

Epidemiological and Evolutionary Profile of HIV-HBV Co-Infected Patients Followed at Ambulatory Treatment Center in Fann Hospital Dakar-Senegal

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Abstract

Context: Human immunodeficiency virus (HIV) and Hepatitis B virus (HBV) infections are major global public health problems because of their frequency, complications and probable socio-demographic consequences.

Viral hepatitis B is identified as more frequent cause of morbidity and mortality in people living with HIV.

The objective of this study was to describe the epidemiological and evolutionary profile of HIV-HBV co-infected patients, treated at CTA/CHNU Fann, in Dakar, Senegal.

Methodology: This is a retrospective, descriptive and analytical study of patients aged at least 18 years, co-infected with HIV-HBV and followed-up at CTA under ART for at least one year from January 2010 to December 2014.

Results: The study included 457 patients. 58 of these patients were diagnosed positive, (12.7%) of HIV-HBV prevalence. The average age of patients was 39.62 ± 10.12 years with extremes ranging from 21 to 61 years. The sex ratio was 1.23. (96%) of patients were infected with HIV-1 and those at WHO stages III and IV were (67%). The average CD4 count at baseline was 235 cells/mm³ [3-936]. Plasma HIV viral load average at baseline was 4.1 log copies/ml [3.89-5.12] copies/ml. The average body mass index (BMI) was 21.42 ± 3.82 Kg/m². Fever and degraded general status were respectively (65%) and (60%) followed by hepatomegaly and jaundice. The lethality was 3.45%. Of the 58 patients co-infected with HIV-HBV, 51/58 (87.93%) were under a therapeutic regimen containing Tenofovir/lamivudine or Tenofovir/Emtricitabine and 7 patients under a regimen containing lamivudine. At 48 weeks of treatment a good evolution of the biological parameters was noted: (90%) had a controlled viral load, (91%) a normal transaminase, (79%) a normal serum creatinine. Only 29% had a CD4 cell count <350 cells/mm³.

Conclusion: The Seroprevalence of viral hepatitis B remains relatively high (12.70%) among PLHIV in Dakar. While active search for hepatitis B has been effective in all PLHIV since 2010, overall management remains a challenge as hepatitis B markers and viral DNA assay are not at the reach of patients.

Keywords: HIV/HBV co-infection, Seroprevalence

1. Introduction

Human immunodeficiency virus and hepatitis B virus (HIV/HBV) co-infection is common due to similar methods of transmission.

HBV infection in people living with human immunodeficiency virus (PLHIV) in sub-Saharan Africa is characterized by high prevalence, vertical and horizontal transmission, late diagnosis, and severe prognosis due to late diagnosis (Attia et al., 2012). In addition, the incidence of ARV-related hepatotoxicity increases with co-infection.

The prevalence of co-infection with hepatitis B virus (HBV) is high in the population of **PLVIH**. This is observed in 5 to 15% of patients infected with the human immunodeficiency virus (HIV) in the world (OMS, 2013). However, few epidemiological data are available on this co-infection (Thio et al., 2013).

In Africa, the prevalence of co-infection ranges from 20 to 30% (Atia, 2007). Vertical and perinatal transmissions are the most frequent routes, including sexual and blood transmissions.

The prevalence of occult HBV infections is underestimated (Raimondo, Caccamo, Filomia, & Pollicino, 2013). In PLHIV, the proportion of occult replication can reach 40%. This rate is estimated at 2% in mono-infected patients with HBV. It varies from 0 to 89.5% depending on the area concerned (Mehdi, Sakineh, Mohammad, Mansour, & Alireza, 2012). This occult infection is more common in PLHIV and those co-infected with HCV (Mehdi, 2013). In Senegal, studies conducted in 2008 showed 16.8% of HBV seroprevalence in PLHIV with a similar prevalence for HBV in the general population (17%) (Diop-Ndiaye et al., 2008). A study conducted at the same site in 2012 found 11% of prevalence of HBV in pregnant women (Lô et al., 2012).

HIV infection alters the natural history of HBV infection and aggravates the overall prognosis of chronic hepatitis B (Joshi, O'Grady, Dieterich, Gazzard, & Agarwal, 2011). The appearance of active pharmaceutical drugs on both HIV and HBV such as Tenofovir (TDF), Lamivudine (3TC), and Emtricitabine (FTC) have improved the survival of patients co-infected with the two HIV viruses (James, Lai, Seta, & Yuen, 2011). HAART should be initiated as soon as possible in all HBV-co-infected patients, regardless of CD4 T-cell count. Treatment should include pharmaceutical drugs with dual anti-HIV and anti-HBV activity (OMS, 2013, Mialhes et al., 2013).

