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Prevalence and Disease Burden of HCV Coinfection in HIV Cohorts in the Asia Pacific Region: A Systematic Review and Meta-Analysis

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Abstract

Background: ***Estimates of the prevalence and disease burden of HIV/HCV coinfection in the Asia Pacific Region are uncertain.*** **Methods:** ***A systematic review of indexed (PubMed, Embase and Web of Science) and non-indexed cross-sectional and cohort studies (2009-2015) reporting HCV seroprevalence in HIV-positive adults living in the Asia Pacific region was performed. Pooled prevalence estimates were calculated with a DerSimonian-Laird random-effects model.*** **Results:** ***39 studies from 10 countries in the Asia Pacific region comprising 89,452 HIV-positive individuals were included. In the high-income Asia Pacific region, HCV coinfection prevalence was 3.8% (95% confidence interval (CI): 3.1-4.5) in Singapore. In East Asia, HCV coinfection prevalence was 8.0% (95% CI: 6.4-9.8) in Hong Kong and 25.5% (95% CI: 17.5-34.4) in general HIV cohorts in China. In South Asia, HCV coinfection prevalence was 4.1% (95% CI: 1.7-7.3) in India and 42.6% (95% CI: 38.7-46.5) in Nepal. In Southeast Asia, HCV coinfection prevalence was 5.5% (95% CI: 4.9-6.1) in Cambodia, 5.3% (95% CI: 4.9-5.7) in Myanmar, and 5.1% (95% CI: 2.7-8.2) in Thailand, but higher in Vietnam (42.5%; 95% CI: 40.8-44.2) and Indonesia (17.9%; 95% CI: 15.0-20.9). The prevalence of HCV coinfection was higher in subpopulations of people who inject drugs (China 81.6%; 95% CI: 74.1-88.0; Nepal 80.8%; 95% CI: 76.4-84.9; Indonesia 81.6%; 95% CI: 71.1-90.3), former blood donors (China 82.9%; 95% CI: 73.9-90.3), and blood transfusion recipients (China 51.0%; 95% CI: 41.7-60.2).*** **Conclusion:** ***HCV coinfection prevalence within HIV populations is highly variable in the Asia Pacific region, between countries and at-risk populations. Enhanced epidemiological data is required to support scale-up of interferon-free HCV therapy.*** **(AIDS Rev. 2016;18:69-80)**

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Key words

HIV. HCV. Coinfection. Epidemiology. Prevalence. Asia.

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Introduction

Infection with HIV and HCV contributes substantially to the global burden of disease, with anti-HCV antibody prevalence estimated at 1.6-2.8%[1,2] and HIV antibody prevalence at 0.8%[3]. Recent estimates suggest that 115 (92-149) million people have been infected with HCV, as evidenced by detectable anti-HCV antibody, while 80 (64-103) million people have HCV viremic infections[2], as compared with an estimated 29.2-35.3 million people living with HIV[3,4]. Based on global HIV and HCV prevalence and estimates of the overlap in these epidemics, 4-5 million people are estimated to be coinfected with HIV and HCV[5], though high-quality epidemiological data is lacking in many settings. In high and upper-middle income countries, 20-25% of people living with HIV are estimated to be coinfected with HCV with somewhat lower estimates in lower-middle (15%) and low (10%) income countries[6].

The natural history of HIV and HCV is significantly impacted by the coexistence of the other virus. Increases in all-cause, AIDS-related, and liver-related morbidity, hospitalization, and mortality are noted, with accelerated liver disease progression and high rates of end-stage liver disease, even in those receiving combination antiretroviral therapy (cART)[7-10]. Given greater access to cART, the number of global deaths related to HIV is falling (2005: 2.3 million deaths; 2012: 1.6 million deaths)[3]. In contrast, the number of HCV-related liver deaths is rising (2010: 500,000 deaths; 2013: 700,000 deaths)[11,12].

No clear estimates exist for the prevalence of HIV/HCV coinfection in the Asia Pacific region. Collectively, the region is home to the largest number of people with HCV[1,2] (Table 1), with China, India, and Pakistan having the largest adult viremic populations in the world (China: 8.8 million; India: 6.0 million; Pakistan: 7.0 million)[2]. Genotype (GT) distribution varies by country and region, with GT1 being common in Australia, China, Taiwan, and other countries in North Asia, while GT6 is found in Vietnam and other Southeast Asian countries. In India and Pakistan, GT3 predominates. Concurrently, 4.9 million (3.7-6.3) people were estimated to be living with HIV in the Asia Pacific region in 2012[13]. While overall HIV prevalence remains low in most countries, certain populations are disproportionately affected, with expanding epidemics concentrated among people who inject drugs (PWID), commercial sex workers (CSW) and their clients, men who have sex with men (MSM), and transgender people[13]. Given shared

Table 1. HCV prevalence by Global Burden of Disease region

GBD region	Countries	2013			
		Total population (millions)	HCV antibody prevalence	No. of persons with HCV antibody (millions)	Viremic prevalence (millions)
High-income Asia Pacific	Brunei, Japan, South Korea, Singapore	182	1.1% (0.5-1.7)	2.0 (0.9-3.0)	1.5 (0.6, 2.2)
Central Asia	Armenia, Azerbaijan, Georgia, Kazakhstan, Kyrgyzstan, Mongolia, Tajikistan, Turkmenistan, Uzbekistan	84	5.4% (3.5-6.8)	4.5 (2.9-5.7)	1.9 (1.3, 2.5)
East Asia	China, Hong Kong, Macau, North Korea, Taiwan	1,434	1.2% (0.4-1.8)	16.6 (6.3-25.3)	10.0 (3.9, 15.1)
South Asia	Afghanistan, Bangladesh, Bhutan, India, Nepal, Pakistan	1,650	1.1% (0.7-1.5)	18.8 (11.3-24.5)	15.2 (8.9, 19.8)
Southeast Asia	Cocos Islands, Christmas Island, Indonesia, Cambodia, Laos, Sri Lanka, Maldives, Myanmar, Mauritius, Malaysia, Philippines, Reunion, Seychelles, Thailand, East Timor, Vietnam	635	1.0% (0.8-1.8)	6.6 (5.3-11.3)	4.2 (3.4, 7.2)

95% CI in brackets. GBD: Global Burden of Disease.
Adapted with permission from Gower, et al.[2].

routes of transmission, this has important implications for the regional coinfection burden.

