DOI: 10.1590/S0004-28032016000300011 ARQGA/1852

HIV AND HEPATITIS C VIRUS COINFECTION. WHO IS THIS PATIENT TODAY?

Vicente Sperb **ANTONELLO**[1,2,3], Ivan Carlos Ferreira **ANTONELLO**[4], Rosana Ferrazza **ZALTRON**[5] and Cristiane Valle **TOVO**[3,6]

Received 24/12/2015
Accepted 20/4/2016

ABSTRACT – ***Background*** – The increase in the survival following the introduction of highly active antiretroviral therapy (HAART) has seen the emergence of hepatitis C virus (HCV) infection, renal and cardiovascular diseases as important morbidity and mortality causes together with HIV. ***Objective*** – The present study aimed to investigate the differences between HIV/hepatitis C virus coinfected and HIV-monoinfected regarding demographic and clinical aspects from a HIV/AIDS clinic in Porto Alegre, Brazil. ***Methods*** – Review of medical records of 1,030 HIV infected individuals aged 18 years or more in an urban HIV/AIDS clinic based in Porto Alegre, Southern Brazil. Clinical and demographical Data were collected from the records of the patients attended between March 2008 and December 2012. ***Results*** – The present study is a cross-sectional study among HIV-infected patients attended at a public HIV/AIDS clinic in Porto Alegre, Brazil. The prevalence of hepatitis C virus in the present study cohort was 11.8% (CI 95%: 9.9%-13.8%). Hypertension and pathological proteinuria were more common in the coinfected compared to monoinfected group. By the other hand, dyslipidemia were more common among monoinfected patients. There was no difference between the groups regarding CD4+ count or HIV-RNA. Variables significant in the univariate analysis with $P<0.05$ were further analyzed using a Poisson regression model with robust variance. Coinfected were likely to be older, with lower lipid levels and higher prevalence of pathological proteinuria compared to HIV-monoinfected patients. Although coinfected patients had higher prevalence of tenofovir-based regimen, there was a strong association between hepatitis C virus individuals to pathological proteinuria and dyslipidemia. ***Conclusion*** – Clinicians should recognize that coinfected and monoinfected individuals are different groups regarding the traditional and HIV-related risk factors and should be managed and screened individually in order to prevent cardiovascular and renal complications.

HEADINGS – AIDS-related opportunistic infections. Hepacivirus. Coinfection. Highly active antiretroviral therapy.

INTRODUCTION

The epidemiologic pattern of the human immunodeficiency virus (HIV) infection and its treatment approaches have changed since this disease, currently considered chronic, was first acknowledged in 1981 [3,24]. Besides HIV, the coinfection HIV/Hepatitis C virus (HCV) has been major prominent in this scenario due to high prevalence and similar transmission routes[3,6,24]. The increase in the survival following the introduction of highly active antiretroviral therapy (HAART) has seen the emergence of HCV infection, renal and cardiovascular diseases as important morbidity and mortality causes together with HIV[22,35].

Hepatitis C virus is linked itself to metabolic abnormalities (diabetes and dyslipidemia) and kidney disease. Some studies report increase of renal and cardiovascular comorbidities in HIV/HCV-coinfected patients[5,13]. Moreover, few authors pointed a negative impact in mortality in coinfected patients compared to HIV-monoinfected ones in HAART era, despite CD4+ counts[2,7].

We aimed in the present study to investigate the differences between HIV/HCV-coinfected and HIV-monoinfected regarding demographic and clinical aspects from a HIV/AIDS clinic in Porto Alegre, Brazil.

METHODS

The present study is a cross-sectional study among HIV-infected patients attended at a public HIV/AIDS clinic in Porto Alegre, Brazil. The patient population consisted of patients all over the city of Porto Alegre and cities nearby who were equal or higher than 18 years old. Data were collected from the records of the patients attended between March 2008 and December 2012. All participants have free access to health care and medications due to national health program.