The general objective of this work is therefore to determine the epidemiological, clinical, biological and evolutionary profile of patients co-infected with HIV-HBV followed at the CTA/Fann Hospital in Dakar, Senegal.

2. Method

This is a retrospective descriptive study. Patient selection was based on the database of Fann CTA/CHNU.

All patients aged at least 18 years, co-infected with HIV-HBV followed-up at CTA, on ART for at least one year from January 2010 to December 2014 were included in this study.

All patients under the age of 18, as well as those in specific research programs, were excluded from the study.

Data extraction was performed using ESOPE database on Microsoft Excel 2003, and data analysis was done using EPI-INFO version 6 software. A total of 58 patients were included.

Statistical parameters used in the analysis of the data were: frequency, proportion (with confidence interval), arithmetic average (with confidence interval), and standard deviation. We used hypothesis tests to compare the different statistical parameters. T-Student test was used to compare the different averages and the Chi-square test to compare the different proportions per group. The threshold of $p=0.05$ was considered significant.

3. Ethical Aspects

An anonymous database was compiled from medical and social records of patients at Ambulatory Treatment Center (CTA-). No information revealing the identity of the patients was included in this study. The database remains a CTA property. The study received prior approval by the head of the Clinic of Infectious Diseases.

4. Results

4.1 Epidemiological and Socio-Demographic Characteristics of the Population Studied at Inclusion

Of the 457 viral hepatitis B screening performed in PLHIV from 1 January 2010 to 31 December 2014, 58 were positive. This represents an HIV-HBV co-infection prevalence of 12.7%. Of the 58 co-infected patients, 11 were screened in 2010, 12 in 2011, 18 in 2012, 9 in 2013 and 8 in 2014.

The average age of patients was 39.62 ± 10.12 years with extremes ranging from 21 to 61 years. Our sample consisted of 32 men for 26 women with a sex ratio of 1.23. The average body mass index (BMI) was 21.42 ± 3.82 Kg/m² with extremes of 14.9 Kg/m² and 32.77 Kg/m². Patients were infected with HIV-1 in 96.55% of cases.

The median CD4 T lymphocyte at inclusion was 235 cells/mm³ [3-936]. The median plasma HIV viral load at inclusion was 4.1log copies/ml [3.89-5.12] copies/ml. The average transaminase (ALT) was 27.22 ± 25.11 UI/l at inclusion. The average creatinine levels were 10.32 ± 3.05 mg/l. The average of plates was 240189.70 ± 93899.06 /mm³ with extremes of 25000 and 457000/mm³. (Table 1)

Table 1. Socio-demographic, clinical and biological characteristics of 58 patients co-infected with HIV-HBV at inclusion

Variables	Pourcentage/Moyenne	
Sex		
Male	55.17%	
Age (years, Average±ET) and age group	39.62±10.12	30-49 ans
Lymphocytoma TCD4 (median, mm³)	235[3-936]	
VIH viral load (log copies/ml)	4.1 [3.89-5.12]	
ALAT (average ±ET, UI/l)	27.22±25.11	
Serum creatinine (average ±ET, mg/l)	10.32±3.05	
Plates (average±ET mm³)	240189.7±93899.06	
BMI (average±ET Kg/m²)	21.42±3.82	

Fever and degraded general status were the most frequent signs (65.52%) and (60.34%), respectively, followed by hepatomegaly and jaundice.

More than half of patients were at stages III and IV as per the WHO staging system, respectively (37.93% and 29.31%) (Table 2).

Table 2. Distribution of Patients according to the WHO Clinical Staging system (N=58)

WHO Staging	Percentage (%)
Stage 1	17.24
Stage 2	29.31
Stage 3	37.93
Stage 4	15.52

We noted that (32.04%) were smokers and 12/58 (20.69%) ethyl. Four patients were using hard drug (6.90%) and 30/58 (51.72%) had already developed an opportunistic disease during their progression to antiretroviral therapy (Table 3).

Table 3. Distribution of patients according to their lifestyle and ATCDS IOs

	n	%
Alcohol	12	20.69
Tobacco	18	32.04
Drug	4	6.90
Opportunistic affections	30	51.72

4.2 Patient Treatment Regimen

Of the 58 patients co-infected with HIV-HBV, 51/58 (87.93%) were under a treatment regimen containing Tenofovir/lamivudine or Tenofovir/Emtricitabine and 7 patients under the lamivudine regimen (Table 4).