This systematic review and meta-analysis will examine the prevalence and disease burden of HIV/HCV coinfection in adults in the Asia Pacific region, a diverse geographical area with burgeoning epidemics in specific subpopulations, and highlight key gaps in our knowledge.

Methods

Search strategy and selection criteria

A systematic review was conducted to gather country or region-specific data on anti-HCV antibody prevalence, HCV genotype distribution, and liver disease stage in HIV-infected adults in the Asia Pacific region. Countries included in the study were limited to those in the Asia Pacific region (excluding Australasia), grouped according to Global Burden of Disease (GBD) region[4] (Table 1). The appendix provides full details of the search strategy. Indexed articles were found by searching Medline (PubMed), EMBASE (Ovid) and Web of Science on 18 March 2015 for articles published in English after 1 January 2009 using the following terms: (hepatitis C OR HCV) and (human immunodeficiency virus OR HIV) and (Asia OR [country name]) and (epidemiology OR prevalence OR disease burden). A total of 669 titles, abstracts, and full texts were screened and reviewed for relevance (MEDLINE 394, Embase 136, Web of Science 139; duplicates 278). Additional studies were identified through manual searches of references noted in the publications. Non-indexed sources were identified through searches of Google Scholar (with the same search terms), international health agency reports, and abstracts from key international conferences.

Cohort and cross-sectional studies were included for quantitative analysis if the study population was recruited as an HIV-positive cohort and reported anti-HCV antibody prevalence (Fig. 1). Study populations including less than 50 individuals were excluded (n = 17). No study was discounted on the basis of HCV diagnostic assay; this review includes studies using both non-confirmatory (ELISA, EIA, screening assays) and confirmatory (RIBA, western blots, PCR) assays. The following data were extracted by one author (Marianne Martinello) from full articles or abstracts: study period, study design, studied population (including proportions of PWID, MSM, former blood donors [FBD] or blood product recipients, and CSW), region studied, analysis scope (urban, rural, both or unknown), region/s studied (one hospital/clinic, multiple hospitals/clinics, city, multiple cities, region, multiple regions, national, other, or unknown) and anti-HCV antibody prevalence. Demographic details, HCV genotype and HCV viremic proportion or prevalence were recorded if available.

Cohort classification

For HCV coinfection prevalence estimates, cross-sectional and cohort studies reporting anti-HCV antibody status in HIV-positive adults (age > 15 years) in the Asia Pacific region were included. Cohorts for analysis were divided based on geographic (country or GBD region) and enrolment characteristics. For HIV cohorts published longitudinally, the most recent publication was used for data extraction. Where possible, for general HIV cohort prevalence estimates by country, studies enrolling “high-risk groups” or specific subpopulations (i.e., PWID, FBD, etc.) were excluded. If a study included a separate subanalysis of PWID, MSM, FBD, or blood product recipients, this cohort was included as separate for the subpopulation pooled prevalence, but was not included as a separate cohort in the analysis of overall prevalence.

Statistical analysis

Point estimates and 95% confidence intervals were calculated for the proportion of people with HIV/HCV coinfection in each study. Data were pooled using a DerSimonian-Laird random effects model, which incorporates an estimate of between study variance, allowing that the true effect size could vary between studies. To assess heterogeneity and between-study variance for the estimates of pooled prevalence, the Cochrane Q, I_2 and t^2 statistics were calculated. The variance of raw proportions was stabilized with double arcsine transformation. Statistical analysis was performed with Stata (version 13.0; StataCorp, College Station, TX).

Results

The HCV seroprevalence in HIV-positive adults was reported in 39 studies (cross-sectional 56%, n = 22; cohort 44%, n = 17) comprising 89,452 individuals in 44 cohorts. Sixty-five percent (n = 29) of the cohorts included ≥ 500 individuals (with one cohort of < 100 individuals). Only 10 countries in the Asia Pacific region