Data collected from records included age, gender, ethnicity, body mass index (BMI), use of smoke,

Declared conflict of interest of all authors: none
Disclosure of funding: no funding received

[1] Serviço de Atendimento Especializado em AIDS/DSTs IAPI, Prefeitura de Porto Alegre, RS, Brasil; [2] Departamento de Prevenção e Controle de Infecção, Hospital Fêmina, Porto Alegre, RS, Brasil; [3] Pós-Graduação em Hepatologia, Universidade Federal de Ciências da Saúde de Porto Alegre, RS, Brasil; [4] Programa de Pós-Graduação em Medicina, Pontifícia Universidade Católica do Rio Grande do Sul, Porto Alegre, RS, Brasil; [5] Programa de Graduação em Medicina e Ciências da Saúde, Faculdade de Medicina, Pontifícia Universidade Católica de Pelotas, RS, Brasil; [6] Programa de Graduação em Medicina e Ciências da Saúde, Universidade Federal de Ciências da Saúde de Porto Alegre, RS, Brasil.
Correspondence: Vicente Sperb Antonello. Hospital Fêmina. Departamento de Prevenção e Controle de Infecção. Rua Mostardeiro, 17. Moinhos de Vento - CEP: 91430-001 – Porto Alegre, RS, Brasil. E-mail: vicente_antonello@hotmail.com

illicit drugs and alcohol, previous diagnosis of hypertension, diabetes mellitus, chronic hepatitis B infection, HCV and dyslipidemia, lipid levels, glucose level, urianalysis, measure of arterial hypertension, drugs in use, current CD4 counts (cells/mm^3), current plasma HIV RNA level (viral load), and type of antiretroviral under use. Patients with previous history of HCV treatment, regardless their virological response were excluded from analysis. All HCV patients were confirmed by polymerase chain reaction and genotype identification (Abbott diagnostics).

Diagnosis of proteinuria was made by a urinary protein-to-creatinine ratio (PCR) in single-spot urine analysis. Overt proteinuria was defined as PCR higher than 150mg/g, according to KDIGO[19]. Blood pressure was measured using a calibrated automated machine with each participant sitting in a relaxed, upright position. Hypertension was defined using standard definitions by the Eighth Joint National Committee guidelines. Patients receiving an antihypertensive medication, irrespective of blood pressure, were also defined as hypertensive[16]. The criteria for definirion of diabetes and dyslipidemia followed, ADA e AACE, respectively[1,17].

Statistical analyses included descriptive statistics with numbers (proportions) for categorical, and mean (with standard deviation) for continuous variables, respectively. Categorical variables were associated by chi-square test or exact test of fisher, and quantitative variables compared by *t*-test student. Adjusted residual analysis was done to detect the categories with two-tail (higher and lower) frequency expected.

Variables significant in the univariate analysis with $P<0.05$ were further analyzed using a Poisson regression model with robust variance. A value of $P<0.05$ was considered statistically significant. All statistical analyses were performed using the SPSS version 18 software (IBM, Armonk, NY, USA).

The present paper was approved by Research Ethics Committee from Municipal Council of Health of Porto Alegre city, under the number 05773912.1.0000.5338 in January, 2013.

RESULTS

From a initial of 1,119 HIV-infected individuals, a total of 1,030 patients with hepatitis C virus serology status were included. The group mean age was 41.4 years (± 11.7); 53.5% were male; 61.9% Caucasian; and 38.1% African-American. Diabetes mellitus was present in only 6.3% of the study population, while dyslipidemia was present in 24.8%. Smoke habit was present in 38.7%, and 15.5% of the patients evaluated had body mass index (BMI) higher than 30. Regarding CD4 count, 10.7% had a current count <200 cells/mm^3, 43.2% between 200 and 500 cells/mm^3 and 46.1% greater than 500 cells/mm^3. Fifty-seven percent presented an undetectable viral load (<50 copies/mL) and 74.8% were currently receiving HAART, with both groups under use of antiretrovirals in similar proportion, but coinfected were prone to use more tenofovir (46.2%) and monoinfected zidovudine (48.2%). HIV/HCV-Coinfected represented 11.8% versus 88.2% HIV-monoinfected of the total individuals in the study.

The prevalence of HCV in the present study cohort was 11.8% (CI 95%: 9.9-13.8%). Regarding HCV genotype, 87 individuals (71.3%) were from genotype 1, four (3.0%) genotype 2, 30 (24.8%) genotype 3 and one (1.0%) genotype 4. Regarding age, in the coinfected group, individuals were significantly older ($P<0.001$). The demographics values comparing the groups are presented in Table 1. When evaluated most prevalent HCV genotypes (1 and 3) for age, sex, ethnicity, smoke, obesity, diabetes, dyslipidemia, hypertension, pathological proteinuria, CD4 counts and HIV RNA no significantly differences were found between groups.

