

Retraction Notice

Title of retracted article: **Prevalence and Profile of Hepatitis B Virus Infection among HIV-Infected Adults at Panzi Referral Hospital, in the Post-Conflict South Kivu Province, Eastern Democratic Republic of Congo**

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Retraction initiative (multiple responses allowed; mark with X):

- ☐ All authors
☒ Some of the authors
☐ Editor with hints from ☐ Journal owner (publisher)
☐ Institution
☐ Reader
☐ Other

Date initiative is launched: 2019-09-12

Retraction type (multiple responses allowed):

- ☒ Unreliable findings
☐ Lab error ☐ Inconsistent data ☐ Analytical error ☐ Biased interpretation
☒ Other: Missing Important Background, Results and Discussion Contents
☐ Irreproducible results
☐ Failure to disclose a major competing interest likely to influence interpretations or recommendations
☐ Unethical research
☐ Fraud
☐ Data fabrication ☐ Fake publication ☐ Other:
☐ Plagiarism ☐ Self plagiarism ☐ Overlap ☐ Redundant publication *
☐ Copyright infringement ☐ Other legal concern:
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☐ Other:

Results of publication (only one response allowed):

- ☐ are still valid.
☒ were found to be overall invalid.

Author's conduct (only one response allowed):

- ☒ honest error
☐ academic misconduct
☐ none (not applicable in this case – e.g. in case of editorial reasons)

* Also called duplicate or repetitive publication. Definition: "Publishing or attempting to publish substantially the same work more than once."

History

Expression of Concern:

☒ yes, date: 2019-09-12

☐ no

Correction:

☐ yes, date: yyyy-mm-dd

☒ no

Comment:

This article has been retracted to straighten the academic record. In making this decision the Editorial Board follows [COPE's Retraction Guidelines](#). Aim is to promote the circulation of scientific research by offering an ideal research publication platform with due consideration of internationally accepted standards on publication ethics. The Editorial Board would like to extend its sincere apologies for any inconvenience this retraction may have caused.

Editor guiding this retraction: Prof. Linda D. Moneyham (EiC of WJA)

Prevalence and Profile of Hepatitis B Virus Infection among HIV-Infected Adults at Panzi Referral Hospital, in the Post-Conflict South Kivu Province, Eastern Democratic Republic of Congo

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Abstract

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Background: Little is known about the prevalence of co-infection with hepatitis B virus (HBV) and human immunodeficiency virus (HIV) in the post-conflict South-Kivu Province, Eastern Democratic Republic of the Congo. Therefore, we aimed to determine such data at Panzi Referral Hospital. **Methods:** We conducted a cross-sectional study of 198 HIV-positive patients seen in consultation from June to 31 November 2017. Socio-demographic and clinical data were collected by interview and clinical examination. Blood sample was taken for serological analyses. The presence of HBV serological markers was determined by enzyme linked immunoassay (ELISA) tests. CD4+ T cell counts were determined for all patients. Data analysis was done using the JMP 7.1 software. Proportions were compared using a Chi-square test or Fisher test. **Results:** Fourteen of 198 participants (7.07%, 95% confidence interval [CI]: 4.35 - 11.51) were HBsAg-positive. Overall, 33.33% of the subjects had been in contact with HBV and 36.87% were carriers of the immunization marker.



Among co-infected patients, 28.57% had a chronic replicative viral B infection, 57.14% a chronic non-replicative infection and 14.29% were inactive carriers. No patient had an acute infection. Co-infection was higher in participants who were aged 55 and over (8.3%), men (12.90%, $p = 0.0306$), married (12.00%, $p = 0.0063$), or of Lega ethnicity (14.3%, $p = 0.0100$). Some clinical signs such as hepatomegaly and jaundice ($p < 0.0001$), fever ($p = 0.0095$), splenomegaly ($p = 0.0007$), ascites ($p = 0.0173$) and viral encephalitis ($p \leq 0.0001$) were associated with co-infection. Severe immunosuppression (50.00%, $p = 0.0110$) and WHO clinical stage III/IV (10.64%; $p = 0.0301$) were associated with HIV/HBV co-infection. **Conclusions:** The relative high prevalence of HIV/HBV co-infection and chronic nature call for the need of integrating HBV screening programs into HIV routine care to reduce morbidity and mortality levels caused by HIV/HBV co-infection.

