



ORIGINAL ARTICLE

HIV and Hepatitis Coinfection among HIV-1 Infected Individuals in Republic of the Congo

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Abstract

Background: HIV and Hepatitis co-infection is common and contribute significantly to morbidity and mortality in persons living with HIV (PLWH). The objective of this study was to determine the prevalence of this co-infection in patients receiving second-line antiretroviral therapy in Pointe-Noire and Brazzaville.

Methods: A cross-sectional study was conducted between January and July 2014 to collect demographic data and perform blood sampling from consenting patients who came for routine visits in sites that provide comprehensive care for PLWH in Pointe-Noire (Centre de Traitement Ambulatoire, Hopital de Base de Tie-Tié and Hopital Général Adolph Sicé) and Brazzaville (Centre de Traitement Ambulatoire and Centre Médico-Social de l'Eglise Evangélique du Congo). Standard enzyme immunoassays were used to confirm the serological prevalence of hepatitis B (HBsAg) and C (anti-HCV antibodies) using of the Hepa-Scan HBsAg Card Test and the Hepa-Scan HCV Card Test kits, respectively.

Results: Out of a total of 261 HIV-positive patients, women accounted for more than half (55.17%), and slightly more than half (54.88%) were older than 40 years. Regarding co-infection, 4.21% (11/261) were co-infected with HIV/HBV, 6.89% (18/261) were co-infected with HIV/HCV and 0.38% (1/261) carried all three viruses. The overall prevalence of

patients co-infected with hepatitis and HIV was 11.49%. Conversely, CD4+ cells are low, and less than 350 cells/μl stained CD4+ positive in all groups.

Conclusion: Although the rate of HIV and hepatitis co-infection seem to be low compare with what is known in sub-Saharan Africa, our results highlight the importance of screening PLWH for hepatitis in developing countries, especially in Congo.

Keywords

HIV-1, Hepatitis, Co-infection, Republic of Congo

Introduction

Human immunodeficiency virus (HIV), hepatitis B (HBV) and hepatitis C (HCV) infections are common worldwide and are a major public health problem [1]. The similarity of their transmission pathways (unprotected sex, blood transfusion, injecting drug use, mother-to-child transmission) probably explains the high frequency of co-infections of these viruses [1,2].

Globally, WHO estimates that 325 million people live with chronic HBV or HCV infection, with 50% living in

Africa and Southeast Asia [3]. Although HCV infection spares no Region, there are major differences between countries but also within a country [3]. The Joint United Nations Program on HIV/AIDS (UNAIDS) 2017 report indicates that in 2015, of the 36.7 million people living with HIV worldwide, 2.7 million are also chronically infected with HBV and 2.3 million are infected with HCV [4]. These co-infections accelerate the progression of hepatic diseases in HIV-positive patients [3,5]. Indeed, HIV infection exacerbates the prognosis of HBV and HCV infection, with a faster progression of fibrosis and the development of cirrhosis and hepatocellular carcinoma [6-8]. It also increases the risk of maternal-fetal transmission (between 3 to 20%) and sexual transmission (up to 3%) of HCV compared with HCV mono-infection [6]. HIV/HBV and/or HIV/HCV co-infections have become important contributors to comorbidity and mortality due to the increased lifespan of patients receiving antiretroviral therapy [6]. Also, the treatment of hepatitis C among HIV patients under antiretroviral drug therapy exposes to drug interactions and requires special support [9].

In the Republic of Congo (RoC), very few studies have been done on these co-infections with most studies limited to evaluate the seroprevalence of hepatitis in blood donors and patients in hospital settings. Indeed, hepatitis B prevalence ranges from 3.27 to 20.8%, and hepatitis C infection ranges from 1.5 to 13.9% [10-15]. These rates place the Republic of Congo in an area of high prevalence for hepatitis B, and it is the country's leading cause of cirrhosis and hepatocellular carcinoma [5,13,16]. In some groups, such as female sex workers, the prevalence of hepatitis B and C are 4.2 and 0.7%, respectively [17].

