

Prevalence of Seropositive and Seronegative Chronic HCV Infections in Southern Thai HIV Patients

Pathipat Durongponkasem MD¹, Pimsiri Sripongpun MD¹,
Naichaya Chamroonkul MD¹, Narongdet Kositpantawong MD², Sujinda Ruangchan MD³,
Roongrueng Jarumanokul MSc⁴, Chanon Kongkamol MD⁵, Teerha Piratvisuth MD¹

¹ Division of Gastroenterology and Hepatology, Department of Internal Medicine, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand

² Division of Infectious Diseases, Department of Internal Medicine, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand

³ Department of Internal Medicine, Songkhla Hospital, Songkhla, Thailand

⁴ Immunology and Virology Unit, Department of Pathology, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand

⁵ Research Unit of Holistic Health and Safety Management in Community, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand

Objective: Hepatitis C virus [HCV] shares common transmission pathways with human immunodeficiency virus [HIV]. HIV-HCV co-infection is associated with negative impacts on both HIV and HCV when compare with mono-infection. Anti-HCV test is the main screening method for HCV infection. However, in HIV patients, false-negative anti-HCV may occur as a result of impaired immunity, and HCV RNA may be the sole investigation to diagnose HCV infection in those patients. Data regarding prevalences of both seropositive (anti-HCV+) and seronegative HCV (anti-HCV- but HCV RNA+) infection in HIV individuals in Thailand are limited. The aims of this study are to define the prevalence of seropositive and seronegative HCV infection in Southern Thai HIV patients.

Materials and Methods: This is a cross-sectional study in 2 centers in Southern Thailand: Songklanagarind and Songkhla Hospital. Inclusion criteria were known adult HIV patients with available CD₄ count within 6 months of enrollment. Exclusion criteria were patients with coexisting autoimmune disease, renal dialysis, immunosuppressive therapy including corticosteroids treatment, and history or clinical condition that cannot exclude acute HCV infection. Plasma samples were obtained from all eligible patients and test for anti-HCV (third-generation enzyme immunoassay) and HCV RNA.

Results: A total of 117 HIV patients were enrolled, with mean age of 44 years and 51.3% were male. The median CD₄ level was 524 cells/mm³. The major HIV transmission route was heterosexual (83.8%), and intravenous drug use [IVDU] was found 3.42% of patients. Nine patients (7.7%) were positive for anti HCV and, among those, HCV RNA was detectable in 8 patients (6.8%). However, no HCV RNA was detected in all patients with negative anti-HCV. When compared with no HCV co-infection group, lower CD₄ count (343 vs. 549 cells/mm³; $p = 0.035$), more IVDU (33.3% vs. 0.9%, $p = 0.001$), lower heterosexual as a route of transmission (55.6% vs. 86.1%, $p = 0.037$), and more elevated aspartate aminotransferase [AST] level (31 vs. 24 U/L, $p = 0.019$) were observed in seropositive HCV group.

Conclusion: The prevalence of seropositive HCV infection in Southern Thai HIV patients was 7.7%. Low CD₄ count, IVDU and elevated AST were significantly associated with HCV co-infection. No seronegative HCV infection was detected in our HIV patients.

Keywords: Hepatitis C, Seropositive, Seronegative, HIV, Negative anti-HCV, HCV infection, Chronic HCV, AIDS, Co-infection

J Med Assoc Thai 2018; 101 (Suppl. 4): S72-S79

Full text. e-Journal: <http://www.jmatonline.com>

Correspondence to:

Sripongpun P, Division of Gastroenterology and Hepatology, Department of Internal Medicine, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand.

Phone: +66+74-451479

E-mail: spimsiri@medicine.psu.ac.th

How to cite this article: Durongponkasem P, Sripongpun P, Chamroonkul N, Kositpantawong N, Ruangchan S, Jarumanokul R, Kongkamol C, Piratvisuth T. Prevalence of seropositive and seronegative chronic HCV infection in Southern Thai HIV patients. J Med Assoc Thai 2018;101;Suppl.4:S72-S79.

