risk groups ranged from 12% to 92%. HCV prevalence in IDUs surpassed 50% in each country represented in the analysis for which estimates were available [13,18-19].

Figure 1 shows the scatter plot between HCV and HIV prevalence in these communities. The relationship is strongly positive ($r = 0.97$, $p < .001$) and linear, indicating that communities with high HCV prevalence also have high HIV prevalence in the general population. The correlation remains robust after removing the extreme observation of Muse ($r = .83$, $p < .01$). The simple linear regression formula for the 12 communities is HIV prevalence (%) = $0.32 + 0.45$ HCV prevalence (%).

Discussion

HCV and HIV prevalences are very strongly correlated in the general populations of Asian communities with reservoirs of HIV infection in injection drug users or prostitute women. In sub-

Table 1. HCV and HIV prevalence estimates in 12 Asian communities

Community	HCV in general population			HIV in general population			HIV in high-risk groups		
	Sample ^a	Year	Estimate	Sample ^a	Year	Estimate	Group ^a	Year	Estimate
New Delhi, India	ANC, n=8,130 ³⁰	2004-2006	1.03%	ANC, n=3,529 ⁴¹	2003-2006	0.88%	IDU, n=246 ⁴²	2003 ^b	37.0%
Kathmandu, Nepal	ANC, n=81 ¹³	1994-1996	0.0%	FP, n=300 ⁴³	1999	0.3%	IDU, synthesis ⁴⁴	1998-2003	40.0-80.0%
Muse, Myanmar	CS all ages, n=349 ⁴⁵	2004-2006	13.5%	ANC, n=200 ⁴⁶	1999	6.5%	IDU, n=26 ⁴⁶	1999	92.4%
Kawthaung, Myanmar	CS all ages, n=380 ⁴⁵	2004-2006	4.2%	ANC, n=200 ⁴⁶	1999	2.0%	IDU	1999-2000 ^c	13-92% ^c
Pathumthani province, Thailand	ANC, n=530 ³²	2002-2003	1.3%	ANC ⁴⁷	2004	1.6%	IDU ⁴⁸	1990-2001	19.2%-29.4%
Bangkok, Thailand	NS, n=234 ⁴⁹	1994	0.0%	NS, n=234 ⁴⁹	1994	0.0%	IDU ⁴⁸	1990-1994	19.8%-27.5%
Central region, Thailand	PS ages 13-25, n=415 ⁵⁰	2000-2002	0.7%	ANC, n=18,304 ⁵¹	2004	1.3%	IDU, n=757 ⁵¹	2004	39.0%
Selected provinces, Thailand	PS, married women age < 45, n=84 ⁵²	2002-2004	1.2%	PS, married women age < 45, n=84 ⁵²	2002-2004	1.2%	IDU, national synthesis ⁴⁴	1998-2003	20.0-56.0%
Takeo province, Cambodia	ANC, n=154 ²⁶	1990-1991	3.9%	ANC, n=590 ⁵³ + PS women age 15-49, n=603 ^{53, 54}	1999-2000	1.6%	Pro, n=158 ⁵⁴	2000	11.5-19.4%
Thai Binh province, Vietnam	PS, women age 16-39, n=195 ³¹	2002	0.0%	PS, women age 15-49, n=1,701 ⁵⁵	2005	0.06%	IDU	2001 ^d	23-72% ^d
Ho Chi Minh City, Vietnam	Check-ups, n=100 ⁵⁶	1998-2001	2.0%	ANC, n=1,699 ⁵⁷	2002	0.9%	IDU, n=218 & 300 ¹⁰	1997-1998	38.5-44.0%
Bali, Indonesia	ANC, n=2,450 ⁵⁸	2003	0.04%	ANC, n=2,450 ⁵⁸	2003	0.0%	IDU	2001 ^e	56% ^e

Note: Numbers in superscript indicate reference numbers.

^aANC = pregnant women receiving antenatal care; Check-ups = healthy persons (no clinical symptoms or abnormal laboratory test results) seen for medical check-ups; CS = community sample of apparently health adults; FP = women receiving family planning services; IDU = injection drug users; NS = nursing students; Pro = prostitute women; PS = probability sample of community.

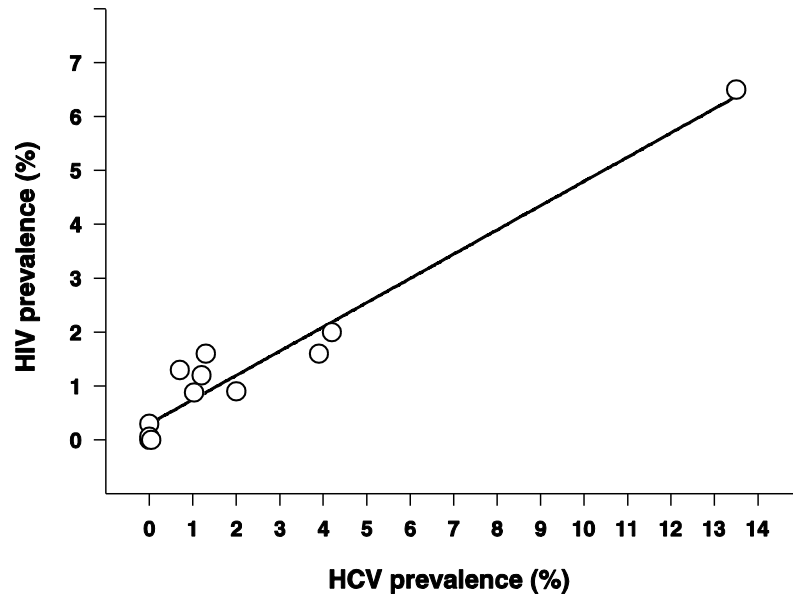
^bEstimate published in 2003.