Co-infections between hepatitis viruses and HIV are very common and although HBV is a DNA virus, structural similarities between HBV DNA Polymerase enzyme pocket and HIV-1 reverse transcriptase are the basis on which some drugs inhibit both enzymes and therefore the replication of both viruses. Indeed, the efficacy of the mutagenicity of HIV and HBV, although usually HIV-1 infection exacerbates the evolution of infection and the pathogenicity of hepatitis B. The opposite seems more nuanced [18]. Similarly, the significant impact of HIV co-infection on the natural history of hepatitis C has been documented by increasing the chronic rate of acute HCV infection and accelerating progression to cirrhosis, hepatic decompensation and hepatocellular carcinoma [19,20]. Similarly, regarding the therapeutic aspects, antiretroviral therapy is highly beneficial for patients co-infected with HIV/HBV and HCV, but carries a risk of developing drug-induced resistance and hepatotoxicity [18,21]. Indeed, it was documented that the drugs used in the management of HIV infection such as lamivudine (3TC), could be used for the treatment of hepatitis B infection. However, the use of this molecule alone is no longer recommended because of the emergence

of the M204V/I mutation responsible for resistance to INRT in around 20% of cases [22]. Regarding hepatitis C treatment, the therapeutic impact of this co-infection remains to be determined.

In order to further the HIV patient management in the country, this study aimed to determine the prevalence of hepatitis B and C viruses in patients receiving antiretroviral therapy in Pointe-Noire and Brazzaville.

Materials and Methods

This cross-sectional study has been conducted between January and July 2014. Patients on second-line AR vs. have been recruited at the HIV treatment centers in Pointe-Noire (Centre de Traitement Ambulatoire, Hôpital de Base de Tié-Tié and Hôpital Général Adolph Cisé) and Brazzaville (Centre de Traitement Ambulatoire « CTA » and Centre Médico-Social de l'Eglise Evangélique du Congo). These centers were selected because they receive 95.63% of all patients on second-line AR vs., according to the audit of patients currently receiving care in 2013 [16]. The Table 1 shows the number of patients followed per site and the number of patients included in the study from the active queue.

The criteria used were that patients must: i) Voluntarily accept to participate in the study on the basis of informed consent; ii) Be on second-line AR vs. treatment for at least one year at the date of consent and iii) be \geq 18-years-old.

Due to the relative small number of patients on second-line treatment (Table 1), all patients were included into the study in some treatment centers. Both the Hôpital de Base de Tié-Tié and Hôpital Général Adolph Cisé in Pointe-Noire had small numbers of participants. In Brazzaville, at the Ambulatory Treatment Center and CMS-EEC center, patients were included randomly and consecutively for 7 months.

After inform consent was obtained, clinical and demographic data such as age, sex were recorded through interviews or by consulting the medical records. For each patient, 5 ml of whole blood were collected in EDTA tube containing as an anticoagulator of which 50 μ l of whole blood was used for CD4+ T cell counting through the FacsCount automaton (Becton Dickinson, San Jose, California, USA), and the remaining blood was centrifuged at 5000 rpm for 5 minutes to collect the plasma. All plasma samples were tested for HBV and HCV using the Hepa-Scan HBsAg Card Test and Hepa-Scan HCV Card Test kits (M/s Bhat Biotech India Pvt., Bangalore. Category: RAPID) respectively. In case of positive result, the confirmation tests namely Monolisa™ HBsAg ULTRA ELISA Kit for Hepatitis B and Monolisa™ HVC Ag-Ab ULTRA for Hepatitis C (Bio-Rad Monolisa HBV Ultra and Bio-Rad Monilisa HCV Ultra, Marne la Coquette, France, respectively) were used.

The data were collected in a Microsoft®Excel spreadsheet (2010 release), and statistical analysis

Table 1: Number of patients included per treatment center according to the number of patients by sites evaluated in 2013 [16].

Study sites	Total patients of the 2 nd line of the active queue	Patient included	
		N	%
Centre de traitement ambulatoire of Pointe-Noire	138	56	40.58
Hôpital de base Tie-Tié	29	29	100.00
Centre de traitement ambulatoire of Brazzaville	155	110	70.97
A. Sicé General Hospital	25	25	100.00
Centre Medico social Mayangui (ECC)	60	41	68.33
Total	407	261	64.13

Table 2: Distribution of patients with HIV and HIV/hepatitis co-infection: prevalence, age and clinical characteristics.