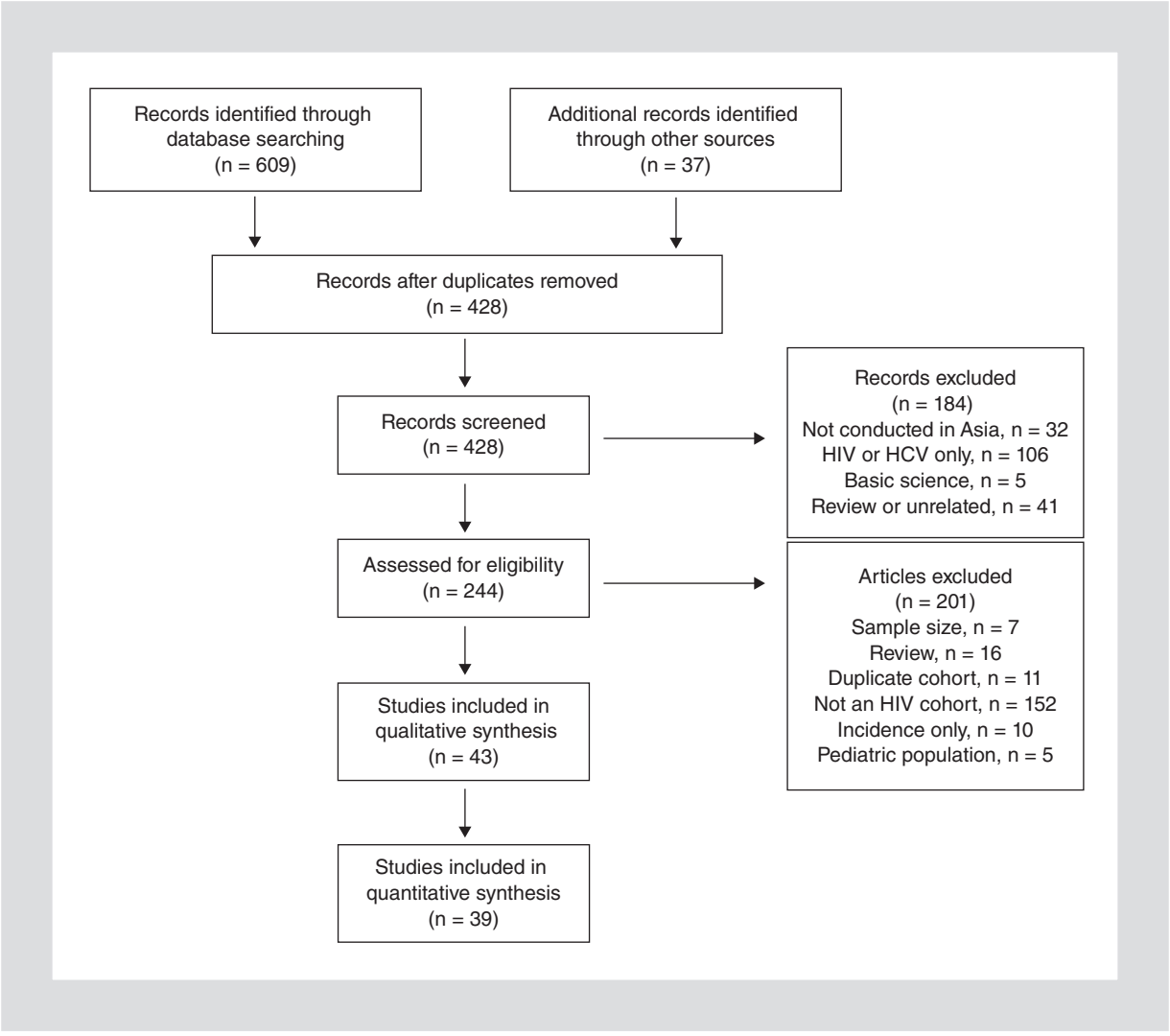

Figure 1. *Study selection.*

were included, with no studies performed in Central Asia. Study populations were predominantly male (median 70%, range 0-100) with median age 35 years (range 25-43). Cohorts were largely recruited from single hospitals or clinics (41%, n = 18) in urban settings (urban 43%, n = 19; rural 7%, n = 3; both 30%, n = 13; unknown/not stated 20%, n = 9). Three (7%) studies were performed at a national level (China, Myanmar, Thailand). Most cohorts were composed of the general HIV-positive population, while a few studies enrolled specific cohorts including people who inject or use drugs (n = 3), MSM (n = 3), FBD (n = 3), and pregnant women (n = 1). Significant inter-group heterogeneity was observed (I^2 = 99.73%, t^2 = 0.22; p < 0.001) (Table 2 and Supplementary Fig. 1). Therefore, a single overall summary estimate across the Asia Pacific region is not presented.

High-income Asia Pacific region

In the high-income Asia Pacific region, two cross-sectional studies involving 2,891 individuals were performed in Singapore. The HCV coinfection prevalence was 2.0 and 4.6%, respectively[14,15], with pooled HIV/HCV coinfection prevalence 3.8% (95% confidence interval (CI): 3.1-4.5) (Fig. 2).

East Asia

In East Asia, 18 studies involving 51,268 participants were undertaken in China (n = 17)[16-32] and Hong Kong (n = 1)[15]. In Hong Kong, HCV coinfection prevalence was 8.0% (95% CI: 6.4-9.8) (Fig. 2)[15]. In this cohort, HIV transmission was predominantly via heterosexual (45%) and homosexual (35%) contact; PWID comprised only

Table 2. HCV coinfection prevalence in HIV-positive cohorts by Global Burden of Disease region and country

