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MORBIDITY AND MORTALITY PROFILE OF HIV INFECTED PATIENTS, WITH AND WITHOUT HEPATITIS C COINFECTION

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Abstract

Purpose—Hepatitis C virus (HCV) and human immunodeficiency virus (HIV) coinfection is an important and frequent scenario, predominantly in injecting drug users (IDUs). The present study evaluated morbidity and mortality variation in HIV infected patients with and without HCV coinfection.

Methods—Coinfection prevalence was determined in 356 HIV infected persons. Their clinical manifestations, laboratory findings, risk factors, HIV therapies and mortality rates were evaluated.

Results—HCV prevalence was 54% in the overall group and 81% in IDUs, with predominance of HCV genotype 1. Mortality rates were similar in patients with and without coinfection; however coinfected patients had significantly higher liver damage as a cause of mortality when compared with those who were not coinfected.

Conclusions—The high HCV prevalence and the emerging mortality from liver diseases, revealed the significance of this coinfection in HIV epidemic. Primary and secondary prevention are necessary to reduce the expanding impact of HCV infection in HIV patients.

Keywords

Hepatitis C and HIV coinfection; Intravenous Drug Use; Mortality causes

INTRODUCTION

The introduction of highly active antiretroviral therapy (HAART) has increased the life expectancy among subjects infected with the human immunodeficiency virus (HIV). The primary reason for the increased longevity is the declining rates of opportunistic infections, which often were one direct cause of demise. This scenario has introduced a number of issues, which are interdisciplinary in nature and will define newer aspects on the HIV epidemic until a viral eradication is a possibility. Some of these issues concern the emergence of chronic conditions which are compatible with a prolonged survival. The presence of Hepatitis C viral (HCV) infection is one of the chronic infections that are often seen co infecting HIV patients, particularly in subject who are injecting drug users (IDUs).[1--11]

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Between 30% to over 50% of HIV infected persons have a concurrent HCV coinfection.[1,10,11] The impact of the coinfection appears to be more relevant in certain ethnic groups and particularly amongst IDUs. In this latter group the prevalence exceeds 80% with important variations according to the patients' age and the duration of the risk practice.[11--13]

Many of the details regarding the interaction between HIV and HCV remain controversial. Certain studies suggest that HCV related hepatic damage is worsened in patients with HIV infection and that HCV mutates more readily in HIV patients with low CD4+ lymphocyte count.[14--16] A more controversial point is the impact of HCV infection on the course of HIV infection. Several studies suggest that HCV does not affect the natural history of HIV infection. Some authors found that coinfection does not influence the rate of progression to either clinical or immunologic endpoints in coinfected HIV patients.[17--19] Other studies suggest that the coinfection worsens the immunologic deterioration and thus accelerates the progression to AIDS.[20--22] An important variable that is emerging in the literature is the impact that variations in the HCV genotype may have on the progression of HIV infection. HCV genotype 1a and 1b have been reported to be more often associated to a rapid progression to AIDS and death than other genotypes.[11]

The present paper evaluates differences of HCV coinfected and not coinfected in a cohort of HIV/AIDS patients followed in Puerto Rico.

MATERIALS AND METHODS

Study population

The study population was comprised by 519 HIV infected patients that entered the Retrovirus Research Center (RRC) cohort between February 1998 and August 2000. All persons were invited to participate, 365 accepted, and 356 (69% of 519) completed the HCV laboratory tests. Case recruitment and follow up were performed at the Ramón Ruiz Arnau University Hospital at Bayamón, Puerto Rico or in the HIV ambulatory clinics. Once an informed consent was obtained, a baseline questionnaire was completed and appropriate laboratory tests were performed. Data were gathered via personal interviews and medical record review and abstraction. A questionnaire which includes socio-demographic, HIV risk factors, clinical manifestations, antiretroviral therapy (ART), laboratory findings and mortality was used to collect the data. Presumptive and confirmed diagnosis of opportunistic infections such as esophageal candidiasis, *Pneumocystis jirovecii* pneumonia (PJP), cerebral toxoplasmosis, recurrent bacterial pneumonia, pulmonary tuberculosis, Kaposi sarcoma, herpes simplex virus and wasting syndrome were recorded. A complete explanation of the RRC questionnaires is described by Gómez and collaborators.[23] Highly Active Antiretroviral Therapy (HAART) was defined as patients with three or more antiretroviral treatments at study entry. Selected candidates were patients over 18 years old, in whom a HCV qualitative test was performed. HCV viral load and HCV genotype were additionally done in HCV positive cases. Those cases with detectable HCV viral load composed the coinfected study group. The remaining cases formed the not coinfected group. The death status of the study participants as of December 2003 was used to measure the mortality of the study group.