After the adjustment of all variables with $P<0.05$ in the univariate analysis using a Poisson regression model, coinfected were likely to be older, with lower lipid levels and higher prevalence of pathological proteinuria compared to HIV-monoinfected patients. Although coinfected patients had higher prevalence of tenofovir-based regimen, there was a strong association between hepatitis c virus individuals to pathological proteinuria and dyslipidemia. The values of regression model are shown in Table 2.

DISCUSSION

Dramatic improvements in survival and disease progression in the HAART era led to liver, cardiovascular and renal diseases to emerge as important causes of morbidity and mortality among HIV-infected patients[30]. Those individuals have nowadays a higher risk of myocardial infarction and cardiovascular death than age-matched uninfected controls. Furthemore, HIV–related renal diseases are the third leading cause of end-stage renal disease (ESRD) among adult African Americans[33]. The presence of ongoing inflammation secondary to other chronic viral infections may promote development of atherosclerosis and subclinical cardiovascular disease in HIV-infected patients. Coinfection with HCV has been linked to endothelial dysfunction[9] and modulates known risk factors for cardiovascular and renal diseases in coinfected individuals[5,12,34].

The present study examinated the influence of HCV in a large cohort of HIV-infected patients, comparing coinfected and monoinfected patients, regarding demographic aspects. HIV/HCV-coinfected had prominent different characteristics compared to HIV-monoinfected patients. First of all, they were older, predominantely from male gender and had higher proportion of African-American inside the group. Regarding literature, coinfected patients are up to three times older than other comparative control groups. Aditionally our results indicate that in our population black race were predominant among coinfected individuals, which is consistently with general literature[3,25,31].

Regarding abuse on drugs, they had higher prevalence on all substances evaluated; alcohol, tobaco, crack cocaine, inhaled cocaine and cannabis. Although coinfected individuals are prone to abuse on alcohol and intravenous drugs, only a few authors associate coinfection to other ilicit drugs as inhaled cocaine[3,6,23]. On the other hand, coinfected and monoinfected had similar pattern of CD4+ counts and HIV viral load control. Regarding use of HAART both groups were under use of

TABLE 1. Demographic data comparing groups of HIV/HCV-coinfected and HIV-monoinfected individuals

Factors			N (%)	Coinfected HIV/HCV N=122 (11.8%)	Monoinfected HIV N=908 (88.2%)	*P* value
Age, years (n=1,030)						< 0.001
	18-39		477 (46.3)	33 (27.0)	444 (48.9)	
	> 40		553 (53.7)	89 (73.0)	464 (51.1)	
Gender, male (n=1,030)	Male gender		551 (53.5)	83 (68.0)	468 (51.5)	0.001
Ethnicity (n=903)	Caucasian		559 (61.9)	60 (52.2)	499 (63.3)	0.028
Abuse on drugs						
	Alcohol	n = 886	140 (15.8)	35 (33.7)	105 (13.4)	< 0.001
	Tabaco	n = 886	343 (38.7)	57 (54.8)	286 (36.6)	0.001
	Crack cocaine	n = 886	48 (5.4)	16 (15.2)	32 (4.1)	< 0.001
	Inhaled cocaine	n = 885	34 (3.8)	8 (7.6)	26 (3.3)	0.051
	Cannabis	n = 884	29 (3.3)	8 (7.7)	21 (2.7)	0.015
Body mass index (n=497)	Obese > 30.0		77 (15.5)	06 (8.7)	71 (16.6)	0.133
Diabetes mellitus		n = 1,025	65 (6.3)	11 (9.2)	54 (6.0)	0.249
Dyslipidemia		n = 1,023	254 (24.8)	11 (9.2)	243 (26.9)	< 0.001
Hypertension		n = 1,001	222 (22.2)	14 (11.8)	208 (23.6)	0.005
Chronic hepatitis B		n = 1,028	29 (2.8)	6 (4.9)	23 (2.5)	0.143
Pathological proteinuria		n = 664	133 (20.0)	29 (36.3)	104 (17.8)	< 0.001
Current CD4 count, cells/mm3 (n=1,029)						0.136
	≥ 500		474 (46.1)	46 (37.7)	428 (47.2)	
	200-500		445 (43.2)	60 (49.2)	385 (42.4)	
	< 200		110 (10.7)	16 (13.1)	94 (10.4)	
HIV RNA, copies/ mL (n=1,030)						0.444
	< 50		590 (57.3)	68 (55.7)	522 (57.5)	
	50 - 1000		163 (15.8)	24 (19.7)	139 (15.3)	
	> 1000		277 (26.9)	30 (24.6)	247 (27.2)	
HAART regimen (n=1,002)	Yes		749 (74.8)	95 (79.8)	654 (74.1)	0.212
Current use of NRTI (n=974)						< 0.001
	TDF+3TC		269 (27.6)	54 (46.2)	215 (25.1)	
	AZT+3TC		452 (46.4)	39 (33.3)	413 (48.2)	
	NAIVE		253 (26.0)	24 (20.5)	229 (26.7)	
Based-therapy (n=1,030)						
NNRTI						
	Efavirenz		292 (28.3)	46 (37.7)	246 (27.1)	0.020
	Nevirapine		12 (1.2)	1 (0.8)	11 (1.2)	0.999
Protease inhibitors						
	Lopinavir		228 (22.1)	26 (21.3)	202 (22.2)	0.906
	Atazanavir		191 (18.5)	18 (14.8)	173 (19.1)	0.306
	Fosamprenavir		16 (1.6)	1 (0.8)	15 (1.7)	0.709
	Darunavir		10 (1.0)	3 (2.5)	7 (0.8)	0.104