Human immunodeficiency virus [HIV] and hepatitis C virus [HCV] infections are global public health problems⁽¹⁾. Thirty-five million people were estimated to be infected with HIV globally, and about 180 million people for HCV infection worldwide^(2,3). HCV and HIV share common transmission pathways which may explain the high rate of co-infection between these 2 viruses. It was estimated that 4 to 5 million individuals (11% to 14% of all HIV patients) have concomitant HCV co-infection⁽⁴⁾. Despite both of them are transmitted via blood contact, HCV infection are more common in transfusion of blood components, intravenous drug users [IVDU] rather than sexual, and mother-to-child transmission⁽⁵⁾.

Comparing with either HIV or HCV mono-infection, HIV/HCV co-infection results in more severe clinical outcomes than mono-infected patients⁽⁶⁾. Impacts of HIV on HCV infection are accelerated progression of HCV-related liver diseases, especially in patients with low CD₄ count, and high HIV viral load^(7,8). HCV also adversely affects progression of HIV disease. Liver disease is a leading cause of mortality for HIV-infected individuals in the antiretroviral therapy era. Patients with co-infection have shorter median survival times than patients with HIV mono-infection⁽⁹⁻¹¹⁾.

Aside from negative impacts on clinical outcomes, HIV/HCV co-infection was also previously known as ‘difficult-to-treat’ population among all HCV patients in the era of peg-interferon/ribavirin therapy. Long duration of treatment for all HCV genotypes, and selective high CD₄ count HIV hosts were needed, yet the sustained virological response [SVR] rates were not satisfactory high in this group of patients. However, with the discovery of novel HCV ‘direct antiviral agents [DAA]’, nowadays, current treatment of HIV/HCV co-infection with DAAs exhibits remarkably high SVR rates (>90%), comparable to treatment outcomes of HCV mono-infection. Making this group of patients should be identified and treated⁽¹²⁻²¹⁾.

To identify patients with HIV/HCV co-infection, there are some considerations in this subgroup of patients. In general population, antibody testing (anti-HCV) is the main screening method for HCV infection, which high sensitivity and specificity were demonstrated⁽²²⁻²⁶⁾. Nevertheless, HCV serological screening in HIV-infected patients may not be the optimal method. Chronic HCV viremia (detectable HCV RNA) in the absence of HCV antibody, or so-called “seronegative HCV” were addressed in patients with HIV infection, hemodialysis, and organ transplanta

tion⁽²⁷⁻³⁰⁾. Immunosuppression by HIV infection may impair antibody formation and results in false negative HCV antibody tests^(12,16). Prevalence of false-negative anti-HCV by enzyme-linked immunosorbent assay [ELISA], or seronegative HCV, were reported by several studies in range from 1.3 to 38.2%⁽³¹⁻³⁹⁾.

Given the clinical significance of HCV co-infection, experts and national guidelines including American Association for the Study of Liver Diseases [AASLD], European Association for the Study of the Liver [EASL], Infectious Diseases Society of America [IDSA], and Thai Association for the Study of the Liver [THASL] recommend HCV RNA testing in HIV patients with suspected chronic liver disease whose anti-HCV results are negative⁽⁴⁰⁻⁴²⁾. But data regarding prevalence of both seropositive and seronegative HCV infection in Thai HIV patients are limited.

In this study, we aim to define the prevalence of seropositive and seronegative chronic HCV infections in Thai HIV patients.

Materials and Methods

We conducted a cross-sectional study at the Infectious Diseases Clinic in 2 centers: Songklanagarind, and Songkhla Hospital, which located in different districts of the same province; Songkhla, in Southern Thailand. Songklanagarind Hospital is a tertiary care hospital and the only university hospital in Southern Thailand, whereas Songkla Hospital is a secondary care hospital. The study was performed from August to November, 2016. Inclusion criteria were: known HIV patients, age of at least 18 years, with available CD₄ count within 6 months of enrollment, and never underwent HCV RNA testing before enrollment. Exclusion criteria were: patients with coexisting autoimmune disease, renal dialysis, immunosuppressive therapy including corticosteroids treatment, and history or clinical condition that cannot exclude acute HCV infection; as the above-mentioned patients could have false negative anti-HCV results themselves. We also excluded patients who were already known as HIV/HCV co-infection before enrollment, and patients who refused to participate in the study.

Baseline characteristics such as, but not limit to, gender, age, and route of HIV transmission were collected. Laboratory data of CD₄ level within 6 months of enrollment and liver function test were also collected. Patients without previous anti-HCV result within 6 months of enrollment would underwent both anti-HCV, and HCV RNA testing; while patients with known being

negative for anti-HCV, plasma samples would be obtained only for HCV RNA level.

