ISSN: 2469-584X

Mayimona et al. J Clin Gastroenterol Treat 2022, 8:089
DOI: 10.23937/2469-584X/1510089
Volume 8 | Issue 2
Open Access

Journal of
Clinical Gastroenterology and Treatment

ORIGINAL ARTICLE

Factors Associated with Hepatic Cytolysis in HIV-HBV and/or HCV Coinfected Patients in Kinshasa, Democratic Republic of the Congo: Multicenter Cross-Sectional Study

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Abstract

Background and Objective: Liver cytolysis is extremely common and sometimes severe in individuals infected with human immunodeficiency virus, but data for this disorder is sketchy in the developing countries. The objective of this study is to identify factors associated with hepatic cytolysis in HIV-HVB-HCV co-infected patients in Kinshasa.

Methods: Cross-sectional and analytical study that included 180 PLWHIV mono-infected or co-infected with HBV / HCV during the period from November 10, 2013 to January 10, 2014 in the city of Kinshasa. Sociodemographic, clinical, biological, serological and immunological data were analyzed. Hepatic cytolysis was retained for elevated SGOT and / or SGPT.

Results: The mean age of the patients was 44.2 ± 11.0 years; the female sex was predominant (76.7%).The HBs antigen was positive in 6.1% of patients with Elisa. Anti-HCV antibody was found in 2.8% of patients (2.8%) on Elisa, 21.7% of patients experienced a concomitant elevation of both transaminases. Factors associated with hepatic cytolysis were age ≥50 years (adjusted OR: 2.7; 95% CI: [1.4-5.5], P =?), duration of HIV infection > 3 years (adjusted (OR: 2, 7; 95% CI: [1.4–5.5), P =?] and CD4 count ≤ 303 cells / mm³ (adjusted OR: 2.2; 95% ; CI: [1.1-4.5], P = ?).

Conclusions: Hepatic cytolysis is frequent in patients co-infected with HIV-HBV-HCV. It is determined by aging, immunodeficiency and length of illness.

Keywords

Hepatic cytolysis, HIV-HBV-HCV, associated factors, Kinshasa, DRC

Introduction

Liver cytolysis is extremely common and sometimes severe in people infected with human immunodeficiency virus (HIV) [1]. Abnormalities in liver laboratory tests appear in more than two-thirds of these subjects [1]. These disturbances may be due to co-infection with HIV and hepatotoxic viruses, associated alcohol poisoning, fatty liver disease following malnutrition, opportunistic conditions, drug abuse, and the direct role of HIV is discussed [2].

HIV infection has favored the emergence of many diseases and infections that take place on a different epidemiological and course pattern [1-3]. Most of these opportunistic infections and neoplastic conditions occur

Citation: Mayimona JPK, Natuhoyila AN, Nlombi CM, Bompeka FL, Nsukini SM, et al (2022) Factors Associated with Hepatic Cytolysis in HIV-HBV and/or HCV Coinfected Patients in Kinshasa, Democratic Republic of the Congo: Multicenter Cross-Sectional Study. J Clin Gastroenterol Treat 8:089. doi.org/10.23937/2469-584X/1510089

Accepted: July 20, 2022: **Published:** July 22, 2022

at an advanced stage of immunosuppression.

However, tuberculosis and kaposi's disease can be observed despite a moderately impaired immune status, at circulating CD4 T lymphocyte levels between 250 and 500 / mm³. In 2007 in the USA and Western Europe, the prevalence of chronic HBV / HCV infection in HIV-infected patients was around 5-10% while in Africa and Asia it varied between 20% to 30% [4]. This prevalence for HCV in the USA and Western Europe was in the order of 75 to 90% in hemophiliacs and 1 to 12% in homosexuals [4]. For Martinez, et al. [5], steatosis was observed in 62% of HIV / HCV co-infections.

In year, in Burkina Faso, Ilboudo, et al. [3] found a hospital frequency of liver abscesses at 41.57% in HIV-positive subjects. In year, in Mali, a previous study reported the prevalence of HBsAg and anti-HCV ac in 23% and 20% of HIV positive patients, respectively. In the DRC, studies evaluating hepatic cytolysis in PLHIV are absent.

The objective of this study is to assess factors associated with liver cytolysis in people mono-infected with HIV or co-infected with HBV-HCV in Kinshasa.