Laboratory measures

The following laboratory test were performed at study entry.

CD4+ Lymphocyte measurement by flow cytometry—A four-color modular flowcytometry analyzer (FACSCalibur Becton/Dickinon, San Jose, CA) was used for CD4+

cell count. For this assay, peripheral blood samples were collected in the presence of EDTA and prepared utilizing a lysed whole blood method. Samples were stained with murine monoclonal antibodies directly conjugated with flourochrome FOTC and PE (Simultest reagents, Becton/ Dickinson) for the quantitation of CD3 (total T cells) and CD3/CD4 lymphocyte.

HIV and HCV virion RNA quantitation—HIV viral load was determined by RNA RT-PCR (Amplicor HIV monitor v.2, Roche Diagnostic System Inc, Indianapolis, IN). This test has a sensitivity of 400 to 750,000 copies/ml. Those specimens with a viral titer of less than 400 were tested with the Roche's RT-PCR modified ultrasensitive version which has a detection range of 50 to 75,000 copies/ml. HCV viral load was determined by RNA RT-PCR (COBAS Amplicor HCV Monitor, Roche Diagnostic Inc,). This test has a detection limits between 100 and 500,000 International Units (IU)/ml. Some of the samples with a viral load below 100 copies/ml were tested with the Taq Man RNA Real Time PCR (Roche Diagnostic System Inc) that has a detection range of 10 to 200 × 10^6 IU/ml.

HCV genotyping—The Bayer's Truegene HCV Genotyping sequencing method (Norcross, GA) was performed on PCR-amplified product for the HCV genotype/subtype determination. For all these analysis, appropriate controls were included.

Mortality

Mortality data were obtained from a review of the institutional medical records and from the Puerto Rican AIDS surveillance system. In addition the mortality registry of the Puerto Rican Health Department was reviewed in order to confirm the death status of the participants. The reported causes of death were tabulated and organized into several categories. These categories included: 1) systems or organ failure (Cardio-vascular, Pulmonary, Gastrointestinal, Renal, Neurological and Metabolic), 2) AIDS conditions (PJP, cerebral toxoplasma and wasting syndrome) and 3) drug overdose or poisoning. A subgroup of liver conditions which included liver failure (chronic and acute) and cirrhosis was included.

Statistical analysis

The Statistical Package of Social Sciences (SPSS) program was used to perform univariate, bivariate and multivariate analyses. Univariate analysis described the frequencies of clinical conditions, immunological findings and antiviral drugs regimens used. Quality differences between patients with and without coinfection were analyzed with the Chi-square or Fisher exact test. ANOVA and student *t* test were used to evaluate means differences. Mann Whitney test, a non parametric test, was used to evaluate median differences between groups. Group differences were also evaluated after stratifying by the use of injecting drug (IDU) as HIV risk factor.

Differences in mortality rates, causes of death and disease duration were evaluated and analyzed in the HIV cohort. Time of follow-up was defined as the time between the patient's enrollment and their death or as of December 2003. HIV disease duration was defined as the time between the first documented positive HIV test and the last follow up or death of the patient. Kaplan Meier analysis was performed to explore the variation in the survival time.[24] The influence of covariate factors was studied with the help of Cox proportional-hazards analysis.[25] P value level used to determine statistical significance was less than 0.05.