GBD region	Reference	Study period	Location	Sample size (n)	Population	MSM (%)	PWID (%)	FBD or blood product recipients (%)	HCV prevalence (%)
High-income Asia Pacific	(15)	2006-2013	Singapore	2,098	HIV	33.0	3.0	< 0.1	3.8
	(14)*	2006-2011	Singapore	793	HIV	NA	NA	NA	2.02
East Asia	(15)	2003-2013	Hong Kong	981	HIV	35.0	4.0	1.0	8.0
	(19)	NA	China	498	HIV PWID	NA	100	NA	90.8
	(22)*	2012-2013	China	1887	HIV	NA	NA	NA	14.9
	(28)	2010-2012	China	33,861	HIV	10.0	22.0	1.3	18.2
	(30)	NA	China	164	HIV FBD	NA	NA	90.1	84.7
	(17)*	NA	China	513	HIV MSM	100	NA	NA	1.9
	(18)	2006-2008	China	978	HIV	NA	53.0	NA	62.4
	(23)	2001-2010	China	395	HIV	NA	33.0	2.3	24.8
	(25)	2009-2010	China	2,040	HIV	NA	13.3	3.9	14.7
	(31)	2007-2010	China	356	HIV	23.0	19.9	NA	25.8
	(16)	NA	China	1,112	HIV	2.2	5.0	16.8	26.9
	(32)	2000-2010	China	2,087	HIV	13.0	23.0	14.2	41.2
	(21)	1990-2008	China	1,110	HIV	1.2	31.8	34.8	59.0
	(26)*	NA	China	61	HIV MSM	100	NA	NA	0
	(27)	2007-2008	China	4,306	HIV	14.4	25.1	26.8	41.8
	(29)	2004-2005	China	305	HIV FBD	NA	NA	89.1	76.4
	(20)*	2008	China	149	HIV MSM	100	NA	NA	24.2
	(24)	NA	China	465	HIV (high-risk groups)	NA	38.3	27.5	69.5
South Asia	(15)	1998-2013	India	2,421	HIV	NA	2.0	2.0	4.1
	(38)	2009-2011	India	120	HIV	NA	0	NA	10.8
	(39)	2002-2008	India	680	HIV	0	0	0	3.5
	(34)	NA	India	1,426	HIV	NA	NA	NA	0.2
	(35)	2005-2009	India	1,953	HIV	8.33	22.62	NA	1.7
	(36)	2006-2009	India	204	HIV	0	NA	NA	7.4
	(33)	2006-2007	India	1,178	HIV	NA	NA	NA	6.3
	(37)	2005-2008	India	1,487	HIV	NA	4.64	10.75	3.02
	(41)	2010-2011	Nepal	313	HIV	NA	65.5	0.6	42.0
	(42)	2010	Nepal	319	HIV	NA	40.8	NA	43.3

(continue)

Table 2. HCV coinfection prevalence in HIV-positive cohorts by Global Burden of Disease region and country *(continued)*

GBD region	Reference	Study period	Location	Sample size (n)	Population	MSM (%)	PWID (%)	FBD or blood product recipients (%)	HCV prevalence (%)
Southeast Asia	(15)	2004-2013	Cambodia	2,588	HIV	1.0	NA	1.0	5.5
	(43)	2003-2012	Cambodia	3,089	HIV	NA	NA	NA	5.3
	(15)†	2003-2013	Indonesia	545	HIV	6	13	0	17.9
	(52)	NA	Indonesia	187	HIV	1.1	62.6	NA	63.6
	(50)	2010	Indonesia	126	HIV	14.0	34.0	NA	38.9
	(51)	1996-2008	Indonesia	773	HIV PWUD	NA	81.9	NA	71.8
	(44)‡	2005-2012	Myanmar	11,032	HIV	1.6	3.7	3.4	5.3
	(46)	NA	Thailand	222	HIV	NA	NA	NA	7.7
	(47)	2000-2002	Thailand	700	HIV	1.0	0.7	NA	3.3
	(45)	2005-2008	Thailand	500	HIV	NA	20.0	13.33	8.4
	(48)	1997-1999	Thailand	1,435	Pregnant women	NA	0.6	2.8	2.9
	(15)	1998-2013	Vietnam	2,496	HIV	1.0	33.0	< 0.1	42.5
	(49)	2005-2011	Vietnam	724	HIV	NA	61.2	NA	41.9

*Abstract only available; †HIV/HCV prevalence refers to adults only; ‡Sample includes children.
GBD: Global Burden of Disease; PWID: people who inject drugs; FBD: former blood donors; MSM: men who have sex with men; PWUD: people who use drugs.

4% of the population[15]. In mainland China, marked heterogeneity in HIV/HCV prevalence was noted, with individual study estimates ranging between 0 to 90.8% (t^2 = 0.21). If reported, the study populations included variable proportions of PWID (0.4-100%) and FBD or blood product recipients (1.0-90.1%) contributing to the broad range of individual study estimates. In general HIV-positive cohorts[16,22,23,25,27,28,31,32], HCV coinfection prevalence ranged between 14.7-41.8%, with a pooled HCV coinfection prevalence of 25.5% (95% CI: 17.5-34.4; t^2 = 0.07) (Fig. 2). This is in keeping with a recent national cross-sectional study of HIV-positive adults on cART (HCV coinfection prevalence: 18.2%; 95% CI: 17.8-18.6)[28]. In this study, in those with HIV mono-infection, heterosexual transmission accounted for 80.1% and infecting drug use (IDU) 6.3%, in contrast to those with HIV/HCV coinfection, in whom heterosexual transmission accounted for 20.2% and IDU 75.9%[28]. In HIV-positive PWID (n = 10,389)[16,18,19,21,24,25,27,28,31,32], HCV coinfection prevalence ranged between 55.1 and 96.6%, with pooled prevalence 81.6% (95% CI: 74.1-88.0; t^2 = 0.06) (Supplementary Fig. 3). In FBD (n = 1,166)[16,21,24,28,29,32], HCV coinfection prevalence ranged between 60.0 and 93.0%, with pooled prevalence 82.9% (95% CI: 73.9-90.3; t^2 = 0.07) (Supplementary Fig. 4). In blood transfusion recipients (n = 255)[16,25,30-32], HCV coinfection prevalence ranged between 40 and 60%, with pooled prevalence 51% (95% CI: 41.7-60.2; t^2 = 0.02) (Supplementary Fig. 5). In HIV-positive MSM (n = 4,702)[17,20,26-28,31], HCV coinfection was documented in 0-24.2%, with pooled prevalence 4.0% (95% CI: 1.4-7.9%; t^2 = 0.03) (Supplementary Fig. 6).