3TC: Lamivudine; AZT: Zidovudine; HAART: highly active antiretroviral therapy; NRTI: nucleoside reverse transcriptase inhibitors; NNRTI: Non- nucleoside reverse transcriptase inhibitors; TDF: Tenofovir.

TABLE 2. HIV/HCV-coinfected: Poisson regression model of all variables with $P<0.05$ in univariate analysis

Variable	*P*	Prevalence rate	95% Confidence Interval for PR	
			Lower	Upper
Age higher 40 years	0.001	3.569	1.938	6.573
Male gender	0.205	1.376	0.840	2.253
Caucasian	0.551	0.865	0.537	1.393
Alcohol abuse	0.060	1.673	0.979	2.858
Smoke	0.107	1.531	0.913	2.569
Inhaled crack abuse	0.166	1.741	0.795	3.811
Dyslipidemia	0.002	0.277	0.124	0.619
Hypertension	0.165	0.613	0.307	1.223
Pathological proteinuria	0.009	1.950	1.183	3.212

medication in similar proportion, however coinfected were prone to use tenofovir and monoinfected to zidovudine. This particulariry probably is due to previous national guidelines in whose zidovudine plus lamivudine were recommend as first line backbone therapy. The option for tenofovir on coinfected individuals were probably due to a better interaction with ribavirin to future HCV treatment options. Finally the HIV/HCV coinfected group represented only 11.8% of the individuals in study population, in agree with newly reports which observe decline across all risk groups with decrease of burden of HCV in general population[25,31].

Few studies suggest that elevations in cholesterol levels may actually be blunted in patients coinfected with HCV[5,8,10,21,26,34]. In a retrospective study of 357 HIV-monoinfected patients and 115 HIV/HCV-coinfected patients taking HAART, mean changes in cholesterol were significantly lower in coinfected than in monoinfected patients[8]. Another study evaluated the incidence and risk factors associated with the development of lipid abnormalities in 282 patients initiating HAART, and a protective effect against developing hypercholesterolemia was seen among HCV-infected patients[26]. The related mechanism is unclear but it is likely to be due to impaired cholesterol synthesis and enhanced cellular lipid uptake in patients with HCV-coinfection[5,10,27].

Although HCV may be associated with a lower risk of developing hypercholesterolemia it does not appear that this reduces overall cardiovascular risk, probably because any benefit to the lipid profile may be offset by modulation of other risk factors, as tobacco, illicit drugs and other comorbidities as hypertension and diabetes[5,12,34]. In the present study, coinfected had a significantly lower prevalence of dyslipidemia compared to monoinfected individuals, although there was no difference between the groups regarding other metabolic disorders as obesity, diabetes and hypertension.