RESULTS

General findings

Of the 356 HIV infected patients entered into the study, 193 (54.0%) had HCV viral load greater than 100 copies/ml. Of the 356 HIV infected patients, 249 (69.9%) were male and the mean age at enrollment was 37.6 ±8.8 years. Injecting drug used (IDU) as the main risk factor for HIV infection was reported in 57.6% of the patients. This risk factor was slightly higher than that reported for the overall RRC cohort (51.7%). At study enrollment, 16 (4.6%) of the patients had history of PJP, 21 (5.9%) cerebral toxoplasmosis, 16 (4.5%) recurrent pneumonia, 5 (1.4%) pulmonary tuberculosis, 2 (0.6%) Kaposi sarcoma and 49 (13.8%) had wasting syndrome. The median CD4+ cell count was of 150 cells per ml and over 57% of the patients had a CD4+ cell count below 200 cells per ml. The median CD8+ cell count was of 660 cells per ml with a median CD4/CD8 ratio of 0.24. The median white blood cell count per ml was of 5,400 cells per ml with an absolute lymphocyte count median of 1,200 cells per ml. The median HIV viral load was 10.8×10^4 copies per ml. Over 43% of the cases were ART naive at study entry. Conversely, over 44% of patients were on HAART at study entry. As of December 2003, 168 of the 356 study patients (47.2%) were dead. This mortality was slightly lower than that reported for the overall RRC cohort (52.5%).

Group differences

Table 1 presents the most relevant parameter differences between the 193 HCV coinfected and the 163 not coinfected patients. Both groups had similar mean age (37.1 ± 7.9 vs. 38.2 ± 9.7, $p = 0.256$). The coinfected group had a higher proportion of men (79.8% vs. 58.3%, $p < 0.01$) and IDUs (85.5% vs. 24.5%, $p < 0.01$). The median time of injecting drug use was similar in both groups (17.8 years in coinfected and 18.4 years in not coinfected). Men having sex with men were less frequently reported in coinfected (8.5% vs. 33.3%, $p < 0.01$).

The prevalence of the AIDS defining conditions at study enrollment were; PJP (3.1% vs. 6.1%), recurrent pneumonia (3.1% vs. 6.1%), wasting syndrome (11.9% vs. 16.0%) and esophageal candidiasis (3.6% vs. 6.1%). These conditions were lower in coinfected group although statistical significance was not reached. A higher median CD4 + cell count (189 vs. 120) and a lower median HIV viral load (10.5×10^4 vs. 11.5×10^4) were seen in the coinfected group. The HIV/HCV coinfected individuals had lesser clinical and immunological evidence of HIV infection. Antecedent of HAART at enrollment was similar in both groups (42% vs. 48%, $p = 0.207$). However, their compliance and adherence could not be measured. Conversely, the mortality rate was slightly higher in the coinfected groups (57.7% vs. 51.1%), but this difference did not reach statistical significance.

Of the 356 study cases, 205 were IDUs and 81% of them were HCV sero-positive (Table 2). Coinfected IDUs had higher prevalence of men (82.4% vs. 72.5) and lower prevalence of PJP (3.6% vs. 5.0%), recurrent pneumonia (3.6% vs. 10.0%), and wasting syndrome (12.7% vs. 27.5%) when compared to not coinfected IDUs. The median CD4+ cell count (180 vs. 120) and the HIV vial load median (10.7×10^4 vs. 10.3×10^4) were slightly higher in this coinfected group. Only the wasting syndrome difference reached statistical significance. HAART antecedent (35.8% vs. 35.0%) and mortality rates (51.5% vs. 55.0%) were similar in these IDUs' groups.