South Asia

In South Asia, 11 studies (n = 10,876) were performed in India (n = 9)[15,33-40] and Nepal (n = 2)[41,42]. The proportion of PWID and blood product or transfusion recipients was reported in seven (range 0-65.5%) and five studies (range 0-10.8%), respectively. Marked differences were noted in HIV/HCV prevalence between countries. In India, HCV coinfection prevalence ranged between 0.2 and 10.8%, with pooled prevalence 4.1% (95% CI: 1.7-7.3; t^2 = 0.05) (Fig. 2). Heterosexual transmission predominated in these HIV cohorts, with few PWID (range 0-22.6%). In Nepal, HCV coinfection prevalence was substantially higher, with pooled prevalence 42.6% (95% CI: 38.7-46.5; t^2 = 0) (Fig. 2). The PWID accounted for significant proportions (40.8-65.5%) of the sampled Nepalese populations, with pooled HCV prevalence in HIV-positive PWID 80.8% (95% CI: 76.4-84.9; t^2 = 0) (Supplementary Fig. 3).

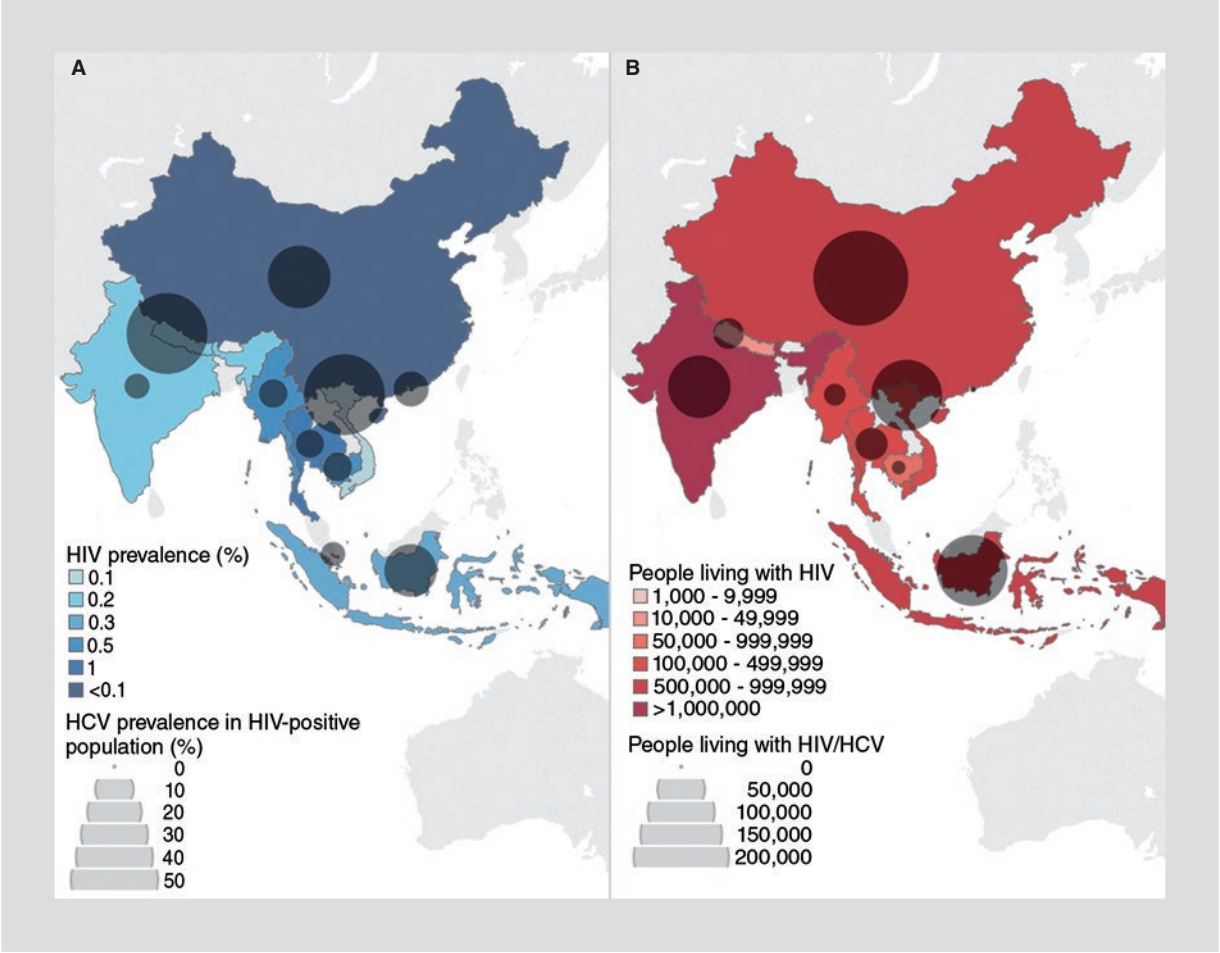

Figure 2. *Estimated HCV coinfection burden among HIV-positive adults aged 15-49 years.* ***A:*** *HCV coinfection seroprevalence in the HIV-positive adult population.* ***B:*** *Estimated number of people with HCV coinfection among the HIV-positive adult population. HIV data from WHO/UNAIDS 2013[3,13] and Ministry of Health websites[64,65].*