^cNo published estimate of HIV prevalence in Kawthaung IDUs is available; however, in 1999-2000, the HIV prevalence in IDUs ranged between 13% and 92% in the communities surrounding Kawthaung in Myanmar⁴⁶ and Thailand.⁵⁹

^dNo published estimate of HIV prevalence in IDUs in Thai Binh province is available; however, Thai Binh residents are noted for their temporary labor migration⁵⁵, and in 2001, the HIV prevalence in IDUs ranged between 23% and 72% in provinces adjacent to Thai Binh.⁶⁰

^eThe only published estimate is for imprisoned IDUs in Bali (56%)⁶¹; other sources^{11, 62} note epidemic transmission.

Figure 1. Relationship between HCV and HIV prevalences in 12 Asian communities (circles represent communities, shown with regression line)



Saharan Africa, HCV and HIV prevalences are also positively, but more weakly, correlated ($r = .20$, $n = 62$ studies) [20]. Furthermore, at the individual level, there is a strong tendency toward HCV-HIV co-infection among women who are not IDUs in some Asian communities, including wives of HIV seropositive IDUs in Manipur, India (OR = 5.2) [21] and prostitute women in Yunnan Province, China (OR = 27.8) [22]. The tendency towards HCV-HIV co-infection is more moderate in sub-Saharan Africa (median OR = 1.52, IQR = 0.99-6.12, $n = 25$ studies) [20]. A strong association between HCV and HIV infection might not be expected in sub-Saharan Africa because of the insensitive HCV tests and other potential measurement problems in the African studies [20]. Given that blood-to-blood contact is the overwhelmingly dominant means of HCV transmission worldwide, the very strong ecologic correlation between HCV and HIV prevalences in Asia suggests that blood exposures may contribute significantly to HIV transmission in Asia.

In the 12 communities that we analyzed, HCV prevalence tended to be higher than HIV prevalence. This observation could be due to the longer history of endemic HCV infection in Asia [23-24] or greater premature mortality in HIV infected persons, each of which could cause HIV prevalence to be lower than HCV prevalence. Also, the infection with greater prevalence in a community tended to be the one that

had been measured more recently; HCV and HIV prevalences in a community tended to be similar when measured in the same year. It is not likely that the difference in HCV and HIV prevalences is due to dramatically different transmission efficiencies of the viruses because occupational transmission studies indicate similar transmission probabilities for HCV and HIV through blood exposures [25].

It is unlikely that HCV transmission in Asia is due to singular mass exposure events, such as vaccination or treatment campaigns focused on a single disease. Rather, diverse blood exposures are associated with HCV infection in several of the countries represented in our analysis [26-33]. In many parts of Asia, unsterile injections [34] and perhaps other unhygienic invasive procedures are particularly common, suggesting widespread risk for HCV and HIV transmission; therefore, coordinated interventions to ensure safe health care and cosmetic care are urgently needed in Asia to prevent the spread of blood-borne pathogens.

The positive association between HCV and HIV prevalences in Asia and sub-Saharan Africa contrasts markedly with the inverse cross-sectional and longitudinal relationship between sexually transmitted infection and HIV prevalences in sub-Saharan Africa [35-38]. These combined results are inconsistent with the notion that sexual exposures account for nearly all and that blood exposures

account for hardly any HIV transmission in the general populations of Asia and Africa.

The concentrated HIV epidemics in IDUs and prostitute women in the 12 communities we analyzed began between the late 1980s and late 1990s. Concentrated epidemics have developed more recently in other Asian communities. Our results suggest that communities with high HCV prevalence and recently established concentrated HIV epidemics may be at the greatest risk for generalized HIV epidemics. This prediction rests on the assumption that the association we observed between HCV and HIV prevalences describes the ultimate trajectory of HIV spread into the general population in Asia. Of course, infection control measures in health care and cosmetic care settings could improve substantially in such communities over the next several years, and thus decouple HCV prevalence from HIV prevalence.

Prevalence data were available for relatively few Asian communities, and some prevalence estimates, especially for HCV, were based on small samples and had correspondingly wide uncertainties. Nonetheless, the communities included in this analysis represent seven countries and the positive correlation we observed is strong, linear, and statistically reliable.

Ecologic analyses such as ours cannot provide decisive evidence of the forces underlying epidemic HIV transmission in Asia and sub-Saharan Africa. Our findings, along with prior research [2], however, should prompt investigations that could yield definitive data on the key modes of transmission. Such studies would involve comprehensive assessment of blood and sexual exposures in incident HIV cases and controls, tracing of their corresponding contacts, and DNA sequencing of infected persons' HIV isolates [39-40].

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