On the other hand, 28 (18.5%) of the 150 non-IDUs were positive for HCV (Table 2). These coinfected patients had lower rates of AIDS defining conditions, higher CD4+ cell count median (210 vs. 128, $p < 0.05$), lower HIV viral load median (8.3×10^4 vs. 11.5×10^4copies) and higher antecedent of HAART used (78.6% vs. 52.0%, $p < 0.05$), than the not coinfected, non-IDUs. Mortality rate was slightly higher in this coinfected group (42.9% vs. 39.8%, $p > 0.05$). In addition, the study found a higher HCV viral load median in coinfected

cases who were IDUs when compared to non-IDUs (50×10^4 vs. 31.6×10^4 copies/ml). However, this difference was not statistically significant.

HCV genotypes

Of the 193 coinfected study cases, 164 were tested for HCV genotype. Genotype 1 was the most prevalent (82.3%), followed by genotype 3 (8.5%), genotype 4 (3.7%) and genotype 2 (3.1%). In four cases (2.4%) the genotype was indeterminate. In those where the genotype was determinate, the most prevalent virus subtypes were: 1a (53.1%), 1b (31.3%) and 3a (8.9%). Genotype 1 was more prevalent in the IDUs than in the non IDUs (88.9% vs. 80.0%). Patients with genotype 1 had higher HCV viral median load (53×10^4 copies per ml vs. 40.1×10^4 copies per ml), higher HIV viral median load (12.7×10^4 copies per ml vs. 4.9×10^4 copies per ml) and lower CD4+ cell count median (188 cells per ml vs. 200 cells per ml) (data not shown). These differences did not reach statistical significance. We did not detect any other changes in the morbidity or mortality of patients when analyzed according to HCV genotypes.

Mortality

As of December 31, 2003 a total of 168 of the 356 study cases were known to be dead. A Cox proportional hazard analysis revealed that patients with a CD4+ cell count of less than 200/ml, or with antecedents of wasting syndrome had a significant increment in the mortality risk (Table 3). The antecedents of HAART and PJP prophylaxis at study entry produced a non significant decrement in the mortality risk. It can also be stated that the presence of HCV coinfection or the IDU as a risk factor produced a non significant increment of the mortality risk. In the analysis of causes of death, several significant differences were seen between HIV/HCV coinfected and not coinfected persons. Of the 168 patients who died, 97 (57.7%) were HCV positive and 71 (42.3%) were HCV negative. As shown in Table 4, male gender (83.5% vs. 57.7%) and the antecedent of IDU were more prevalent in the coinfected death cases (87.6% vs. 31.0%). Men having sex with men were associated with a lower mortality in the coinfected cases (6.2% vs. 29.3%). Coinfected death cases had longer HIV disease duration (4.1 years vs. 3.2 year), slightly higher antecedent of HAART (40.2% vs. 36.6%) and lower AIDS prevalence (68.0% vs. 88.7%) at study entry than not coinfected death cases. Causes of death related to hepatic dysfunction, cirrhosis or failure were significantly higher in the HCV infected persons (19.6% vs. 1.4%). In general, the presences of gastrointestinal conditions as causes of death were seen more often in the coinfected patients as compared to the other group (28.9% vs. 9.9%). Liver related dysfunction as a cause of death was more commonly reported in patients infected with HCV genotype 1 as compared to other HCV genotypes (19.1% vs. 7.7%, $p > 0.05$) (Data not shown). On the other hand, coinfected cases had significantly lower rate of pulmonary conditions such as pneumonia (38.1% vs. 57.7%) reported as the cause of death in their certificates as compared to the non-coinfected group.

DISCUSSION

The implementations of HAART along with an increase in the presence of chronic conditions of the HIV survivors are producing important changes in the natural history of HIV/AIDS. These changes deserve evaluation. The coinfection with HIV and HCV is emerging as an important and frequent finding in patients seeking therapy for one or the other viral entity. The fact that both viruses share a similar route of transmission and mechanisms of epidemic spread appears to be the most important reason for the growing nature of the coinfection.[20--22] It is known that the highest prevalence of the coinfection is occurring in patients with a current or previous history of injecting drug used. The HIV cohort of the Bayamón RRC is characterized by a high prevalence of IDUs; as such the

expanding nature of this coinfection becomes an important issue for our health care delivery system. Our data revealed a coinfection prevalence of 54% for the entire group and 82.5% in the IDUs. These findings are consistent with other published information, reporting a high prevalence of the coinfection associated to the risk scenario and risk practices of IDUs.[11--13] MacDonald and collaborators reported an HCV prevalence over 50% among this high-risk group and Sulkowski and collaborators found a coinfection prevalence of 44.6% among 1,955 cases of the John Hopkins HIV cohort.[11,26]