Southeast Asia

In Southeast Asia, 13 HIV cohorts (n = 24,417) were included from Cambodia (n = 2), Indonesia (n = 4), Myanmar (n = 1), Thailand (n = 4), and Vietnam (n = 2). The proportion of PWID and blood product recipients was reported in nine (range 0.3-81.9%) and five (range 0.05-13.3%) studies, respectively. Marked regional diversity was evident, with HCV coinfection documented in 2.9-71.8%, with the lowest HCV coinfection prevalence stemming from a cohort of pregnant women in Thailand. In Cambodia[15,43], pooled HCV coinfection prevalence was 5.5% (95% CI: 4.9-6.1; $t^2 = 0$) (Fig. 2). In Myanmar[44], HCV coinfection prevalence was 5.3% (95% CI: 4.9-5.7) (Fig. 2). In Thailand[45-48], pooled HCV coinfection prevalence was 5.1% (95% CI: 2.7-8.2; $t^2 = 0.01$) (Fig. 2). In contrast, in Vietnam[15,49] and Indonesia[15,50], pooled HCV coinfection prevalence was 42.5% (95% CI: 40.8-44.2; $t^2 = 0$) and 17.9% (95% CI: 15.0-20.9; $t^2 = 0$), respectively (Fig. 2). In HIV-positive PWID across the region, HCV coinfection ranged between 47.0 and 87.7% ($t^2 = 0.24$). In HIV-positive PWID in Indonesia[50-52], pooled coinfection prevalence was 81.6% (95% CI: 71.1-90.3; $t^2 = 0.04$), while in single studies, HCV prevalence in HIV-positive PWID was 49.4% (95% CI: 44.8-54.1) in Vietnam[49] and 47.0% (95% CI: 42.17-51.86) in Myanmar[44] (Supplementary Fig. 3).

HCV viremic prevalence and genotype distribution

Ten studies reported HCV viremic proportion or prevalence[16,19,23,30,36,37,48,50,53,54] (Supplementary Table 1). Of those who were anti-HCV-antibody positive, the pooled HCV viremic proportion was 73.5% (95% CI: 65.0-81.3; $t^2 = 0.07$) (Fig. 3).

The HCV genotype distribution in HIV/HCV coinfection was reported in nine studies[19,30,31,36,37,48,50,53,54] (Table 2). In three Chinese studies, GT1b (21.4-65.9%)

and GT2 (34.1-78.6%) clustered in FBD, and GT3 (27.8-61.9%) and GT6 (18.6-39.3%) in PWID. This compares with recent general population estimates in which GT1b (56.8%) and GT2 (24.1%) comprised the majority and GT3 (9.1%) and GT6 (6.3%) were infrequent[2]. In PWID, there was no significant difference in HCV genotype distribution between HCV monoinfection and HIV/HCV coinfection[30,31]. Two studies reported genotype distribution in India. Ponamgi, et al. identified GT1 (68.8%) and GT3 (31.1%) in a HIV-positive cohort in south India[37]. In contrast, in a cohort in Calcutta, Saha, et al. reported a predominance of GT3 (GT1 20%, GT3 80%), in keeping with the general Indian population (GT1 24%, GT3 54.4%)[2]. In Southeast Asia, a Thai cohort of HIV/HCV-coinfected pregnant women[48] and two Indonesian HIV-positive cohorts[50,52] largely paralleled their respective general population HCV genotype distributions[2]. While GT6 infection appears to be predominant in Cambodia and Vietnam[2], in the sampled HIV/HCV-coinfected populations, the majority had GT1 infection (Cambodia GT1 68%, GT6 25%, GT2 7%[54]; Vietnam GT1 43%, GT4%[53]). However, the number of HIV/HCV-coinfected individuals is small.

Risk factors for HCV coinfection in HIV-positive adults

Throughout the Asia-Pacific region, the reported mode of HIV acquisition is predominantly heterosexual transmission[15,28]. The HCV transmission risk is significantly higher among individuals who acquire HIV infection via parenteral rather than sexual exposure, with PWID representing one of the groups at highest risk of transmitting and acquiring infection[19,24,51,55]. In an Indonesian HIV-positive cohort, HIV/HCV coinfection was noted in 87.7% of PWID, with no coinfection in non-IDU[51]. Similarly, in Myanmar, the prevalence of HCV coinfection was 47.0% for PWID, 7.5% for blood transfusion recipients, 3.6% for heterosexuals, and 3.4% for MSM[44]. The HIV-positive PWID (RR 13.04; 95% CI: 11.2-15.13) and blood transfusion recipients (RR 2.09; 95% CI: 1.44-3.03) had a much higher risk of HCV coinfection in comparison with the heterosexual group[44].

In low- and middle-income countries, unsafe medical procedures contribute to the burden of disease. Goyet, et al. conducted a case-control study in Cambodia, comparing those with HIV monoinfection to those with HIV/HCV coinfection[56]. Factors associated with coinfection were exposure to multiple parenteral infusions before the year 2000 (aOR 3.4; 95% CI: 1.5-7.6), surgery (aOR 2.6; 95% CI: 1.2-5.7) and fibroscopy (aOR 2.4; 95% CI: 1.0-5.7). Similarly, in a national cross-sectional study of male military recruits in Thailand, unsafe medical injection and transfusion was reported by 10.3% and 13.3% of a pre-specified cohort of 500 HIV-positive recruits, compared with 3.6% (unsafe medical injection) and 2.4% (transfusion) in 5,246 general recruits (HIV-positive 0.4%).

Unregulated commercial blood collection among rural populations in central China during the 1990s resulted in an epidemic of HIV and HCV infection in FBD. Fortunately, this practice appears to have ceased and screening for blood-borne viruses across the Asia Pacific region has reduced transmission from blood products. Zhao, et al. examined the prevalence (HIV/HCV 41.2%) and risk factors for HCV coinfection in 2,087 HIV-positive individuals in Shandong province, China. On multivariate logistic regression, HCV coinfection was associated with FBD (aOR 3.36), blood transfusion (aOR 2.91), and PWID (aOR 1.98)[32].