Patients and methods

Study setting and design and period

This was a cross-sectional and analytical study, carried out in the city of Kinshasa, the political capital of the Democratic Republic of Congo. In this city, HIV care is organized in all general hospitals, in certain general and university hospitals, in certain private medical centers and in the medical training of certain NGOs. Depending on the availability and completeness of the information sought in our study, we considered two NGOs located in urban-rural areas, namely: the Pediatric Foundation of Kimbondo and the NGO "Community Actions AIDS / Better Future for Orphans du Congo (ACS / AMO-Congo) "which are among the oldest centers in Kinshasa for HIV care. The study took place during the period from November 10, 2013 to January 10, 2014.

Study population

The present study consecutively included elderly people, at least 18 year old known to have HIV who consulted during the study period at the two selected sites and who freely consented to participate in the study. Inclusion criteria were to be PLWHIV at least 18 in the study and years of age consenting to participate followed in one of the two treatment centers selected for the study, to have a medical file including the parameters sought.

To carry out the present study, were used as materials data collection sheet, informed consent sheet, strips for rapid qualitative tests HBsAg and AcVHC of the brand "ACCURATE of Indian manufacture", quantitative tests for the determination of the markers of the hepatitis B (ELISA) brand "DIALAB Austrian manufacture", test for determination of HCV antibodies (ELISA) brand "DIALAB Austrian manufacture", tests for evaluation of hepatic synthetic function.

Data collection method

The data collection involved in 3 stages: 1) administering a questionnaire to patients to collect socio-demographic information, medical history and risk behaviors for viral hepatitis; 2) the blood test for the determination of markers of the hepatic functions studied and of HBV and HCV; 3) analysis of the medical file of each patient selected in search of clinical, immunological and therapeutic information relating to HIV infection.

Sociodemographic parameters included age, sex, occupation, marital status, level of education and religion. Regarding the medical history and risky behavior, we looked for the concept of previous blood transfusion, vaccination against HBV, the number of sexual partners, the type of sexual intercourse, the concept of scarification, circumcision, excision, piercing, drug addiction, knowledge of one's HBV and HCV serological status and the notion of surgical intervention in the past. The analysis of the medical file of each patient allowed us to gather information on the year of the diagnosis of HIV, the clinical stage of the HIV infection, the current ARV treatment regimen and, if applicable, the highest rate, recent CD4; only CD4 counts not older than 3 months before the survey were taken into account.

On the blood test, the HBV biological markers sought were HBs Ag, anti-HBs Ab, anti-HBc Ab, HBe Ag and anti-HBe Ab. For HCV, total anti-HCV Abs were assayed. Transaminases (SGOT and SGPT) were the desired markers of hepatic cytolysis. To explore cholestasis, we assayed for γGT, total and direct bilirubin as well as alkaline phosphatases. To assess hepatic synthetic function, prothrombin, serum albumin, and INR were assayed. In terms of the collection process, any patient selected for the study received, after consultation by the center's medical team, the survey questionnaire. After completing the questionnaire, the patient was directed to the laboratory with a token bearing an identification code. Once arrived at the laboratory, a 5 cc venous blood sample was taken in two tubes, a dry tube for hematological and biochemical analyzes and another tube with citrate for serological analyzes. The samples were centrifuged using a German brand A-RD-42-26 device at 1500 revolutions / min / 5min, decanted and then stored in the refrigerator at a temperature between 2 to 8 °C at the site laboratories. Studies Qualitative tests for HBsAg and for total HCV antibodies were performed on site; the rest of the samples were sent to the Lomo Médical laboratory where hematological, biochemical and serological analyzes were carried out. A spectrophotometer of the brand

"Spectrum" and a "Bain Marie of the HUMAN brand" and ELISA reader "HIMARETADR-FINGLE of the HUMAN brand" were used to carry out the hematological and biochemical analyzes according to the manufacturer's standards. Kinetic methods for GOT, GPT, PAL, γGT; enzymatic for serum albumin, total and direct bilirubin, prothrombin and INR; and immunoenzymatic type ELISA for quantitative tests for viral hepatitis B and C were used. The results were transcribed on an ad hoc form with the corresponding codes.