Plasma samples were consecutively obtained from all eligible patients at the time of OPD encounter. Serum creatinine, liver function test were evaluated from laboratory centers in both hospitals. Samples for anti-HCV and HCV RNA testing were stored at -20°C for <14 days. HCV antibody tests were performed by a third-generation assay (Abbott ARCHITECT anti-HCV chemiluminescent microparticle immunoassay) which detects multiple antigenic determinants (core, NS3, NS4 and NS5). HCV RNA amplification was done by COBAS® AmpliPrep/COBAS® TaqMan® HCV Test with a detection limit of less than 15 IU/mL.

Informed consent was obtained from all patients and this study was approved by Human Research Ethics Committees [HREC] at Faculty of Medicine, Prince of Songkla University.

Statistical analysis

Data were expressed as mean and standard deviation [SD], or median and interquartile range [IQR] regarding distribution of the data. Prevalence was calculated in percentage. Categorical variables were compared by Chi-square test or Fisher's exact test, whereas Wilcoxon rank-sum test or Student's t-test was used for comparison of continuous variables. The percentages were expressed with 95% confidence interval (95% CI). Comparison values with $p < 0.05$ were considered statistically significant. The R version 3.3.1 (The R Foundation for Statistical Computing Platform) was used for analysis.

Results

Study population

Of 138 patients who were screened, 21 patients were excluded, and a total of 117 HIV-positive patients were enrolled in this study (Figure 1). Baseline characteristics of the eligible patients are shown in Table 1. The mean age of patients was 44 years old with slightly male predominance. The mean CD₄ level was high and most of the patients were on antiretroviral therapy. The major HIV transmission route was heterosexual (83.8%), and intravenous drug use [IVDU] was found in 3.42% of patients.

Seropositive and seronegative HCV infection in HIV patients

Nine patients (7.7%) were positive for anti-HCV (seropositive HCV), and HCV viremia were detectable in 8 of 9 patients (6.8%). However, no HCV

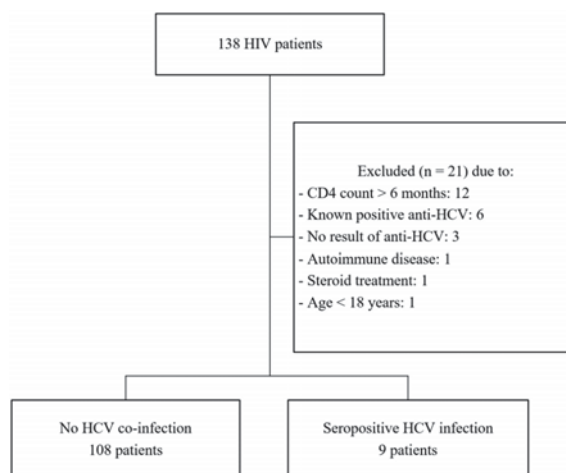


Figure 1 Study population.

Table 1. Baseline characteristics of all eligible HIV patients

Characteristics	Patients (n = 117)
Age (year)	44.1±10.3
Male	60 (51.3)
BMI (kg/m ²)	22.1±3.4
Smoking	25 (21.4)
Alcoholic drinking	21 (17.9)
Comorbidities	
Ischemic heart disease	2 (1.7)
Chronic lung disease	1 (0.8)
Chronic kidney disease	3 (2.5)
Diabetes mellitus	9 (7.6)
Hypertension	8 (6.8)
CD ₄ count (cells/mm ³)	533±281.4
Antiretroviral therapy	109 (93.1)
HIV transmission route	
IVDU	4 (3.4)
Heterosexual	98 (83.8)
Homosexual	12 (10.3)
Blood transfusion	2 (1.7)
Mother-to-child	1 (0.8)
Tattooing	2 (1.7)
AST (U/L)	29.7±19.7
ALT (U/L)	30.4±22.6
Serum creatinine (mg/dL)	0.89±0.5

ALT = alanine aminotransferase; AST = aspartate aminotransferase; BMI = body mass index; HIV = human immunodeficiency virus; IVDU = intravenous drug use

* Data are expressed as number (%) or mean ± standard deviation.