Characters	HIV-only (%)	HIV/HBV (%)	HIV/HCV (%)	HIV/HBV/HCV (%)	Total
Total (%)	231 (88.51)	11 (4.21)	18 (6.9)	1 (0.38)	261
M	81 (90.01)	3 (3.33)	6 (6.66)	0	90
F	132 (91.66)	6 (4.17)	6 (4.17)	0	144
Not done	18 (66.67)	2 (7.41)	6 (22.22)	1 (3.7)	27
Age (years)	41 ± 13	40 ± 11	44 ± 13	0	41 ± 13
M	43 ± 16	46 ± 16	49 ± 21	0	42 ± 15
F	40 ± 12	36 ± 8	40 ± 12	0	41 ± 13
Not done	22	2	6	1	31
CD4+ cells/μl	305 ± 245	316 ± 176	245 ± 206	0	305 ± 245
M	249 ± 194	446 ± 126	302 ± 249	0	249 ± 194
F	340 ± 266	237 ± 160	176 ± 131	0	340 ± 266
Not done	36	3	7	1	47

was done using SPSS software version 19.9.

Ethical Considerations

All eligible patients gave their written consent to participate in the study prior to collection of demographic data and samples. Therefore, a statement summarizing the objectives of the investigation was read to each individual, in French or in one of the two national languages (Lingala and Kituba). The interviews were conducted in private to ensure the confidentiality of the information collected. The study obtained ethical clearance from the Comité d’Ethique pour la Recherche en Sciences de la Santé.

Results

Demographic characteristics of the study population

A total of 261 patients were included into the study. In both cities, the largest inclusions were recorded in CTA’s comprising more than 67.43% of all patients (Table 1).

A majority of patients were women (55.17% vs. 34.48%). Gender was not reported in 10.34% cases. Regarding the age, the majority of the patients (54.88%) had a mean age of 41 ± 13 years as detailed in Table 2. The majority of patients (57.85%) included came from Brazzaville, and 42.15% were from Pointe-Noire.

Prevalence of hepatitis B and C

In this study, 11 patients (4.21%) were positive for HBV, and 18 (6.89%) for HCV. However, only one patient (0.38%) was co-infected with HIV/HBV/HCV as shown in Table 2. The overall prevalence of HIV and HBV or HCV co-infection in the population was 11.49%; and 90% of men and 91.66% of women were not co-infected with neither HBV nor HCV.

The prevalence of HBV was 3.33% in men and 4.17% in women. In 7.41% of positive cases, the sex was not recorded. Similarly, 6.66% of men, 4.17% of women and 22.22% of non-recorded gender were co-infected with HCV.

Biological features

A mean CD4+ count was found in the HIV/HBV patient group (316 cells/μl vs. 245 cells/μl for HIV/HCV, pvalue). An average of 305 cells/μl expressing CD4 was detected in patients that are not infected with hepatitis viruses. The distribution by sex shows that the average number of CD4+ cells is higher in women than in men (340 cells/μl vs. 249 cells/μl) regardless the type of co-infection. Similarly, in non-co-infected women, the mean number of CD4+ cells was higher (340 cells/μl vs. 249 cells/μl). However, an inverse trend is observed in the groups of patients co-infected with HIV/HBV and HIV/HCV that favors men (446 cells/μl vs. 237 cells/μl and 302 cells/μl vs. 176 cells/μl, respectively).

Table 3: Distribution of HIV/hepatitis co-infection in patients under second-line ARVs by town and center.

Town	Center	HIV	HIV/HBV	HIV/HCV	HIV/HBV/HCV	Total
		N (%)	N (%)	N (%)	N (%)	N (%)
Pointe-Noire	CTA-PN	44 (78.57)	4 (7.14)	8 (14.29)	0	56 (50.91)
	HBTT	25 (86.21)	1 (3.45)	3 (10.34)	0	29 (26.36)
	HGAS	25 (100)	0	0	0	25 (22.73)
Total		94 (85.45)	5 (4.55)	11 (10)	0	110 (100)
Brazzaville	CTA-BZV	98 (89.09)	6 (5.45)	5 (4.55)	1 (0.91)	110 (72.85)
	CMS-EEC	39 (95.12)	0	2 (4.88)	0	41 (27.15)
Total		137 (90.73)	6 (3.97)	7 (4.64)	1 (0.66)	151 (100)

The comparison by town shows that 90.73% of patients were mono-infected in Brazzaville compared to 85.45% in Pointe-Noire (Table 3). Consequently the co-infections were prevalent in Pointe-Noire compared to Brazzaville (4.55% vs. 3.97% for HIV/HBV and 10% vs. 4.64% for HIV/HCV). The only patient with HIV/HBV/HCV co-infection was from Brazzaville.

Discussion

To our knowledge, this is a first study reported the prevalence of hepatitis among HIV patients under second-line AR vs. treatment in the Republic of Congo.