Liver disease burden

Liver disease stage was assessed very infrequently and with different methodologies. Durier, et al. assessed fibrosis stage by transient elastography (FibroScan®) in 120 HIV-positive individuals in Indonesia, Malaysia, Thailand, and Vietnam[53]. Significant fibrosis (≥ F2) was reported in 67%, with cirrhosis (F4) in 20%. Only fibrosis stage, not median liver stiffness measurement, was reported. Lerolle, et al. performed FibroTest-ActiTest in 31 HIV/HCV-coinfected individuals and demonstrated a FibroTest score equivalent to F2-F4 in 68%[54]. The FibroTest score was not reported. Anggorowati, et al. calculated the AST to platelet ratio index (APRI) in a cohort of HIV-positive individuals in Indonesia[50]. Forty percent (12/77) with HIV and 60% (18/49) with HIV/HCV had an APRI > 0.5, consistent with significant fibrosis.

Discussion

The burden of disease attributable to HIV/HCV coinfection in the Asia Pacific region is significant. Given the regional diversity, the country level estimates of HCV coinfection within HIV populations are varied and do not all conform to the previous 10-15% estimate for lower-middle and low-income countries[6]. While the coinfected population may represent a small proportion of the estimated 32.8 million viremic HCV infections in the Asia Pacific region[2], accelerated HCV disease progression, together with increasing rates of IDU in

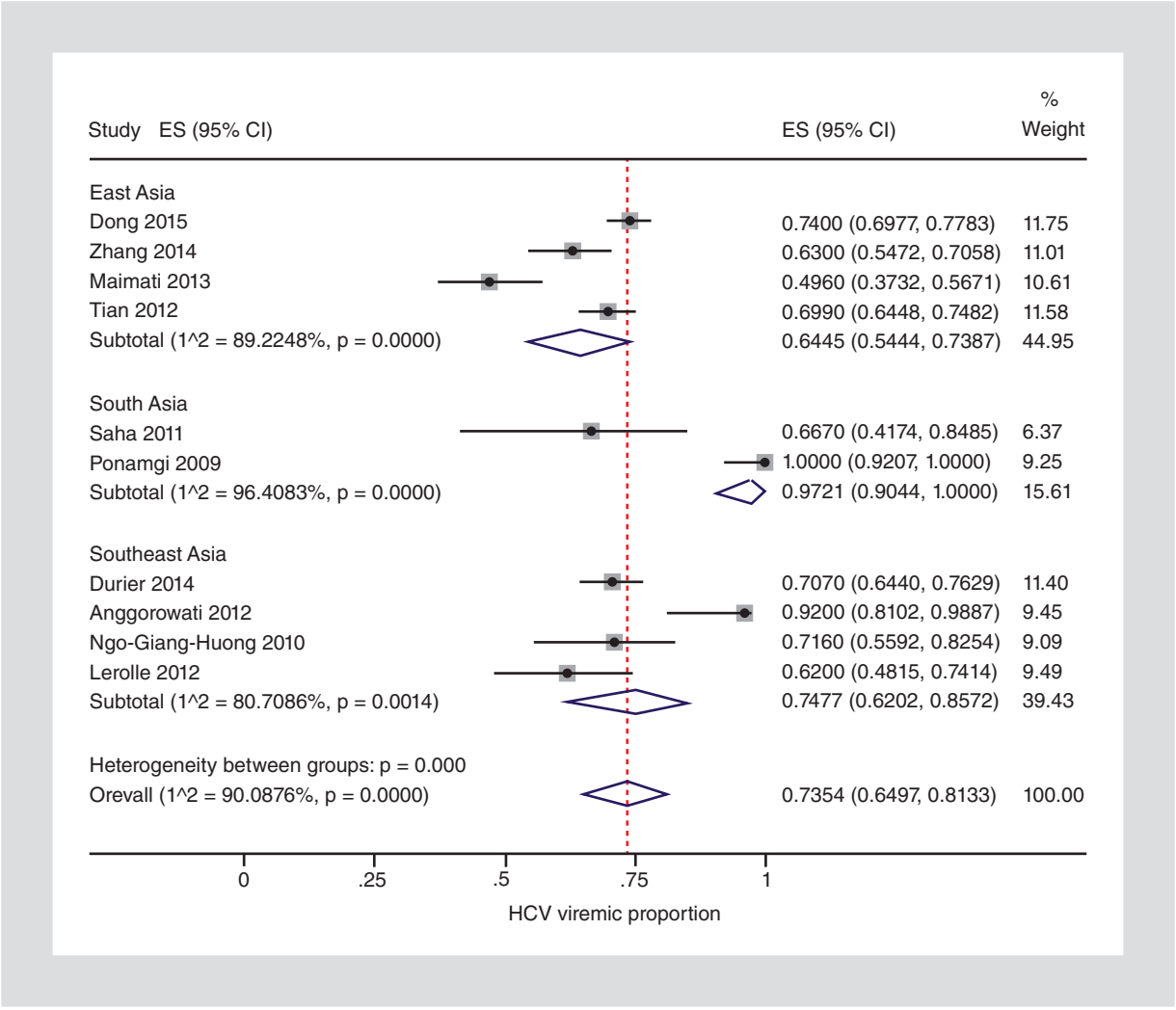

Figure 3. *Proportion of positive HCV serology samples with detectable HCV RNA by polymerase chain reaction, subdivided by Global Burden of Disease region.*

many countries within the region, means that HIV/HCV coinfection is likely to emerge as a major public health issue in the future.

