

Prevalence of hepatitis C among HIV-1, HIV-2 and dually reactive patients: A multi-country cross-sectional survey in West Africa

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Abstract

Little is known on the impact of HIV-2 infection on HCV viral replication. The aim of the study was to compare HCV prevalence and viral replication based on HIV types in West Africa.

A cross-sectional survey was conducted within the IeDEA HIV-2 West Africa cohort from March to December 2012. All HIV-infected adult patients who attended participating HIV clinics during the study period were included. Blood samples were collected and re-tested for HIV type discrimination, HCV serology and viral load.

A total of 767 patients were enrolled: 186 HIV-1, 431 HIV-2 and 150 HIV-1&2 dually reactive. At time of sampling, 531 (69.2%) were on ART and median CD4+ cell count was 472/mm³. Thirty (3.9%, 95% CI 2.7-5.5) patients were anti-HCV positive (4.3% in HIV-1, 4.0% in HIV-1&2 dually reactive and 3.7% in HIV-2; $p=0.91$). Detectable HCV RNA was identified in 21 (70.0%) patients (100% in HIV-1 and HIV-1&2 dually reactive vs. 43.8% in HIV-2; $p=0.003$).

Systematic screening should be promoted and performed in this population, since HCV is now potentially curable in sub-Saharan Africa.

Introduction

Hepatitis C virus (HCV) infection is a growing public health concern^{1,2} in resource limited settings. In Sub-Saharan Africa (SSA), a recent meta-analysis estimated the HCV prevalence at 3.0% (95% CI 2.9–3.1), varying from 6.8% (95% CI 6.0–7.6) in the Central African region to 4.3% (4.0–4.7) in West Africa and 0.9% (0.8–1.0) in Southeast Africa.³ Chronic HCV infection has been strongly correlated to the development of hepatocellular carcinoma (HCC).^{4,5} Thus, all efforts must be made to prevent and control this disease.

West Africa is also characterized by a high prevalence of HIV and the circulation of both HIV type 1 and 2, which can lead to co-infections with HIV-1 and HIV-2 (HIV-1&2).⁶⁻⁸ Due to shared routes of transmission, HCV and HIV co-infection is common and globally 6.0% of HIV-infected people are co-infected in SSA, with some regional differences.^{1,2} Co-infection with HIV adversely affects the course of HCV infection, and co-infected people, particularly those with advanced immunodeficiency have a significantly accelerated progression from liver disease to cirrhosis and hepatocellular carcinoma than HCV mono-infected people.⁹⁻¹² Therefore, HCV screening is very important among HIV-infected patients especially with the availability of new, highly effective anti-viral treatments that can cure HCV.^{13,14} To our knowledge, only one small-scale study from Guinea Bissau has estimated the prevalence of HCV co-infection according to HIV types and did not find any difference between HIV-1 and HIV-2.¹⁵

The objectives of this study were to estimate the prevalence of HCV according to HIV types in the West Africa Database on Antiretroviral Therapy (WADA) HIV-2 cohort in two West African countries and to identify risk factors for HCV positivity.

Materials and Methods

A cross-sectional survey was conducted from March to December 2012 in two countries (Burkina Faso and Côte d'Ivoire) within the WADA HIV-2 cohort. The method of this survey was described in details elsewhere.¹⁶

This cohort is embedded in the International epidemiological Database to

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Contributions: DKE, PAC and BT conceived the study, participated in its design and coordination, performed the statistical analyses and wrote the first draft of the manuscript. AJ, AP, FD and SPE participated in the design of the study and helped to draft the manuscript. FD is the Primary Investigator of the IeDEA West Africa (WADA) cohort. All authors read and approved the final manuscript.

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Evaluate AIDS (IeDEA) West Africa Collaboration, which is part of the global IeDEA network.¹⁷ All patients aged 18 years and above, registered in the WADA cohort as HIV-2 or dually reactive, who attended one of the participating clinics during the study period and who agreed to participate were included in this survey regardless of ART initiation according to WHO 2010 guidelines.¹⁸