Increasing access to highly active antiretroviral therapy (HAART) in developing countries such as the Republic of Congo has led to a significant improvement in the quality of life of people living with HIV/AIDS [1,23,24]. However, co-infection with HBV and/or HCV has been shown to contribute significantly to morbidity and mortality in the seropositive population [1,24]. These co-infections increase the risk of hepatotoxicity in antiretroviral therapy and the likelihood of opportunistic infection [25,26].

The current study shows a female predominance (55.17%) of HIV consistent with the feminization of the infection observed at the national level, where more than 67% of HIV-infected subjects are women [16]. The study conducted in Cameroon, one of the neighboring countries, have also shown a predominance of women receiving second-line treatment [27]. UNAIDS reports that twice as many women as men are infected in sub-Saharan Africa [28], correlating with the increased vulnerability of women to HIV infection [29]. More than 47% of the study population have the age between 20 and 49-years-old, with the majority between 40 and 49-years-old. These observations corroborate other data from the national seroprevalence survey conducted in 2009 [30]. Regarding the HBV infection, the current rate of 4.21% was, similar to those reported by Niama, et al. [17], in contrast, to other studies that have reported higher prevalence [10-13]. These conflicting data provided in this country maybe due to the difference of the study population. However, the current prevalence corroborate reports in Africa, specifically in the DRC, with a co-infection rate of 5.5% [31], 4.2% in

Nigeria [32], 4.26% in Kenya [24] and 4.7% in Ethiopia [33]. Unlike the WHO distribution placing the Republic of Congo a high prevalence area (greater than 8%) [5], the current shows a tendency towards a decrease in the prevalence of HBV infection. This decrease could be explained by the reduced risk of blood transfusions of hepatitis B probably associated with increased immunization coverage in the Republic of Congo.

Regarding the HCV, few data are available on HIV/HCV co-infection in RoC. In the current study, we report a prevalence of 6.9%. This result concurs with other studies that report variable prevalence ranging between 0.7 and 13.9% [14,17]. Similar prevalences were found in Cameroon and Gabon [34,35]. These results, remain below to the WHO estimates and probably reflect a downward trend from previous studies. This trend could be explained by the low incidence of intravenous drug use, one of the main routes of transmission of the HCV. Indeed, it has been shown that in the Republic of Congo, sexual transmission was not the preferred route for HCV infection [17]. However, the lack of an effective vaccine against HCV infection makes all efforts fragile to prevent and control this infection.

Only one case of triple infection (0.38%) was reported in this study. Similarly low rates of triple infection were reported in Kenya (0.15% and 0.30%) and in Nigeria 0.7 [24,36,37]. This prevalence is linked to the low frequency of injecting drug abuse. However, the true prevalence of this triple infection remains to be determined.

The mean CD4+ values of the three groups (HIV-only, HIV/HBV and HIV/HCV) show that they are less than 350 cells/mm³, a sign of some immune deficiency [38]. Given the low number of patients co-infected with HIV/ HBV and HIV/HCV (see Table 2), it is difficult to draw conclusions. However, the trends observed in this study seem to confirm the negative impact of ARV treatment on HCV infection. Indeed, some studies indicate that antiretroviral therapy leads to a net increase in HCV viremia [6,39].

Limits of the Study

Our study has certain limitations, namely, the diffi-

culty of counting exhaustively all patients on the second line of treatment, given the absence of an updated active queue due to frequent ARV ruptures; in addition, the use of serological tests may introduce false results, as these tests do not detect recent infections, although their sensitivity is generally greater than 90%.

Conclusion

The HIV/HBV and/or HIV/HCV co-infections are a reality in the Republic of Congo. The data we report show a decrease in these co-infections rates compared to WHO estimations, with a predominance of HIV/HCV co-infection. In addition, the overall prevalence of HIV/hepatitis co-infection observed is high (11.49%). From these facts, the combined action of routine screening of these co-infections coupled with the vaccination of HBV-naïve subjects would contribute to the improvement of hepatitis B management.

However, further studies throughout the national territory will help to better understand the problems of HIV/hepatitis co-infection and its impact in the management of HIV infection in the Republic of Congo.

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Conflicts of Interest

No conflicts of interest are declared by the authors.

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Author's Contributions

FRN, PIM, ESBK, ASPDB, MND and MD conceived and designed the study, LI, LBNC, organized the data collection and finalized the manuscript. TSM performed HIV, and hepatitis testing, OIRB, MMG and HJP participated in the design and the coordination of the study; RFN and TSM drafted the manuscript. All authors read and approved the final manuscript.

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