RNA was detected in all patients with negative anti-HCV, making prevalence of seronegative HCV infection in our study was zero. High HCV viral loads ($\geq 100,000$ IU/mL) were detected among all HCV viremia patients. Comparing with HIV patients without HCV co-infection, patients with seropositive HCV had a significant lower CD₄ count, higher AST level, and more IVDU and less heterosexual as risks of HIV transmission (Table 2).

Discussion

The present study is the first study to define prevalence of both seropositive and seronegative HCV infection in Thai HIV patients. Our study shows that 7.7% of Southern Thai HIV patients were positive for anti-HCV, and true HCV viremia were observed in all but one patients. The prevalence of seropositive HCV infection among HIV patients in our study was almost identical to previous studies in Central Thailand (7.7% to 7.8%)^(43,44), and it was much greater than the prevalence of HCV mono-infection in general Thai

population (0.98% to 2.9%)^(45,49), as HIV and HCV share common routes of transmission. However, the prevalence of HCV and HIV co-infection in Thailand was much lower than US and European countries (17% to 33%)^(4,47). This result indicates that the transmittal efficiency may differ between each viruses despite similar transmission. The majority proportion of HCV spread through exposure to contaminated blood products, especially in IVDU patients, while sexual transmission of HCV is quite low. The main HIV risk factor of patients in our study was heterosexual, whereas IVDU was the main route of transmission of HIV in the US and European studies^(4,47).

In the present study, we demonstrated that factors associated with the presence of seropositive HCV co-infection among HIV patients are; lower CD₄ count, IVDU as an HIV risk factor, and more elevated AST level when comparing to HIV mono-infection. These are in contrast to the previous study in Thailand by Phuangchoei et al⁽⁴³⁾, which no associated factor of

Table 2. Comparison of parameters between HIV patients with and without HCV co-infection

	No HCV co-infection (n = 108)	HCV co-infection (n = 9)	p-value
Age (year), mean \pm SD	44.5 \pm 10.3	39.9 \pm 11.5	0.200
Male	53 (49.1)	7 (77.8)	0.164
BMI (kg/m ²), median (IQR)	21.8 (20.2, 23.9)	19.6 (17.6, 22.4)	0.051
Smoking	22 (20.4)	3 (33.3)	0.605
Alcoholic drinking	20 (18.5)	1 (11.1)	0.607
Comorbidities			
Ischemic heart disease	1 (0.9)	1 (11.1)	0.149
Chronic lung disease	1 (0.9)	0	1
Chronic kidney disease	3 (2.8)	0	1
Diabetes mellitus	8 (7.4)	1 (11.1)	0.526
Hypertension	6 (5.6)	2 (22.2)	0.116
CD ₄ count (cells/mm ³), mean \pm SD	549.2 \pm 276.5	343.6 \pm 286.2	0.035
Antiretroviral therapy	102 (94.4)	7 (77.8)	0.116
HIV transmission route			
IVDU	1 (0.9)	3 (33.3)	0.001
Heterosexual	93 (86.1)	5 (55.6)	0.037
Homosexual	10 (9.3)	2 (22.2)	0.231
Blood transfusion	2 (1.9)	0	1
Mother-to-child	1 (0.9)	0	1
Tattooing	1 (0.9)	1 (11.1)	0.149
AST (U/L), median (IQR)	24.5 (20, 34.8)	31 (29.2, 43.5)	0.019
ALT (U/L), median (IQR)	23 (17, 37.2)	34 (20, 38)	0.262
Serum creatinine (mg/dL), median (IQR)	0.8 (0.6, 1)	0.8 (0.7, 0.9)	0.861

ALT = alanine aminotransferase; AST = aspartate aminotransferase; BMI = body mass index; HCV = hepatitis C virus; HIV = human immunodeficiency virus; IQR = interquartile range; IVDU = intravenous drug use
Data are expressed as number (%) except being specified.

HIV-HCV co-infection could be observed. Nonetheless, our study results are concordant with the earlier studies in other countries that low CD₄ count^(4,48,49), IVDU^(4,48-50), and elevated liver enzymes⁽⁴⁹⁾ were associated with HCV co-infection among HIV patients.