A standardized survey form was used to collect data on patients' demographics, clin-

ical and biological characteristics. Two EDTA tubes of blood were collected from each patient and sent to the referral laboratory of the study (CeDReS, Treichville Hospital in Abidjan, Côte d'Ivoire) to perform HIV type discrimination and hepatitis analyses. All patients identified as HIV-2 or dually reactive on clinical site according to the national algorithms were screened *de novo* with two immuno-enzymatic tests: Immunocomb II HIV 1 & 2 BISPOT (Organics Ltd. Yavne, - Alere), a World Health Organization (WHO)-endorsed indirect, immuno-enzymatic test (sensitivity 100%; specificity 99%)¹⁹ and an in-house ELISA test, developed by the French National Aids and Viral Hepatitis Research Agency (ANRS).²⁰ The results of this rescreening were previously reported.²¹ The aim of this retesting was to perform an accurate HIV type discrimination, since HIV type misclassification has previously been reported in many West African cohorts, especially for HIV-1&2 dually reactive patients.²²

HCV antibodies (anti-HCV) was done using a sequential algorithm with two tests: screening was performed using DIA.PRO

HCV Ab Version 4.0 (DIA.PRO Diagnostic Bioprobes Srl, Italy). A second serological test was used as confirmation: INNOTEST® HCV Ab IV (INNOGENETICS N.V, Belgium) a 4th generation enzyme Immuno assay. Samples with positive HCV serology were tested for HCV viral load quantification by PCR using the COBAS(R) AmpliPrep/COBAS(R) TaqMan(R) v2.0 Roche® kit.

The prevalence of HCV was expressed with a 95% confidence interval (95% CI). Groups' comparisons were performed using Student's t test or non-parametric Wilcoxon rank-sum test (non-normal distribution) for continuous variables and using Chi-2 test or Fisher's exact test for categorical variables.

This survey was approved by the national ethics committee of each participating country: the *Comité d'Ethique pour la Recherche en Santé au Burkina Faso* (CERS_BF) in Burkina-Faso and the *Comité National pour l'Ethique et la Recherche en Santé* (CNER_CI) in Côte d'Ivoire. All patients were informed and had to give their written consent before being included in the study.

Results

From March to December 2012, 767 HIV-positive patients were included in this study: 232 (30.2%) from Burkina Faso, 535 (69.8%) from Côte d'Ivoire. The population consisted of (made of) 186 (24.2%) HIV-1 patients, 431 (56.2%) HIV-2 and 150 (19.6%) as HIV-1&2 dually reactive. At time of sample collection, the overall median age was 47 years [IQR: 40-53], 453 (59.1 %) were women; median CD4+ cell count was 472 cells/mm³ [IQR: 294-644]; 531 (69.2%) were on ART with 3.6 years [IQR: 1.9-6.2] median duration on ART.

Thirty patients were tested positive for anti-HCV giving a anti-HCV prevalence of 3.9% (95% CI 2.7-5.5). This rate did not significantly vary according to neither HIV type (4.3% in HIV-1, 4.0% in HIV-1&2 dually reactive and 3.7% in HIV-2; p=0.91), nor gender (4.8% in males vs. 3.3% in females; p=0.35) (Table 1).

However, the prevalence of anti-HCV positivity varied based on the country (7.8% [95% CI, 4.7%-11.1%]) in Burkina Faso and 2.2% [95%CI, 1.2%-3.9%] in Côte d'Ivoire; p=0.001).

Table 1. Characteristics of patients at time of blood collection by Hepatitis viral C status – Burkina Faso, Côte d'Ivoire and Mali – IeDEA West Africa cohort (2012).