A feature of the epidemiology of HIV-HCV coinfection in the Asia Pacific region is the considerable heterogeneity within GBD regions, between and within countries, and across population groups. The PWID are at particularly high risk of HIV/HCV coinfection, an important feature given that 3-4 million PWID reside in the region[13] and rates of IDU are increasing. The HIV prevalence in PWID varies across the Asia Pacific region (China 6.5%, India 7.2%), but is particularly high in Southeast Asia (Indonesia 36.4%, Cambodia 24.1%, Myanmar 18%, Thailand 16%, Vietnam 11.6%)[13]. Given transmission efficiency, HCV acquisition usually precedes HIV infection among PWID. Thus, rising HIV prevalence among PWID will be inextricably linked to increasing HIV/HCV coinfection. While sexual transmission of HIV may be declining in many regions, transmission in PWID continues unabated with important implications for the HIV/HCV coinfection epidemic. Chanbancherd, et al.[57] demonstrated that the HIV prevalence in Thai military recruits declined from 2.4 to 1.1% between 1995 and 2000, while among those with HIV, the HCV-coinfected proportion increased from 20.8 to 49.5%, suggesting a switch from predominantly sexual to injecting-related HIV transmission. In many regions in East and Southeast Asia, HCV coinfection is almost universal in HIV-positive PWID[19,24,51].

Over the last decade in Australia, Europe, and North America, an epidemic of acute HCV infection has been observed in HIV-positive MSM, largely associated with sexual and non-IDU behavior[58-60]. Outside of Australia,

Table 3. HCV genotype distribution in HIV/HCV coinfection*

GBD region	Reference	Population	Location	HIV/HCV prevalence (%)	HCV GT distribution (%)						
					1	1a†	1b†	2	3	3a†	3b†	6
East Asia	(19)	HIV-positive PWID	China	90.8	19.5	3.0	16.5		61.9	19	42.9	18.6
	(30)	HIV-positive FBD	China	84.7	65.9		65.9	34.1				
	(31)	HIV-positive	China	25.8	24.7		24.7		27.8	9.8	18.0	39.3
South Asia	(36)	HIV-positive	India	7.4	20.0				80.0			
	(37)	HIV-positive	India	3.02	68.8				31.1			
Southeast Asia	(54)	HIV-positive	Cambodia	100	68.0			7.0				25.0
	(53)	HIV-positive	Malaysia	100	42.9	14.3	14.3		57.1			0
	(50)	HIV-positive	Indonesia	38.9	52.0	52.0			27.0			
	(53)	HIV-positive	Indonesia	100	81.0	78.6	0		7.1			0
	(53)	HIV-positive	Thailand	100	43.8	28.1	9.4		40.6			12.5
	(48)	HIV-positive pregnant women	Thailand	2.9	41.0	19.0	22.0		38.0			19.0
	(53)	HIV-positive	Vietnam	100	48.0	28.0	8.0		0			4.0

*HCV genotype is reported only for those with HIV/HCV coinfection; those with HCV monoinfection are not included; †HCV subtype provided if available.
GBD: Global Burden of Disease; GT: genotype; PWID: people who inject drugs; FBD: former blood donor.

little is known about whether this also occurs in other Asia Pacific countries. A systematic review and meta-analysis of 35,203 MSM in China (including 363 HIV-positive and 625 CSW) estimated HIV and HCV prevalence at 4.7% (95% CI: 3.9-5.6%) and 1.2% (95% CI: 1.0-1.6%), respectively[61]. In HIV-positive MSM, HCV prevalence was 8.4% (95% CI: 3.9-17.3%), similar to our pooled prevalence estimate. The available but limited data would suggest that the prevalence in MSM is low, but that the incidence may be increasing. In Taiwan, a prospective observational cohort study assessed HCV incidence in 892 HIV-infected individuals who denied IDU[62]. Overall HCV incidence was 0.7 per 100 person years (py), with a significant increase over the duration of the study (1994-2000: 0/100 py; 2006-2010: 1.0/100 py). Similar increases in incidence over the last decade were noted in Japanese HIV-positive MSM (2005-2006: 0/100 py; 2011-2012: 2.5/100 py)[63]. Consistent with the international literature, recent syphilis infection[62] and illicit drug use[63] were associated with HCV seroconversion.

There are several limitations to this study that should be noted. First, it is likely that there are additional data on HIV/HCV prevalence in the Asia Pacific region that were not identified. While broad search terms were employed and the grey literature was searched, further discussions with key researchers in the field may have provided additional results. Secondly, as in any systematic review and meta-analysis, subsequent assessment is limited by the data and analyses contained in the original reports. In one large study[15] (n = 30,153), a large proportion of individuals (total study population, 63%; India 87%; Indonesia 61%), did not undergo anti-HCV Ab testing. Given the proportion with detectable anti-HCV Ab cannot be assumed to be the same in those tested compared with those not tested, only those screened for anti-HCV Ab were included in calculations of prevalence estimates. Prevalence estimates in many regions are based on data obtained from single countries in specific populations, with little data available in certain regions, particularly Central Asia. Among the included studies, there were diverse recruitment methods, which may have led to study populations being non-representative samples in some locations. Likely due to socio-cultural factors, women appear to be underrepresented. However, gender differences in risk factors for HIV acquisition may also contribute. Thirdly, only studies enrolling HIV-positive individuals were included. This was in order to limit study heterogeneity and allow pooling of results for meta-analysis.

Conclusion

While few studies examine the prevalence of HIV/HCV coinfection in Asia, the available literature highlights the high prevalence and disease burden in HIV-positive PWID, FBD, and blood product recipients. Large gaps in knowledge are evident, particularly in Central Asia where significant populations of PWID reside. Coinfection incidence may be increasing in HIV-positive MSM, but only limited data is available on which to base this observation. These at-risk populations require engagement and assessment in order to determine appropriate intervention.

Given the availability of safe and effective interferon-free direct-acting antiviral therapy for HCV, solid epidemiological data in those populations most at need are required to enhance treatment scale-up within the Asia Pacific region.

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