Similar to the overall RRC cohort, we found a high mortality rate in the study group; despite that no significant mortality differences between coinfected and not coinfected patients were detected. The similarities in their clinical, immunological and therapeutic profile at enrolment could explain this finding. However, comparable findings were previously reported by Sulkowski and collaborators. These authors did not find evidence that HCV coinfection alters significantly the risk of dying or developing AIDS in their HIV study group.[26]

Klein and collaborators argued that the prevalence of IDU increases the morbidity and mortality of HCV infection and prevents an improved health care outcome for this patients.[27] In our study we did not find a significant morbidity or mortality variation between HCV coinfected individuals with and without this risk behavior. On the other hand, contrary to the study of Klein and collaborators in which active drug use was unknown, 77% of our IDUS were actively using drug. Nevertheless, the common presence of injecting drug use, with its social, clinical and psychological dimensions adds an element of therapeutic complexity which needs to be included in the management of these patients with risky lifestyles and behaviors. In addition, the low HAART adherence and the fear of increasing rate of HIV viral variants may allow a worse outcome in this population.[27]

Even though our mortality rates were not significantly different between groups, HCV coinfection introduced significant variation in the causes of death amongst the study groups. HCV coinfection produced a chronic liver damage in HIV patients and over 15% of them developed a severe liver damage or cirrhosis. [28--34] Additionally, HIV/HCV coinfection has been associated with more rapid liver failure progression.[26] The present study found that 10% of coinfected patients developed severe hepatic conditions which likely led to their demise. This specific hepatic related mortality was higher than that reported in previous studies.[2,26] For example, Darby and collaborators reported a 6.5% of death related to liver damage in their coinfected hemophilic patients.[2] This high prevalence of hepatic damage in our group suggests the possibility that some of these patients had been coinfected for long time prior to study enrollment. Furthermore, there were no routine HCV screening tests for our patients prior to the present study.

HCV genetic heterogeneity is a known hallmark of this infection. While genotype “1a” is the most common in our study, genotype “1b” was more commonly reported in the US mainland.[35] This geographic variation could be related to the way patients have acquired the HCV infection. Genotype “1b”, spreads more frequently by blood transfusion while genotype “1a” is more frequently related to the injecting drug use risky practice.[29,35] The higher prevalence of genotype “1a” in our study is in concordance with the high prevalence of IDUs in this group. Prior studies have reported a higher morbidity and mortality in HCV patients attributed to the genotype 1 virus.[10,11,36,37] In addition, HCV genotype 1 has been related to a lower response to the anti- HCV pharmacological therapy.[37,38] Our study found that coinfected patients with HCV genotype 1 presented more often liver related death than patients coinfected with other genotype. However, the mortality rates were not significantly different between patients coinfected with different HCV genotypes. On the other, hand, this study could not evaluate the relationship between HCV genotypes and anti-HCV therapy

outcome because none of the coinfected cases reported the use of antiviral therapy for HCV. HCV therapy in HIV infected persons has substantial complications due to potential drug interactions and treatment related toxicities.[26,39--46] The high prevalence of IDUs in the coinfected patients introduce additional barriers for HCV therapy. The initiation and evaluation of anti-viral therapy for HCV in coinfected patients remains an important challenge particularly for centers, like ours, that provide care to medically indigent patients.