Chronic conditions such as kidney disease associated to HIV infection has increased overall and it vary according to the population studied, with pathological proteinuria ranging from 1% in a HIV-positive military veterans cohort without ESRD to 32% among women in United States and 55% in a cohort from Germany[11,14,28,29]. While HIV is a well-defined cause of acute and chronic kidney disease, HCV coinfection also plays a role in the development and progression of renal condition in this population. Furthermore, coinfected persons are more likely to progress to end-stage kidney disease compared to those with HIV infection alone[4,15,18,28]. In the present study 20% of the patients had pathological proteinuria. When compared both groups, coinfected had significantly higher prevalence than monoinfected individuals (36.6% vs 17.8%). Tenofovir may play a role in this situation because coinfected used more tenofovir than monoinfected, and it is associated with proteinuria and ESRD, due to drug accumulation within proximal renal tubules, leading to mitochondrial injury and depletion[20,28].

The present study has some limitations. As far as we did not evaluate the duration of HIV disease or antiretroviral therapy, some of our findings could be underestimated. Our analyses were based on a cross-sectional study; hence, the influence of HCV over time could not be established to evaluate cardiovascular and renal diseases. By the other side, our study had several strengths. It was conducted in a population of HIV-infected persons with clinical follow-up and reliable information on antiretroviral use. Finally, the group studied is a representative one, for two reasons: a large cohort of patients evaluated; and a similar profile of patients attended in HIV clinics nowadays.

In conclusion, HIV/HCV-coinfected individuals are older, mostly from male gender and african-american. Also this group is prone to abuse on tobacco, alcohol and illicit drugs as inhaled and crack cocaine and cannabis. The presence of hepatitis C coinfection appears to predispose the HIV-infected population to pathological proteinuria, possible associated to tenofovir and risk factors above, and to present lower prevalence of dyslipidemia compared to HIV-monoinfected individuals. Furthermore, clinicians should recognize that coinfected and monoinfected individuals are different groups regarding the traditional and HIV-related risk factors and should be managed and screened individually in order to prevent cardiovascular and renal complications.

Authors' contributions

Antonello VS, Antonello ICF, Zaltron RF, Tovo CV participated in the revision of the manuscript. Antonello VS, Antonello ICF and Tovo CV participated in the design, draft and revision of the study. Antonello VS evaluated the medical records of the case and control patients. Antonello VS conceived the study and participated in its design, coordination and the drafting of the manuscript. All authors read and approved the final manuscript.

Antonello VS, Antonello ICF, Zaltron RF, Tovo CV. Coinfecção por HIV e o vírus da hepatite C. Qual o perfil deste paciente hoje? Arq Gastroenterol. 2016,53(3):180-4.

RESUMO - ***Contexto*** - O aumento da sobrevida após a introdução da terapia antirretroviral nos pacientes vivendo com HIV tem como consequência o aparecimento de doenças emergentes nestes pacientes, como a hepatite pelo vírus C, doenças renais e cardiovasculares. ***Objetivo*** - O presente estudo tem como objetivo investigar as diferenças entre monoinfectados por HIV e coinfectados por HIV/virus da hepatite C, considerando aspectos demográficos e clínicos de pacientes atendidos em uma clínica de HIV/AIDS em Porto Alegre, Brasil. ***Métodos*** - Revisão de prontuários médicos de 1.030 indivíduos vivendo com HIV em uma clínica especializada em Porto Alegre, Brasil. Dados clínicos e demográficos foram coletados a partir dos registros dos pacientes atendidos entre março de 2008 e dezembro de 2012 na referida clínica. ***Resultados*** - O presente estudo é um estudo transversal com indivíduos vivendo com HIV, atendidos em um serviço municipal de HIV/AIDS em Porto Alegre, Brasil. A prevalência de hepatite pelo vírus C na presente coorte de estudo foi 11,8% (IC 95%: 9,9%-13,8%). Hipertensão e proteinúria patológica eram ocorrências mais comuns em coinfectados do que monoinfectados. Por outro lado, dislipidemia foi mais comuns entre monoinfectados. Não houve diferença entre os grupos quanto contagem de linfócitos CD4 totais ou HIV-RNA. Variáveis significativas na análise univariada com $P<0,05$ foram ainda analisadas usando um modelo de regressão de Poisson com variância robusta. Coinfectados eram mais velhos, com os níveis de lipídios mais baixos e maior prevalência de proteinúria patológica em comparação com indivíduos monoinfectados. Apesar de os coinfectados apresentarem maior prevalência de estarem em uso de regime contendo tenofovir, houve uma forte associação dos indivíduos infectados pelo vírus da hepatite C com proteinúria patológica e ausência de dislipidemia. ***Conclusão*** - Clínicos devem reconhecer que coinfectados e monoinfectados pertencem a grupos diferentes quanto aos fatores de risco tradicionais e aqueles associados ao HIV, devendo estes serem manejados e rastreados de forma individual, para prevenir complicações cardiovasculares e renais.