Meanwhile, seropositive HCV data in our study are akin to the previous studies as mentioned above, the data regarding seronegative HCV infection in HIV patients in our study is different. In preceding studies, the prevalence of HCV viremia without detectable anti-HCV antibodies (as known as seronegative HCV infection) in HIV patients varies from 1.3% to 38.2%⁽³¹⁻³⁹⁾. Abnormal antibody production and cellular immune responses to HCV had been described in HIV patients with seronegative HCV infection⁽⁵¹⁻⁵⁴⁾. In contrast to our study, no detectable HCV viremia was found in HIV patients with negative HCV antibodies by third-generation assay.

To explain the surprisingly dissimilarity results between the present study and the previous studies by Hadlich et al and George et al, whose HCV antibody tests were performed by the same generation of enzyme immunoassay method, and seronegative HCV prevalence were 8.3% and 20%, respectively, the differences in baseline characteristics of the HIV patients may play a significant role for such results. Baseline mean CD₄ counts of the patients in our study (533 cells/mm³) is higher than in Hadlich et al and George et al (31 and 225 cells/mm³, respectively^(31,39)). The other factor that might explain the very low prevalence of seronegative HCV in our population is the distinction of HIV transmission routes among study populations. Thio et al demonstrated 8.3% prevalence of seronegative HCV in high CD₄ HIV patients⁽³³⁾ but all of the patients in their study had history of IVDU. Another study from Juniastuti⁽³²⁾ reported the prevalence of seronegative HCV infection in HIV patients was 38.2% and one-third of the population in their study was IVDU. The major route of HIV transmission in our study was heterosexual (>80%) and IVDU was found in only 3.4%.

The limitations of our study are small sample size, and was conducted in the secondary and tertiary care settings, which may not reflect the whole population of Southern Thai HIV patients. Nevertheless, it depicts the real situation of HIV patients in HAART era.

Conclusion

The prevalence of seropositive HCV infection in Southern Thai HIV patients was 7.7%. Low CD₄

count, IVDU and elevated AST were significantly associated with HCV co-infection. No seronegative HCV infection was detected in our HIV patients. Despite the theoretical assumption that impaired immunity in HIV patients has an impact on anti-HCV production, we suggest that HCV RNA should not be tested in every HIV patients with negative anti-HCV. To minimize the unnecessary cost, HCV RNA testing should be evaluated only in high-risk for HIV/HCV co-infection e.g. Low CD₄ count, IVDU, and abnormal liver enzymes. Further cost effectiveness data regarding this issue is needed.

What is already known in this topic?

HIV and HCV share common routes of transmission, making co-infection is not uncommon, and resulting in more severe outcomes compared with mono-infection. In HIV patients, false-negative anti-HCV may occur as a result of impaired immunity, and HCV RNA may be the sole investigation to diagnose HCV infection in those patients, or so-called 'seronegative HCV'. Prevalence of seronegative HCV in HIV patients were reported by several studies in range from 1.3% to 38.2%. There is no data in Thailand

What this study adds?

In our study population (from 2 centers in Southern Thailand), the prevalence of seropositive HCV in HIV patients was 7.7% and associated with lower CD₄ count, history of IVDU, and elevated AST level when compared with no HCV co-infection HIV patients. There was no case of seronegative HCV in our study.

Acknowledgement

The authors are grateful to all participants in this study. The research was supported by grants from Faculty of Medicine, Prince of Songkla University, Thailand, and The Gastroenterological Association of Thailand (GAT).

Potential conflicts of interest

None.

References

1. Naghavi M, Wang H, Lozano R, Davis A, Liang X, Zhou M, et al. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015; 385: 117-71.
2. Mohd HK, Groeger J, Flaxman AD, Wiersma ST.