The present study had some limitations which could introduce potential biases. These biases could have affected the results and their interpretation. First: This was a prevalence and not an incidence study. Thus the real disease duration is this study could not be estimated. This issue could explain the high mortality found after a short period of follow up. On the other hand the clinical, immunological and therapeutic measures were gathered at the time the HCV testing was performed. No further measures were obtained. Consequently the effects of the change of these variables through time were not evaluated. Second: The study group was selected by convenience and not randomized. This issue could introduce some selection biases. And third: No liver function tests such as SGOT or SGPT were measured. The adherence and compliance to anti retroviral therapy were also not measured. Consequently, we could not evaluate the impact of these variables in the study group.

Knowledge about the interaction between HIV and HCV infections has become increasingly crucial to public health.[7,22,26] Lack of knowledge in this area generates delay in the opportune diagnosis and treatment of HCV, which could increase the possibility of severe target organ damage such as the one detected in our patients. Most of our cases became aware of their coinfection with their participation in our study, probably years after their initial HCV inoculum. The urgent implementation of primary and secondary HCV prevention strategies in HIV infected population is essential and necessary to reduce the rate of coinfection and its complications, especially in those persons with high risks behavior. Until now there is no vaccine to prevent the HCV infection; however risk reduction intervention could reduce the virus dissemination and opportune HCV medical treatment could reduce the extent liver damage caused by the HCV. On the other hand, the high mortality and the low prevalence of HAART and PJP prophylaxis in this group of immunocompromised patients illustrate the present limitations of their HIV management. Most of these peoples were medically indigent with financial barriers that could affect directly and indirectly their HIV management. Nevertheless, additional efforts are needed to improve HIV management in order to prevent or reduce future disease complications.

Finally, further studies need to be done in HIV/HCV coinfection, in order to explore in more detail the current prevention strategies and the therapeutic management of this condition. Another area that needs extensive research is the potential detrimental effects of repeated re-inoculums, with both viruses, in the context of IDUs.

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Abbreviations

HCV	Hepatitis C
IDU	Injecting Drug User
HIV	Human Immunodeficiency Virus

ART	Antiretroviral therapies
HAART	Highly Active Antiretroviral Therapy

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Table 1

Demographic, risk factor, clinical manifestation and laboratory findings in the HIV infected patients group, by HCV coinfection

Parameter	HCV (+) (n=193)	HCV (−) (n=163)	p-value
Sex (%)			
Males	79.8	58.3	< 0.01
Mean age (years)	37.1±7.9	38.2±9.7	0.256
Risk Factors			
IDU (%)	85.5	24.5	< 0.01
IDU length median (years)	17.8	18.4	0.718
Man with man sex (%)	8.5	33.30	< 0.01
Laboratories (median)			
CD4 + cells count/ml	189	120	0.261
CD8 + cells count/ml	665	630	0.681
CD4/CD8 Ratio	0.24	0.22	0.796
WBC cells/ml	5.400	5.500	0.821
HIV viral load/ml	105,760	115,020	0.241
HCV viral load/ml	500,000	n/a	
Clinical findings (%)			
PJP^H	3.1	6.1	0.170
Pulmonary tuberculosis	1.0	1.8	0.664
Cerebral toxoplasmosis	5.7	6.1	0.862
Recurrent pneumonia	3.1	6.1	0.170
Kaposi sarcoma	0.5	0.6	1.000
Wasting syndrome	11.9	16.0	0.271
Esophageal candidiasis	3.6	6.1	0.269
Pulmonary candidiasis	0	1.2	0.209
Immunological AIDS	52.2	62.7	0.050
AIDS (Total)	61.8	68.7	0.165
Treatments (%)			
HAART at enrollment	42.0	47.9	0.266
PJP^H prophylaxis	16.6	28.2	< 0.01
Outcome (%)			
Mortality rate	57.7	51.1	0.207

PJP^H: *Pneumocystis jirovecii* Pneumonia

Table 2

Demographic, risk factor, clinical manifestation and laboratory findings in IDUs and in No-IDUs HIV infected patients, by HCV coinfection