Table 4. Distribution of patients according to their treatment regimen (N=58)

Therapeutic regimen	Percentage (%)
TDF+3TC/FTC+NVP/EFV	79.31
TDF+3TC/FTC+LPV/rt	8.62
AZT/ABC+3TC+LP/rt	8.62
AZT+3TC+EFV	3.45

4.3 Evolution

At inclusion, (65%) had severe immunosuppression with CD4 <350 cells/mm³, whereas after 48 weeks of treatment, only 17/58 (29.12%) were severely immunosuppressed. At 24 weeks of antiretroviral therapy, (86.21%) patients had undetectable HIV plasma viral load and (90%) after 48 weeks. Transaminases were normal in (84.48%), after 48 weeks of treatment, (91.38%) had normal transaminase levels.

Serum creatinine levels were high (≥ 13 mg/l) in (60.34%) at inclusion and 12/58 (20.6%) after 48 weeks of ARV therapy ($p = 0.43$) (Table 5).

Table 5. Distribution of patients according to changes in biological parameters at J0; 24 weeks and 48 weeks of antiretroviral therapy

Biological Parameters	J0		M6 (S24)		M12 (S48)		p-value	
	N	%	N	%	N	%		
TCD4 (μ l)	<350	38	65.00	24	41.38	17	29.31	0.002
	≥ 350	20	35.00	34	58.62	41	70.69	
CV VIH (copies/ml)	<50	-	-	50	86.21	52	89.66	0.004
	≥ 50	-	-	8	13.79	6	10.34	
ALAT (UI/l)	<40	49	84.48	50	86.20	53	91.38	0.01
	≥ 40	9	15.52	8	14.80	5	8.62	
Creatinine (mg/l)	<13	23	39.66	-	-	12	20.69	0.43
	≥ 13	35	60.34	-	-	46	79.31	

Of the 58 patients enrolled, 2 died during their progression, (3.45%) of lethality.

5. Discussion

Of the 457 B viral hepatitis tests performed in people living with HIV followed at CTA, from January 1st 2010 to December 31st 2014, 58 were positive, (12.7%) of HIV-HBV co-infection prevalence. This is obviously lower than the (16.8%) prevalence found by H. Ndiaye-Diop *et al.* in Dakar in 2008 (Diop-Ndiaye *et al.*, 2008), but similar to the prevalence found by Lô *et al.*, in 2012 (Lô *et al.*, 2012) (11%) among pregnant women living with HIV in Senegal. This decrease in seroprevalence could be explained by the effectiveness of vaccination against viral hepatitis B in Senegal and the systematic search for HBsAg in the assessment at prenatal consultations.

However, this prevalence corroborates the current global co-infection HIV/HBV trend which is 5-15% worldwide (WHO, 2015). This is higher than those found in African sources. Tremeau-Bravard, A. *et al.* in Nigeria in 2012, Muriuki *et al.* in Kenya in 2013, Kapembwa *et al.* in Zambia in 2011 (Tremeau-Bravard, Ogbukagu, Ticao, & Abubaka, 2012; Beatrice, Michael, Dorcas, Anthony, & Samoel, 2013; Kapembwa *et al.*, 2011), who found respectively 7.9%; 6%; 9.9%. On the other hand, Lukhwareni *et al.* (Lukhwareni, Burnett, Selabe, Mzileni, & Mphahlele, 2009) in South Africa in 2009, found a much higher prevalence than ours (22.9%).

The average age of patients was 39.62 ± 10.12 [21 to 61]. This is higher than the average found in available sources: 34 years in the study of Chloe L. Thio *et al.* (Thio *et al.*, 2013), 36 years in that of Attia *et al.* (Attia *et al.*, 2012), 32 years in that realized by Yitayih M. *et al.* (Yitayih, Meseret, Fanaye, & Yeshambel, 2013), 38 years in the work of H. Diop-Ndiaye *et al.* (Diop-Ndiaye *et al.*, 2008). This could be explained by the youth of the overall African population but also by the fact that the population is sexually active at this age.

In our series, there is a slight male predominance (51.17%) with a sex ratio of 1.23.

The predominant character of men in PLHIV with HBV is generally confirmed by the review of the literature. Previous work on the same site showed that men were more concerned than women $p = 0.002$. (Diop-Ndiaye et al., 2008). Taiwo Modupe Balogun et al. reported that the prevalence of HIV-HBV co-infection was higher ($p = 0.001$) in men (37.5%) than in women (24.3%) (Taiwo Modupe, Samuel, & Emmanuel Folorunso, 2012). Given explanations reveal unprotected multipartner sexual activities.

Of the 5639 HIV patients in the study of Jong Hun Kim *et al.* conducted in the USA, HBsAg seroprevalence was 4.47%. Men were the majority (80.6%). This confirms that the prevalence of HBV in PLHIV is high even in areas of low HBV prevalence (Bado et al., 2013).