- Global epidemiology of hepatitis C virus infection: new estimates of age-specific antibody to HCV seroprevalence. *Hepatology* 2013; 57: 1333-42.
3. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; 380: 2095-128.
 4. Peters L, Mocroft A, Lundgren J, Grint D, Kirk O, Rockstroh J. HIV and hepatitis C co-infection in Europe, Israel and Argentina: a EuroSIDA perspective. *BMC Infect Dis* 2014; 14 (Suppl 6): S13.
 5. Rockstroh JK, Spengler U. HIV and hepatitis C virus co-infection. *Lancet Infect Dis* 2004; 4: 437-44.
 6. Hernandez MD, Sherman KE. HIV/hepatitis C coinfection natural history and disease progression. *Curr Opin HIV AIDS* 2011; 6: 478-82.
 7. Fierer DS, Dieterich DT, Fiel MI, Branch AD, Marks KM, Fusco DN, et al. Rapid progression to decompensated cirrhosis, liver transplant, and death in HIV-infected men after primary hepatitis C virus infection. *Clin Infect Dis* 2013; 56: 1038-43.
 8. Martinez-Sierra C, Arizcorreta A, Diaz F, Roldan R, Martin-Herrera L, Perez-Guzman E, et al. Progression of chronic hepatitis C to liver fibrosis and cirrhosis in patients coinfecting with hepatitis C virus and human immunodeficiency virus. *Clin Infect Dis* 2003; 36: 491-8.
 9. Weber R, Sabin CA, Friis-Moller N, Reiss P, El Sadr WM, Kirk O, et al. Liver-related deaths in persons infected with the human immunodeficiency virus: the D:A:D study. *Arch Intern Med* 2006; 166: 1632-41.
 10. Lohse N, Hansen AB, Pedersen G, Kronborg G, Gerstoft J, Sorensen HT, et al. Survival of persons with and without HIV infection in Denmark, 1995-2005. *Ann Intern Med* 2007; 146: 87-95.
 11. Mira JA, Rivero-Juarez A, Lopez-Cortes LF, Giron-Gonzalez JA, Tellez F, de la S-G I, et al. Benefits from sustained virologic response to pegylated interferon plus ribavirin in HIV/hepatitis C virus-coinfecting patients with compensated cirrhosis. *Clin Infect Dis* 2013; 56: 1646-53.
 12. Carrat F, Bani-Sadr F, Pol S, Rosenthal E, Lunel-Fabiani F, Benzekri A, et al. Pegylated interferon alfa-2b vs standard interferon alfa-2b, plus ribavirin, for chronic hepatitis C in HIV-infected patients: a randomized controlled trial. *JAMA* 2004; 292: 2839-48.
 13. Torriani FJ, Rodriguez-Torres M, Rockstroh JK, Lissen E, Gonzalez-Garcia J, Lazzarin A, et al. Peginterferon Alfa-2a plus ribavirin for chronic hepatitis C virus infection in HIV-infected patients. *N Engl J Med* 2004; 351: 438-50.
 14. Perez-Olmeda M, Soriano V, Asensi V, Morales D, Romero M, Ochoa A, et al. Treatment of chronic hepatitis C in HIV-infected patients with interferon alpha-2b plus ribavirin. *AIDS Res Hum Retroviruses* 2003; 19: 1083-9.
 15. Sulkowski MS, Naggie S, Lalezari J, Fessel WJ, Mounzer K, Shuhart M, et al. Sofosbuvir and ribavirin for hepatitis C in patients with HIV coinfection. *JAMA* 2014; 312: 353-61.
 16. Molina JM, Orkin C, Iser DM, Zamora FX, Nelson M, Stephan C, et al. Sofosbuvir plus ribavirin for treatment of hepatitis C virus in patients co-infected with HIV (PHOTON-2): a multicentre, open-label, non-randomised, phase 3 study. *Lancet* 2015; 385: 1098-106.
 17. Gilmore J, Lynn K, Breen D, Trooskin S, Slim J, Scangarello N, et al. Effectiveness of sofosbuvir/simeprevir for HIV/HCV patients in clinical practice. Poster session presented at: The 22nd Conference on Retroviruses and Opportunistic Infections; 2015 Feb 23-26; Seattle, WA.
 18. Osinusi A, Townsend K, Kohli A, Nelson A, Seamon C, Meissner EG, et al. Virologic response following combined ledipasvir and sofosbuvir administration in patients with HCV genotype 1 and HIV co-infection. *JAMA* 2015; 313: 1232-9.
 19. Naggie S, Cooper C, Saag M, Workowski K, Ruane P, Towner WJ, et al. Ledipasvir and Sofosbuvir for HCV in Patients Coinfected with HIV-1. *N Engl J Med* 2015; 373: 705-13.
 20. Wyles DL, Ruane PJ, Sulkowski MS, Dieterich D, Luetkemeyer A, Morgan TR, et al. Daclatasvir plus Sofosbuvir for HCV in patients coinfecting with HIV-1. *N Engl J Med* 2015; 373: 714-25.
 21. Nelson DR, Cooper JN, Lalezari JP, Lawitz E, Pockros PJ, Gitlin N, et al. All-oral 12-week treatment with daclatasvir plus sofosbuvir in patients with hepatitis C virus genotype 3 infection: ALLY-3 phase III study. *Hepatology* 2015; 61: 1127-35.
 22. Desbois D, Vaghefi P, Savary J, Dussaix E, Roque-Afonso AM. Sensitivity of a rapid immunochromatographic test for hepatitis C antibodies detection. *J Clin Virol* 2008; 41: 129-33.
 23. Lee SR, Kardos KW, Schiff E, Berne CA, Mounzer K, Banks AT, et al. Evaluation of a new,