Parameter	IDUs HCV (+/−) (n=165/40)	Not-IDUs HCV (+/−) (n=28/123)
Sex (%)		
Males	82.4/72.5	64.3/53.7
Risk Factors (%)		
Man with man sex	3.7/20.7**	35.7/30.0
Laboratories (median)		
CD4 + cells count/ml	180/120	210/128♦
CD8 + cells count/ml	640/440*	819/675
CD4/CD8 Ratio	0.22/0.22	0.37/0.22
WBC cell/ml	5,450/6,700	5,350/5,300
HIV viral load/ml	107,370/102,860	83,630/115,020
HCV viral load/ml	500,000/ -	315,890/ -
Clinical findings (%)		
PJP[H]	3.6/5.0	0/6.5
Pulmonary tuberculosis	1.2/2.5	0/1.6
Cerebral toxoplasmosis	6.7/7.5	0/5.9
Recurrent pneumonia	3.6/10.0	0/4.9
Kaposi sarcoma	0/0	3.6/0.8
Wasting syndrome	12.7/27.5*	7.1/12.2
Esophageal candidiasis	4.2/5.0	0/6.5
Immunological AIDS	52.9/69.2	48.1/60.7
AIDS	61.8/67.5	60.7/69.1
Treatments (%)		
HAART at enrollment	35.8/35.0	78.6/52.0♦
PJP[H] prophylaxis	15.2/17.5	25.0/31.7
Outcome (%)		
Mortality rate	51.5/55.0	42.9/39.8

* p-value < 0.05 between HCV (+) and HCV(−) in IDUs

♦ p-value < 0.05 between HCV(+) and HCV(−) in No-IDUs

♦♦ p-value < 0.01between HCV(+) and HCV(−) in No-IDUs

PJP [H]: *Pneumocystis jirovecii* Pneumonia

Table 3

Cox proportional hazard regression analysis: Mortality in 356 HIV infected patients

Parameter	Mortality risks	95% C.I.*	p -value
Female	1.033	0.715–1.492	0.864
IDU	1.069	0.708–1.614	0.751
CD4+ cells count < 200	2.446	1.471–3.581	< 0.01
PJP^H	1.784	0.931–3.418	0.08
PJP^H prophylaxis	0.751	0.492–1.146	0.185
Cerebral toxoplasmosis	1.483	0.830–2.647	0.183
Wasting syndrome	3.566	2.431–5.228	< 0.01
Hepatitis C	1.167	0.790–1.724	0.437
HAART at enrollment	0.802	0.568–1.132	0.201

C.I. = Confidence Interval

PJP^H= *Pneumocystis jirovecii* Pneumonia

Table 4

HIV death cases differences, by HCV coinfection

Variables	HCV(+) (n=97)	HCV(−) (n=71)	p –value
Sex (%)			
Male	83.5	57.7	< 0.01
Mean time (years)			
Mean age at death	40.8	37.6	0.059
Mean time of follow up	1.28	0.88	0.05
Mean HIV duration	4.1	3.2	0.11
Risk Factor (%)			
IDU	87.6	31.0	< 0.01
Man with man sex	6.2	29.3	< 0.01
AIDS (%)			
At enrollment	68.0	88.7	< 0.01
Treatments (%)			
HAART at enrollment	40.2	36.6	0.637
PJP prophylaxis at enrollment	17.5	23.9	0.306
Death causes (%)			
Cardio vascular conditions	9.3	9.9	0.899
Pulmonary conditions	38.1	57.7	0.012
Gastro intestinal conditions	28.9	9.9	0.003
Liver damage	19.6	1.4	< 0.01
Renal condition	8.2	7.0	0.773
Metabolic conditions	10.3	7.0	0.463
Neurological conditions	7.2	9.9	0.540
Drug overdose-Poisson	10.3	1.4	0.021
PJP^{H}	3.1	5.6	0.416
Cerebral toxoplasmosis	8.2	12.7	0.347
Wasting syndrome	5.2	9.9	0.242

PJP^{H}= *Pneumocystis jirovecii* Pneumonia