DESCRITORES - Infecções oportunistas relacionadas com a AIDS. Hepacivirus. Coinfecção. Terapia antirretroviral de alta atividade.

REFERENCES

1. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2010;33 Suppl 1:S62.
2. Anderson KB, Guest JL, Rimland D. Hepatitis C virus coinfection increases mortality in HIV-infected patients in the highly active antiretroviral therapy era: data from the HIV Atlanta VA Cohort Study. Clin Infect Dis. 2004;39:1507-13.
3. Antonello VS, Kliemann DA, Riegel Santos B, Tovo CV. HAART and liver: is it safe? J Infect Dev Ctries. 2014;8:1444-50.
4. Banerjee T, Scherzer R, Powe NR, Steffick D, Shahinian V, Saran R, et al. Race and Other Risk Factors for Incident Proteinuria in a National Cohort of HIV-Infected Veterans. J Acquir Immune Defic Syndr. 2014;67:145–52.
5. Bedimo R, Westfall AO, Mugavero M, Drechsler H, Khanna N, Saag M. Hepatitis C virus coinfection and the risk of cardiovascular disease among HIV-infected patients. HIV Med. 2010;11:462-8.
6. Calza L, Verucchi G, Manfredi R, Chiodo F. Human immunodeficiency virus and hepatitis C virus coinfection: epidemiology, natural history, therapeutic options and clinical management. Infection. 2004;32:33-46.
7. Chen TY, Ding EL, Seage Iii GR, Kim AY. Meta-analysis: increased mortality associated with hepatitis C in HIV-infected persons is unrelated to HIV disease progression Clin Infect Dis. 2009;49:1605-15.
8. Cooper CL, Mills E, Angel JB. Mitigation of antiretroviral-induced hyperlipidemia by hepatitis C virus co-infection. AIDS. 2007;21:71-6.
9. de Castro IF, Micheloud D, Berenguer J, Guzmán-Fulgencio M, Catalán P, Miralles P, et al. Hepatitis C virus infection is associated with endothelial dysfunction in HIV/hepatitis C virus coinfected patients. AIDS. 2010;24:2059-67.
10. Diong C, Raboud JM, Li M, Cooper C and the Ontario HIV Treatment Network Cohort Study Team. HIV/hepatitis C virus and HIV/hepatitis B virus coinfections protect against antiretroviral-related hyperlipidaemia. HIV Med. 2011;12:403-11.
11. Fischer MJ, Wyatt CM, Gordon K, Gilbert CL, Brown ST, Rimland D, et al; VACS Project Team. Hepatitis C and the risk of kidney disease and mortality in veterans with HIV. J Acquir Immune Defic Syndr. 2010;53:222-6.
12. Freiberg MS, Chang CC, Skanderson M, McGinnis K, Kuller LH, Kraemer KL, et al. The risk of incident coronary heart disease among veterans with and without HIV and hepatitis C. Circ Cardiovasc Qual Outcomes. 2011;4:425-32.
13. George E, Nadkarni GN, Estrella MM, Lucas GM, Sperati CJ, Atta MG, et al. The impact of hepatitis C coinfection on kidney disease related to human immunodeficiency virus (HIV): a biopsy study. Medicine (Baltimore). 2011;90:289-95.
14. Gravemann S, Brinkkoetter PT, Vehreschild JJ, Franke B, Ehren K, Bünemann E, et al. Low-grade proteinuria is highly prevalent in HIV-positive patients on antiretroviral treatment. AIDS. 2014;28:1783-89.
15. Izzedine H, Sene D, Cacoub P, Jansen H, Camous L, Brocheriou I, Bourry E, Deray G. Kidney diseases in HIV/HCV-co-infected patients. AIDS. 2009;23:1219-26.
16. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). JAMA. 2014;311:507-20.
17. Jellinger PS, Smith DA, Mehta AE, Ganda O, Handelsman Y, Rodbard HW, et al. American Association of Clinical Endocrinologists' Guidelines for Management of Dyslipidemia and Prevention of Atherosclerosis. Endocr Pract. 2012;18 Suppl 1:1-78.