- rapid test for detecting HCV infection, suitable for use with blood or oral fluid. *J Virol Methods* 2011; 172: 27-31.
24. Lee SR, Yearwood GD, Guillon GB, Kurtz LA, Fischl M, Friel T, et al. Evaluation of a rapid, point-of-care test device for the diagnosis of hepatitis C infection. *J Clin Virol* 2010; 48: 15-7.
 25. Owusu-Ofori S, Temple J, Sarkodie F, Anokwa M, Candotti D, Allain JP. Predonation screening of blood donors with rapid tests: implementation and efficacy of a novel approach to blood safety in resource-poor settings. *Transfusion* 2005; 45: 133-40.
 26. Smith BD, Drobeniuc J, Jewett A, Branson BM, Garfein RS, Teshale E, et al. Evaluation of three rapid screening assays for detection of antibodies to hepatitis C virus. *J Infect Dis* 2011; 204: 825-31.
 27. Brojer E, Liszewski G, Niznik A, Rosiek A, Letowska M, Peterson JE, et al. Detection of HCV core antigen in HCV RNA positive, anti-HCV negative blood donations from Polish blood donors. *Transfusion* 2001; 41: 304.
 28. Schneeberger PM, Keur I, van Loon AM, Mortier D, de Coul KO, van Haperen AV, et al. The prevalence and incidence of hepatitis C virus infections among dialysis patients in the Netherlands: a nationwide prospective study. *J Infect Dis* 2000; 182: 1291-9.
 29. Thomson EC, Nastouli E, Main J, Karayiannis P, Eliahoo J, Muir D, et al. Delayed anti-HCV antibody response in HIV-positive men acutely infected with HCV. *AIDS* 2009; 23: 89-93.
 30. Tugwell BD, Patel PR, Williams IT, Hedberg K, Chai F, Nainan OV, et al. Transmission of hepatitis C virus to several organ and tissue recipients from an antibody-negative donor. *Ann Intern Med* 2005; 143: 648-54.
 31. Hadlich E, Alvares-Da-Silva MR, Dal Molin RK, Zenker R, Goldani LZ. Hepatitis C virus (HCV) viremia in HIV-infected patients without HCV antibodies detectable by third-generation enzyme immunoassay. *J Gastroenterol Hepatol* 2007; 22: 1506-9.
 32. Juniastuti, Utsumi T, Nasronudin, Alimsardjono L, Amin M, Adianti M, et al. High rate of seronegative HCV infection in HIV-positive patients. *Biomed Rep* 2014; 2: 79-84.
 33. Thio CL, Nolt KR, Astemborski J, Vlahov D, Nelson KE, Thomas DL. Screening for hepatitis C virus in human immunodeficiency virus-infected individuals. *J Clin Microbiol* 2000; 38: 575-7.
 34. Bonacini M, Lin HJ, Hollinger FB. Effect of coexisting HIV-1 infection on the diagnosis and evaluation of hepatitis C virus. *J Acquir Immune Defic Syndr* 2001; 26: 340-4.
 35. Honge B, Jespersen S, Medina C, Te D, da Silva Z, Ostergaard L, et al. Hepatitis B virus surface antigen and anti-hepatitis C virus rapid tests underestimate hepatitis prevalence among HIV-infected patients. *HIV Med* 2014; 15: 571-6.
 36. Tien PC, Benson C, Zolopa AR, Sidney S, Osmond D, Grunfeld C. The study of fat redistribution and metabolic change in HIV infection (FRAM): methods, design, and sample characteristics. *Am J Epidemiol* 2006; 163: 860-9.
 37. Chamie G, Bonacini M, Bangsberg DR, Stapleton JT, Hall C, Overton ET, et al. Factors associated with seronegative chronic hepatitis C virus infection in HIV infection. *Clin Infect Dis* 2007; 44: 577-83.
 38. Hall CS, Charlebois ED, Hahn JA, Moss AR, Bangsberg DR. Hepatitis C virus infection in San Francisco's HIV-infected urban poor. *J Gen Intern Med* 2004; 19: 357-65.
 39. George SL, Gebhardt J, Klinzman D, Foster MB, Patrick KD, Schmidt WN, et al. Hepatitis C virus viremia in HIV-infected individuals with negative HCV antibody tests. *J Acquir Immune Defic Syndr* 2002; 31: 154-62.
 40. Craxi A, Pawlotsky JM, Wedemeyer H, Bjoro K, Flisiak R, Fornis X, et al. EASL Clinical practice guidelines: management of hepatitis C virus infection. *J Hepatol* 2011; 55: 245-64.
 41. Chung RT, Davis GL, Jensen DM, Masur H, Saag MS, Thomas DL, et al. Hepatitis C guidance: AASLD-IDS recommendations for testing, managing, and treating adults infected with hepatitis C virus. *Hepatology* 2015; 62: 932-54.
 42. Thai Association for the Study of the Liver (THASL). Thailand practice guideline for management of chronic hepatitis B and C 2015. Bangkok: THASL; 2015: 34-67.
 43. Phuangchoei P, Chotiyaputta W, Chayakulkeeree M. Clinical characteristics of hepatitis B and C virus infections in HIV-infected patients. *J Med Assoc Thai* 2015; 98: 226-31.
 44. Sungkanuparph S, Vibhagool A, Manosuthi W, Kiertiburanakul S, Atamasirikul K, Aumkhyan A, et al. Prevalence of hepatitis B virus and hepatitis C virus co-infection with human immunodeficiency virus in Thai patients: a tertiary-care-based study. *J Med Assoc Thai* 2004; 87: 1349-54.