Our results are different from those reported by most African authors who noted a female predominance. This is the case of Chloe L. Thio *et al.* in a multicentric study (Thio et al., 2013), G. Bado *et al.* in Burkina Faso (Kim, Pseudos, Suh, & Sharp, 2008), Nimzing Gwamzhi Laped *et al.* in Nigeria (Ladep et al., 2013), Yitayih. *et al.* in Ethiopia (Yitayih, Meseret, Fanaye, & Yeshambel, 2013) and Attia *et al.* in Cote d'Ivoire, (Attia et al., 2012).

Monogamous married patients were the most represented group (43.10%), followed by unmarried patients (24.14%).

Our results are similar to those reported by Yitayih W. *et al.* in 2013 in Ethiopia, 50% and 18% (Yitayih et al., 2013); Diombana in 2010 in Mali (Diombana, 2010) who had found 21.18% of unmarried and 19.53% married.

On the other hand, Walter *et al.* in 2007 in Italy (Walter & Miele, 2007) found a remarkable predominance of unmarried (51.50%). This difference is related to the fact that the study by Walter R. et al. focused on detainees who were predominantly young and unmarried.

In our series, fever and alteration of the general health conditions were the most visible symptoms with respectively (65.52%) and (60.34%). Ascites, hepatomegaly and jaundice were present in 19, 12 and 6 patients respectively. These results are similar to those found by Diombana S. in 2010 (Diombana, 2010).

More than half of the patients were included at stages III and II as per the WHO staging system, with (37.93%) and (29.31%) respectively.

Our results are similar to data from available sources, particularly those of DIOMBANA S. in Mali in 2010 (Diombana, 2010), ATTIA *et al.* in 2012 in Côte d'Ivoire (Attia et al., 2012) which found 20.28% and 19.87%; 47.5% and 35% respectively.

This is due to the fact that patients come to the hospital only at an advanced stage of the disease when symptoms of opportunistic infections appear.

In our series, 24.14% of patients were undernourished ($BMI < 18.5 \text{ kg/m}^2$), 15.52% overweight and 3.45% obese. John R. et al. in Rwanda in 2013 (Rusine et al., 2013) found 9.8% undernourished, 32.9% overweight and obese.

Of the 58 patients co-infected with HIV-HBV, 79.31% were on first-line ART containing Tenofovir/lamivudine or Tenofovir/Emtricitabine active for both viruses.

Diombana in Mali in 2010 (Diombana, 2010) 5.36% were actively treated on both viruses.

These contradictory results could be explained by the fact that since 2006, any patient in Senegal with an HIV-HBV co infection is treated with TDF and 3TC or FTC. This is in accordance with the WHO recommendations. As a result, our patients who were not under this regimen were put on 2nd line treatment.

The median CD4 lymphocyte at baseline was 235 cells/all [3-936]. Sixty-five percent of patients had severe immunosuppression (< 350 cells/all). This median of CD4 is similar to that of John. *et al.* in Rwanda (Rusine et al., 2013) who found a median of 222 cells/all [142-289]; Higher than that of Van Greisen J. *et al.* in Cambodia 104 cells/all [26-227] in 2013 (van Griensven, Phirum, Choun, Thai, De Weggheleire, & Lynen, 2014) but lower than that of Attia., In Ivory Coast in 2012 (Attia et al., 2012) who had a median of 341/].

The median HIV viral load at inclusion was 4.11log copies/ml [3.89-5.12]. Our results are similar to those of John. *et al.* in Rwanda (Rusine et al., 2013) and Attia *et al.* in Cote d'Ivoire in 2012 (Attia et al., 2012) who had noted 4.81log copies/ml [4.22-5.33] and 4.87log copies/ml respectively [4.15-5.45].

The average transaminase (ALT) was 27.22 ± 25.11 IU/l at inclusion. ALT was elevated in 13.52% of cases. Attia *et al.* in Cote d'Ivoire in 2012 (Attia et al., 2012), and Van Griensven *et al.* in Cambodia found lower than ours in 2013 (van Griensven et al., 2014), with respectively, 8.6% and 3.9% respectively.

6. Conclusion

The seroprevalence of viral hepatitis B remains relatively high (12.70%) among PLHIV in Dakar. Management of hepatitis B is a challenge due to the lack of public awareness of common symptoms. A low lethality of 3.45% in our patients is noted. Given the results of this descriptive work, it is necessary to conduct a multicenter, in-depth analytical study to better assess not only the profile of HIV-HBV co-infected but also the impact of antiretroviral therapy on the evolution of HBV disease.

Authors' Contributions

NGOM GUEYE Ndeye Fatou, Mahamat Bolti, Cheikh tidiane Ndour: design, data collection, statistical analysis and manuscript review. Other authors: design and manuscript review. All the authors have read and approved the final version of the manuscript.

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Competing Interests Statement

The authors declare that there is no conflict of interests regarding the publication of this paper.

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