Definition of concepts

The duration of HIV infection is the time between discovery of HIV and investigation;

Anti-HBs Ab were found to be positive when in the Elisa test, the anti-HBs Ab titre was> 12 IU / L [2];

HIV-HBV co-infection was selected on the basis of the positivity of HBsAg in HIV + patients [6];

HIV-HCV co-infection was selected on the basis of the positivity of anti-HCV Ab in HIV + patients [6];

SGOT and SGPT> 40 IU / L were considered to be high [7];

Hepatic cytolysis was retained for elevated SGOT and / or SGPT [7].

Statistical analyzes

The processing and analyzes of the data collected was carried out using SPSS version 20 and STATA version 10.1 software. During analyzes, patients' ages were categorized into tertiles (<40 years, 40-49 years and ≥ 50 years). The duration of HIV infection and TL CD4 count were dichotomized at the threshold of their median value (3 years and 303 cells / mm³, respectively). The descriptive statistics applied include the mean ± standard deviation for continuous quantitative variables with symmetric distribution, the median with extreme values for those with asymmetric distribution, and relative (%) and / or absolute (n) frequencies for qualitative variables. . For comparison of means and medians, Student's t test and Wilcoxon / Mann-Whitney nonparametric test were applied. For the analysis of the contingency tables, we used Pearson's chi-square test or Fisher's exact test or linear trend chi-square, as appropriate.

Logistic regression was performed to identify factors associated with hepatic cytolysis. Explanatory variables tested included patient age, sex, jaundice history, substance abuse concept, duration of HIV infection, clinical stage of HIV, TL CD4 count, ARV treatment, and status. of HIV-HBV / C co-infection. We opted for the step-by-step ascending Wald method. The final model, obtained after adjusting the variables significantly associated with hepatic cytolysis, was derived from the adjusted odds ratios (OR) and their 95% confidence intervals (CI). For the tests used, the statistical significance level retained was $p < 0.05$.

Ethical considerations

The protocol was submitted to the Ethics Committee of the School of Public Health of the University of Kinshasa. It was agreed at number ESP/CE/012/14. Thus, recruiting patients, anonymity and confidentiality were guaranteed.

Results

Sociodemographic characteristics

A total of 180 HIV patients were included in the study. Their socio-demographic characteristics are reported in table 1.

The mean age of the patients was 44.2 ± 11.0 years; the female sex was predominant (76.7%). The majority of them were married (38.3%) and widowers (31.7%); about half (53.3%) did not have a professional activity (unemployed). More than 8 out of 10 patients (84.3%) had completed at least high school; 53% prayed in revival churches. The province of Bas Congo was the most represented (40.6%). Clinically, the median time to know HIV status was 3 years (1 to 20 years) and 46.1% of patients were in stage III infection. Immunologically, the median CD4 lymphocyte count was 303 cells / mm³ (2 to 1133 cells / mm³); 40.4% of patients had less than 200 CD4 lymphocytes / mm³. 11.1% of patients were not on ARVs and AZT + 3TC + NVP was the most widely used treatment regimen (73.9%) (Table 1).

Serological profile of patients with viral hepatitis B and C

Table 2 shows the profile of HBV and HCV markers in the study population.

For HBV, the HBs antigen was positive in 11 patients (6.1%) on the qualitative test, while on the Elisa test, 41 people (22.8%) were carriers. Only one subject (0.6%) carried the HBe antigen. Anti-HBc, anti-HBs and anti-HBe antibodies were identified in 60%, 28.9% and 8.9% of patients, respectively. Regarding HCV, the anti-HCV antibody was found in 5 patients (2.8%) in the qualitative test while at Elisa, it was only identified in 3 subjects (1.7%) (Table 2).

Liver function abnormalities in patients according to HIV-HBV and / or HCV co-infection status is indicated in table 3.

Thirty point six percent and 33.9% of patients had an elevation of GOT and GPT, respectively, 42.8% had at least one of the two markers elevated while 21.7% had a concomitant elevation of both transaminases, without significant difference between the 2 groups of patients (Table 3).

Factors associated with hepatic cytolysis in patients

They are reported in table 4.

Table 1: General characteristics of patients.