Variables	Total N=767	Detectable HCV RNA N=21	Undetectable HCV RNA N=9	Anti-HCV negative N=737	P*	P**
Age (years)						
Median [IQR]	47 [40-53]	50 [39-54]	46 [43-51]	47 [40-53]	0.88	0.62
≤30	39 (5.1)	1 (4.7)	0 (0.0)	38 (5.2)	0.73	0.79
31-49	426 (55.5)	9 (42.9)	5 (55.6)	412 (55.9)		
≥50	302 (39.4)	11 (52.4)	4 (44.4)	287 (38.9)		
Gender						
Male	314 (40.9)	11 (52.4)	4 (44.4)	299 (40.6)	0.55	1.00
Female	453 (59.1)	10 (47.6)	5 (55.6)	438 (59.4)		
Country						
Burkina Faso	232 (30.2)	15 (71.4)	3 (33.3)	214 (29.0)	<0.001	0.10
Côte d'Ivoire	535 (69.8)	6 (28.6)	6 (66.7)	523 (71.0)		
HIV-type						
HIV-2	431 (56.2)	7 (33.3)	9 (100.0)	415 (56.3)	0.02	0.003
HIV-1/2	150 (19.6)	6 (28.6)	0 (0.0)	144 (19.5)		
HIV-1	186 (24.2)	8 (38.1)	0 (0.0)	178 (24.2)		
CD4 count (cells/mm ³)						
Median [IQR]	472 [294-644]	390 [250-566]	456 [240-540]	473 [294-646]	0.49	0.84
≤200	100 (13.0)	3 (14.3)	2 (22.2)	95 (12.9)	0.48	0.62
>200	667 (87.0)	18 (85.7)	7 (77.8)	642 (87.1)		
Antiretroviral treatment						
No	236 (30.8)	2 (9.5)	3 (33.3)	231 (31.3)	0.09	0.14
Yes	531 (69.2)	19 (90.5)	6 (66.7)	506 (68.7)		
Antiretroviral regimen*						
Triple NRTI	26 (4.9)	1 (5.3)	0 (0.0)	25 (4.9)	0.82	1.00
NRTI + NNRTI	7 (1.3)	0 (0.0)	0 (0.0)	7 (1.4)		
NRTI + PI	498 (93.8)	18 (94.7)	6 (100.0)	474 (93.7)		
Antiretroviral drugs*					0.01	0.15
3TC alone	382 (71.9)	11 (57.9)	1 (16.7)	370 (73.1)		
TDF + 3TC (FTC)	121 (22.8)	7 (36.8)	4 (66.6)	110 (21.8)		
Others	28 (5.3)	1 (5.3)	1 (16.7)	26 (5.1)		

*Comparison between the three groups, **comparison between patients with detectable HCV RNA and undetectable HCV RNA.

Among the 30 patients with anti-HCV positive, 21 (70.0%) had detectable HCV RNA giving a HCV RNA prevalence of 2.7% (95% CI, 1.7-4.2). The proportion of patient with detectable HCV RNA varied based on HIV type (100.0% in HIV-1 and in HIV-1&2 dually reactive patients' vs. 43.8% in HIV-2 patients ($p=0.003$). Among the 21 patients with anti-HCV positive, the median viral load of HCV was 2.3×10^6 copies/ml, IQR [0.4×10^6 - 4.7×10^6 copies/ml] and did not vary according to HIV type ($p=0.37$).

In multivariable analysis, only the variable *country* was associated with the presence of anti-HCV positivity. The risk of anti-HCV positivity was higher in Burkina-Faso (OR=4.22, 95% CI [1.91-9.29]) compared to Côte d'Ivoire after adjusting for HIV type and CD4 count (Table 2).

Discussion

To our knowledge, this is one of the largest report up to now on HCV co-infection among HIV-positive individuals in West Africa. In this study, the prevalence of HCV infection was high (3.9%; 95% CI 2.7-5.5) based on the positivity of anti-HCV, with statistical difference by country (2.2% in Côte d'Ivoire and 7.8% in Burkina Faso) but not by HIV types.

Our estimate for anti-HCV prevalence is similar to the estimates from a recent meta-analysis conducted among HIV-positive individuals in SSA. In this study, the overall HCV prevalence among the HIV-

infected patients from West Africa was 6.7% (95% CI 4.8-8.5), with a significant difference between countries (between 9-12% in Burkina Faso and Nigeria; between 3-6% in Ghana; and <3% in Côte d'Ivoire, Mali and Senegal).¹ When considering previous studies on HCV prevalence among patients in the two participating countries, the HCV prevalence ranged between 1.1-3.3% in Côte d'Ivoire and between 2.4% and 10.0% in Burkina Faso.²³⁻²⁷ The variation of risk factors for HCV infection (e.g., scarification or medical practice...) according to geographical region, even inside a country, population studied, year of study and diagnostic assay used might explain the difference of HCV prevalence.

Our results were in accordance with the study conducted in Guinea Bissau. In this study, there was no statistical difference of the prevalence of HCV according to HIV types.¹⁵ Thus, the specificity of HIV-2 infection seems to have no impact on the transmission and the rate of HCV infection. However, we found that all (100%) HIV-1 and HIV-1&2 dually reactive patients with HCV infection had detectable viral load versus only 43.8% of HIV-2 infected patients. This interesting result needs to be further explored.