18. Jotwani V, Li Y, Grunfeld C, Choi AI, Shlipak MG. Risk factors for ESRD in HIV-infected individuals: traditional and HIV-related factors. Am J Kidney Dis. 2012;59:628-35.
19. Kidney Disease: Improving Global Outcomes (KDIGO) Chronic Kidney Disease Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int Suppl. 2013;3:1–150.
20. Kohler JJ, Hosseini SH, Hoying-Brandt A, Green E, Johnson DM, Russ R, et al. Tenofovir renal toxicity targets mitochondria of renal proximal tubules. Lab Invest. 2009;89:513-9.
21. Lapadula G, Torti C, Paraninfo G, Castelnuovo F, Uccelli MC, Costarelli S, et al. Influence of hepatitis C genotypes on lipid levels in HIV-positive patients during highly active antiretroviral therapy. Antivir Ther. 2006;11:521-7.
22. Lloyd-Sherlock P, Ebrahim S, Grosskurth H. Is hypertension the new HIV epidemic? Int J Epidemiol. 2014;43:8-10.
23. Mendes-Correa MC, Barone AA, Gianini RJ. Risk factors associated with hepatitis c among patients co-infected with human immunodeficiency virus: a case-control study. Am J Trop Med Hyg. 2005;72:762-7.
24. Mocroft A, Ledergerber B, Katlama C, Kirk O, Reiss P, d'Arminio Monforte A, et al. Decline in the AIDS and death rates in the EuroSIDA study: an observational study. Lancet. 2003;362:22-9.
25. Oliveira SB, Merchán-Hamann E, Amorim LD. HIV/AIDS coinfection with the hepatitis B and C viruses in Brazil. Cad Saude Publica. 2014;30:433-8.
26. Patroni A, Torti C, Tomasoni L, Quiros Roldan E, Bertelli D, Puoti M, et al. Effect of highly active antiretroviral therapy (HAART) and hepatitis C Co-infection on hyperlipidemia in HIV-infected patients: a retrospective longitudinal study. HIV Clin Trials. 2002;3:451-61.
27. Pineda-Tenor D, Berenguer J, García-Broncano P, Jiménez-Sousa MA, Fernández-Rodríguez A, Diez C. Association of adiponectin (ADIPOQ) rs2241766 polymorphism and dyslipidemia in HIV/HCV-coinfected patients. Eur J Clin Invest. 2014;44:453-62.
28. Scherzer R, Estrella M, Li Y, Choi AI, Deeks SG, Grunfeld C, et al. Association of tenofovir exposure with kidney disease risk in HIV infection. AIDS. 2012;26:867-75.
29. Schwartz EJ, Szczech LA, Ross MJ, Klotman ME, Winston JA, Klotman PE. Highly active antiretroviral therapy and the epidemic of HIV+ end-stage renal disease. J Am Soc Nephrol. 2005;16:2412-20.
30. Selik RM, Byers RH Jr, Dworkin MS. Trends in disease reported in U.S. death certificates that mentioned HIV infection, 1987-1999. J Acquir Immune Defic Syndr. 2002;29:378-87.
31. Serrano-Villar S, Sobrino-Vegas P, Monge S, Dronda F, Hernando A, Montero M, et al. Decreasing prevalence of HCV coinfection in all risk groups for HIV infection between 2004 and 2011 in Spain. J Viral Hepat. 2014. doi: 10.1111/jvh.12353.
32. Szczech LA, Gange SJ, van der Horst C, Barlett JA, Young M, Cohen MH, et al. Predictors of proteinuria and renal failure among women with HIV infection. Kidney Int. 2002;61:195-202.
33. U.S. Renal Data System: USRDS 1999 Annual Data Report. Bethesda, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, April 1999. [Accessed 2014 December, 29]. Available from: http://www.usrds.org/atlas00.aspx
34. Weber R, Sabin C, Reiss P, de Wit S, Worm SW, Law M, et al. HBV or HCV coinfections and risk of myocardial infarction in HIV-infected individuals: the D:A:D Cohort Study. Antivir Ther 2010;15:1077-86.
35. World Health Organization (WHO). A Global Brief on Hypertension. 2013. [Internet]. [Accessed 2014, December, 20]. Available from: http://www.who.int/cardiovascular_diseases/publications/global_brief_hypertension/en