Variable	(n=180)	%
Age (year)		44.2 ± 11.0
< 40	60	33.3
40 – 49	62	34.4
≥ 50	58	32.2
Gender	0	
Female	138	76.7
Male	42	23.3
Marital status		
Married	69	38.3
Widower	57	31.7
Single	32	17.8
Divorced	22	12.2
Profession		
Unemployed	103	57.2
Independent	41	22.8
Official	14	7.8
Others	22	12.2
Level of studies		
Illiterate & Primary	28	15.7
Secondary	129	71.5
Higher or university	23	12.8
Religion		
Revival churches	95	52.8
Catholic	44	24.4
Protestant	35	19.4
Kimbanguist	6	3.4
Others ???		
Duration of HIV infection (years) Me (IQS)	3 (1-20)	
Clinical stage of HIV infection		
I	18	10.0
II	55	30.6
III	83	46.1
IV	24	13.3
CD4 count (cells / mm³) Me (IQS)	303(2-1133)	
ARV treatment		
No treatment	20	11.1
AZT + 3TC + NVP	133	73.9
TDF + 3TC + EFV	20	11.1
ABC + DDI + [ALUVIA ou LPV/r]	7	3.9

Table 2: Serological profile of patients with viral hepatitis B and C.

Variable	n=180	%
HBV markers		
Qualitative test (rapid)		
Ag HBs +	11	6.1
ELISA tests		
Ag HBs +	41	22.8
Ag HBe +	1	0.6

Anti-HBs + Ab	52	28.9
Anti-HBe + Ab	16	8.9
Anti-HBc + Ab	108	60.0
HCV markers		
Qualitative test (rapid)		
Anti-HCV + Ab	5	2.8
ELISA test		
Anti-HCV + Ab	3	1.7

Table 3: Liver function abnormalities in patients according to HIV-HBV and / or HCV co-infection status.

Cytolyse hépatique	Over all (n = 180)	HIV (n = 137)	HIV+/HBV+/HCV (n = 43)	p
SGOT ↑, %	30.6	34.3	18.6	0.051
SGPT ↑, %	33.9	37.2	23.3	0.091
SGOT ↑ and/or SGPT ↑, %	42.8	46.7	30.2	0.057
SGOT ↑ and SGPT ↑, %	21.7	24.8	11.6	0.067

Table 4: Factors associated with hepatic cytolysis (univariate and multivariate analysis).

Variable	Univariate analysis		Multivariate analysis	
	OR (95%CI)	p	aOR (95% CI)	P
Age (years)				
< 40	1		1	
40 – 49	1.4 (0.6-3.1)	0.421	1.5 (0.6-3.5)	0.489
≥ 50	3.8 (1.7-8.8)	0.001	3.9 (1.7-9.2)	**0.005**
Duration of HIV infection				
≤ 3 years	1		1	
> 3 years	2.4 (1.3-4.7)	0.004	2.7 (1.4-5.5)	**0.005**
Clinical stage of VIH				
I	1		1	
II	1.8 (0.5-8.7)	0.589	1.1 (0.3-2.7)	0.689
III	4.6 (1.3-20.4)	0.005	1.6 (0.3-2.4)	0.189
IV	1.4 (0.3-8.1)	0.317	1.2 (0.4-3.1)	0.569
CD4 count (cells/mm³)				
> 303	1		1	
≤ 303	1.9 (1.0-3.9)	0.042	2.2 (1.1-4.5)	**0.024**

In univariate analysis, patient age, duration of HIV infection, clinical stage of infection, as well as CD4 count were significantly associated with hepatic cytolysis. In logistic regression, only the variables patient age, duration of HIV infection and CD4 count emerged as factors significantly associated with hepatic cytolysis in our patients. The risk of cytolysis increased linearly with patient age. This risk was higher in patients with known PVV for more than 3 years (adjusted OR: 2.7; 95% CI: 1.4-5.5) and in those with a CD4 count ≤ 303 cells / mm³ (Adjusted OR: 2.2; 95% CI: 1.1 - 4.5) compared to the others (Table 4).

Discussion

The objective of this study is to assess factors associated with liver cytolysis in people mono-infected with HIV or co-infected with HBV-HCV in Kinshasa.