For HCV screening, it is suggested that nucleic acid testing (NAT) for HCV RNA be performed directly following an HCV positive test result to establish a definitive diagnosis of HCV infection in addition to the use of NAT as part of the evaluation for treatment eligibility.²⁸ The proportion of anti-HCV positive participants with a sig-

nificant HCV replication is consistent with previous studies from West Africa.^{15,25-27} In a recent meta-analysis conducted among HIV-positive individuals in SSA, the pooled proportion of positive serology samples that were positive for HCV RNA was 54.0% for patients from West Africa, with a variation ranging from 7.7% to 94.7%.¹

Our study confirms the high prevalence of HCV infection in West Africa. However, most of the people with HCV infection in this region have very limited access to HCV testing and thus remain undiagnosed until they have clinical symptoms of cirrhosis or HCC.²⁹ To date, it is recommended that HCV serology testing be offered to individuals who are part of a population with high HCV prevalence or who have a history of HCV risk exposure and/or behavior.²⁸ Facing the high prevalence of HCV infection among HIV-infected reported here in line with previous reports from West Africa in both HIV-infected and uninfected people HCV testing might be recommended for the general population.²⁵⁻²⁷ Approaches for large-scale HCV testing earlier in the course of disease should be identified.

Today with the availability of direct-acting antiviral agents (DAA), very effective and much less toxic, HCV infection can be cured or even eliminated.¹³ Thus, all efforts, including the availability of screening tests and NAT for HCV RNA, information and training on HCV prevention and care of general practitioners and other health care workers, must be implemented for the control or elimination of this disease.

Table 2. Factors associated with Anti-HCV seropositivity.

Factor	No. of patients with data	Anti-HCV positivity	Univariate analysis			Multivariate analysis		
			OR	95% CI	P	OR	95% CI	P
Age (years)								
31-49	426	14 (3.3)	1.29	0.17-10.09	0.81			
≥50	302	15 (5.0)	1.98	0.26-15.46	0.51			
≤30	39	1 (2.6)	1.00	-	-			
Gender								
Male	314	15 (4.8)	1.46	0.70-3.04	0.31			
Female	453	15 (3.3)	1.00	-	-			
HIV-type								
HIV-2	431	16 (3.7)	0.86	0.36-2.04	0.73	1.20	0.49-2.93	0.69
HIV-1/2	150	6 (4.0)	0.93	0.31-2.73	0.89	0.76	0.25-2.27	0.62
HIV-1	186	8 (4.3)	1.00	-	-	1.00	-	-
Country								
Burkina Faso	232	18 (7.8)	3.67	1.74-7.74	0.001	4.22	1.91-9.29	<0.001
Côte d'Ivoire	535	12 (2.2)	1.00	-	-	1.00	-	-
CD4 count (cells/mm ³)								
≤200	100	5 (5.0)	1.35	0.51-3.62	0.55	1.59	0.58-4.33	0.36
>200	667	25 (3.8)	1.00	-	-	1.00	-	-
Antiretroviral treatment								
Yes	531	25 (4.7)	2.28	0.86-6.04	0.10			
No	236	5 (2.1)	1.00	-	-			

OR: Odds ratio; CI: Confidence Interval.

Our study has some limitations. Data on certain risks of HCV infection, such as body mutilations and drug use, were not collected and genotype test was not performed. In West Africa, genotypes 2 and 1 are predominant.^{24,30-32} The representativeness of our HIV-infected population might be limited as included patients were recruited in selected HIV clinics disregarding patients not in care.²⁵⁻²⁷ Therefore, a population-based survey, involving all subgroups of HIV-infected patients, could provide a more accurate estimate of the HCV prevalence in each country. Despite these limitations, this study has also major strengths. It took place in two different West African countries and included a large sample of HIV-infected patients. In addition, HCV RNA was performed, giving therefore the proportion of chronic HCV infection.

Conclusions

HCV infection is high in West African HIV-infected patients, irrespective of HIV type. Therefore, screening should be systematically performed in HIV-positive patients to allow a better management of this co-infection. Also, since HCV is now curable with the DAA, strategies that will lead to a large-scale diagnosis and care of this disease earlier in the course of the disease are needed.

Ethics approval and consent to participate

This survey was approved by the national ethics committee of each participating country: the *Comité d'Ethique pour la Recherche en Santé au Burkina Faso* (CERS_BF) in Burkina-Faso and the *Comité National pour l'Ethique et la Recherche en Santé* (CNER_CI) in Côte d'Ivoire. All patients were informed and had to give their written consent before being included

Availability of data and materials

All of data used are available and could be requested from the authors.

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