45. Luksamijarulkul P, Thammata N, Tiloklurs M. Seroprevalence of hepatitis B, hepatitis C and human immunodeficiency virus among blood donors, Phitsanulok Regional Blood Center, Thailand. *Southeast Asian J Trop Med Public Health* 2002; 33: 272-9.
46. Verachai V, Phutiprawan T, Theamboonlers A, Chinchai T, Tanprasert S, Haagmans BL, et al. Prevalence and genotypes of hepatitis C virus infection among drug addicts and blood donors in Thailand. *Southeast Asian J Trop Med Public Health* 2002; 33: 849-51.
47. Sulkowski MS. Viral hepatitis and HIV coinfection. *J Hepatol* 2008; 48: 353-67.
48. Sherman KE, Rouster SD, Chung RT, Rajcic N. Hepatitis C Virus prevalence among patients infected with Human Immunodeficiency Virus: a cross-sectional analysis of the US adult AIDS Clinical Trials Group. *Clin Infect Dis* 2002; 34: 831-7.
49. Rockstroh JK, Mocroft A, Soriano V, Tural C, Losso MH, Horban A, et al. Influence of hepatitis C virus infection on HIV-1 disease progression and response to highly active antiretroviral therapy. *J Infect Dis* 2005; 192: 992-1002.
50. Sulkowski MS, Moore RD, Mehta SH, Chaisson RE, Thomas DL. Hepatitis C and progression of HIV disease. *JAMA* 2002; 288: 199-206.
51. Bruno R, Sacchi P, Puoti M, Soriano V, Filice G. HCV chronic hepatitis in patients with HIV: clinical management issues. *Am J Gastroenterol* 2002; 97: 1598-606.
52. Braitstein P, Yip B, Montessori V, Moore D, Montaner JS, Hogg RS. Effect of serostatus for hepatitis C virus on mortality among antiretrovirally naive HIV-positive patients. *CMAJ* 2005; 173: 160-4.
53. Cribier B, Rey D, Schmitt C, Lang JM, Kirn A, Stoll-Keller F. High hepatitis C viraemia and impaired antibody response in patients coinfecting with HIV. *AIDS* 1995; 9: 1131-6.
54. Chamot E, Hirschel B, Wintch J, Robert CF, Gabriel V, Deglon JJ, et al. Loss of antibodies against hepatitis C virus in HIV-seropositive intravenous drug users. *AIDS* 1990; 4: 1275-7.