Analysis of samples from our patients showed that 22.8% n = (41) were carriers of HBsAg. This seroprevalence is higher than that found by other authors in Africa, India and Brazil estimated at around 8-15% [8-14], it is nevertheless close to that found by BA. A in Mali 21.5% [15], in DR Congo another author found it to be 10.1% [16]. This difference could be explained by the small size of our study population and by the fact that we used a more sensitive test. Only 1.7% (n = 3) of our patients had anti HCV + serology. This agrees with data from the literature which classifies sub-Saharan Africa as a region with a low prevalence of hepatitis C virus infection [17,18] but less than that of

Ba A in Mali which found 8 , 3% [9] and Cassia M in Brazil which found 17.7% [6]. The prevalence of triple HIV-viral hepatitis B and C infection was 0.6% (n = 1) close to that of Otegbaya in Nigeria which was 1% [10], Cassia M, in Brazil found 1.8 % [8]. From the typology point of view of our hepatitis B patients, profile 6 may correspond to patients with occult hepatitis B, ie 60% (n = 108), but also to a former contact. This prevalence is consistent with that described in most studies 10-90%, DNA testing for HBV is necessary especially as the outcome of these patients is not clearly defined [6,19-22]. Profile 2 may correspond to patients with acute hepatitis B, ie 8.9% (n = 16). The other profiles, the occurrence, profile 1 can correspond to healing, i.e. 1.1% (n = 2), profile 3, when it comes to chronic hepatitis B, i.e. 0.6% (n = 1) , profile 4 may correspond to an absence of viral replication 2.8% (n = 5), while profile 5 may correspond to convalescence, ie 2.2% (n = 4).

Hepatic cytolysis was observed in 30.6% and 33.9% of patients with elevated GOT and GPT respectively, 42.8% had at least one of the two markers elevated, while 21.7% had elevated concomitant increase in the two transaminases, without significant difference between the 2 groups of patients. The hepatic cytolysis observed in our study can be explained by the fact that 73.7% of our patients were mono-infected with HIV against 74.4% of the co-infected were on antiretroviral treatment containing a protease inhibitor and the duration their average HIV infection was at least 3 years. Our results agree with the data in the literature in fact, hepatic cytolysis increases with the duration of ARV treatment and in the event of HBV and / or HCV co-infection. It is higher in case of triple therapy including a protease inhibitor and / or a non-nucleoside reverse transcriptase inhibitor compared to dual therapy of reverse transcriptase inhibitors [23-26]. Hepatic cytolysis was not statistically associated with HIV-HBV-HCV co-infection but it was more marked in the co-infected than in the mono-infected, thus showing in this study that the three viruses have the same degree of cause viral liver disease.

In univariate analysis the age of the patients, the clinical stage of the infection, the duration of the HIV infection as well as the TL CD4 count were the factors associated with hepatic cytolysis but in logistic regression the age of the patients the duration HIV infection and TL CD4 count were the factors most associated with hepatic cytolysis. The risk of cytolysis increased linearly with patient age. This risk was higher in patients with known PVV for more than 3 years (adjusted OR: 2.7; 95% CI: 1.4 - 5.5) and in those with a TL CD4 count ≤ 303 cells / mm³ (Adjusted OR: 2.2; 95% CI: 1.1 - 4.5) compared to the others. The association between hepatic cytolysis and advancing age has been proven in the literature [27]. In elderly patients (≥50 years), there is an increase in the muscle enzyme creatinine kynase which accelerates muscle lysis. This muscle lysis is accentuated in the presence of HIV-HBV-HCV co-infection, thus leading to hepatic cytolysis [27]. The collapse of TL CD4 is associated with the occurrence of opportunistic infections, which after treatment, will lead to immune reconstitution syndrome. This resumption of immunity is the basis of inflammation at the sites of opportunistic infections. In patients co-infected with HCV and HBV, the syndrome manifests as elevated levels of liver enzymes ALT and AST, hence the presence of hepatic cytolysis more frequent in these patients [28].

Conclusions

This study shows that HIV infection is often associated with HBV and / or HCV. This combination could alter the natural course of HIV infection, and lead to complications such as hepatic cytolysis. The frequency of hepatic cytolysis is higher in the population of PLHIV in Kinshasa. Advanced age, duration of HIV infection and low CD4 count were factors associated with hepatic cytolysis.

Conflict of interests

The authors state that there is no conflict of interests.

Author's contributions

All authors contributed to data analysis, drafting or revising the article, have agreed on the journal to which the article will be submitted, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

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