Keywords

Democratic Republic of Congo, Hepatitis B Virus Infection, HIV-HBV Co-Infection, Prevalence

1. Introduction

Chronic hepatitis B virus (HBV) infection is present in 2.7 million of the 36.7 million people infected with the human immunodeficiency virus (HIV) worldwide [1]. The overall prevalence of HIV/HBV co-infection is estimated at 7.4% with 1.96 million co-infected persons (71%) living in Sub-Saharan Africa [1]. This prevalence varies with rates estimated to be between 5% and 10% in regions such as North America, Europe and Australia compared to higher rates, between 20% and 30%, in Sub-Saharan Africa and Asia where more than 70% of the 36.7 million people infected with HIV live [1] [2]. HIV/HBV co-infection is common because of the shared transmission routes for these two viruses, including the parenteral route, the mother-child route and the sexual route. This co-infection has become one of the morbidity and mortality factors including the rapid progression of hepatic lesions to cirrhosis and for hepatocellular carcinoma associated with HBV infection compared to mono-infected HIV or HBV patients [3]. Although the specific mechanisms through which HBV interacts with HIV to influence the progression of the disease are not clearly understood up today, HIV/HBV co-infection has been identified as being responsible for higher levels of HBV replication and decreased spontaneous clearance of HBV with a higher risk of reactivation of HBV infection and death from liver complications due to hepatic failure, cirrhosis and hepatocellular carcinoma [3] [4] [5].

In sub-Saharan Africa, it is estimated that approximately 10% - 20% of HIV-infected patients are HBsAg positive [6]. In the Democratic Republic of Congo (DRC), the limited number of studies conducted in different regions including the South Kivu region, showed variable prevalences of hepatitis B virus in-

fection among blood donors with prevalences rates between 3.5% and 4.8% [7] [8] [9] [10] [11] and in HIV-infected patients ranging from 0% to 9% [12] [13]. While there are more cases of HBV infection in clinical practice and increasingly, there is an influx of HBV cases into clinical practice, while no screening and treatment program is available in the DRC. Since 2015, World Health Organization (WHO) has recommended a systematic screening for HBsAg in all HIV-infected patients in HIV care programs. But these recommendations are not effective in our region. However, we found few published data on the HIV/HBV co-infection prevalence in our setting, the South Kivu Province of Eastern DRC [12] [13]. This study was therefore conducted to answer the question: what is the prevalence of HIV/HBV co-infection in HIV-infected patients at the Panzi Referral Hospital Therapeutic Center?

2. Methods

2.1. Study Population

A cross-sectional study was conducted between 01 July and 31 November 2017 in an HIV outpatient care center at Panzi Referral Hospital in the post-conflict south Kivu province, DRC. This center provides primary health care services to HIV-infected individuals in outpatient settings. Convenience sampling was used to consecutively select available consenting patients to participate in this study. A total of 225 ART treated HIV-infected patients aged > 18 years were enrolled in the center during the data collection period but only 198 (88%) participants had interpretable results.

2.2. Laboratory Diagnostic Procedures

Plasma samples were collected from HIV-infected patients with unknown HBsAg status attending for routine care. For laboratory analysis, a total of 10 mL of whole blood was collected from each participant and plasma was stored at -20°C . A total of 198 samples were tested for serological markers (HBsAg, HBcAb, HBsAb, HBcAg/Ab and HIV-1/2 p24 Ag/Ab) by enzyme linked immunoassay (ELISA) using the DiaSource kit (DIAsource ImmunoAssays® S.A., Belgium) for each marker tests at the medical research laboratory of the Université Evangélique en Afrique (U.E.A) faculty of medicine in Bukavu, DRC. CD4+ cells count with the BD kit FACSPresto™ Cartridge (BD Biosciences, San Jose, CA 95131 USA) were determined for all enrolled patients at the Panzi Hospital laboratory in Bukavu, RDCat Panzi hospital laboratory in RDC.

2.3. Statistical Analysis

HBV prevalence estimates were calculated with 95% confidence intervals (CI). Sociodemographic characteristics, clinical and laboratory data were recorded in a standardized form and data were entered into an electronic database in Excel (version 10). Descriptive analyses were performed using means and proportion as well as standard deviations and 95% confidence interval where necessary. As-

sociations between demographic, clinical and biologic characteristics with the presence of HBsAg were evaluated using the Pearson's Chi-square test and statistical significance was considered when the p-value was <0.05 . Statistical analyses were performed using JMP software version 7.1.

2.4. Regulatory Approval

Ethics approval was obtained from the Ethics Committee of the Catholic University of Bukavu (Reference No. UCB/CIE/NC/001/7/2017).

3. Results

In our study, 198 HIV-infected patients were enrolled. The median age of the study participants was 43 years old (IQR 41 - 45) and 12.90% (8/62) were men. Fourteen HIV-patients were HBsAg positive yielding a co-infection prevalence of 7.07% (14/198), 33.33% (66/198) of the participants had prior exposure to the hepatitis B virus (presence of anti-HBc antibodies) and 36.87% (73/178) had the HBV immunization marker. By analyzing the profile of the 14 co-infected subjects, we found that 4/14 patients had a chronic viral B replicative infection (circulating virus with HBeAg positive). In contrast, more than half of the participants had non-replicative chronic viral hepatitis B (HBeAb). Only 2/14 patients were asymptomatic carriers. No patient had an acute infection (anti HBc IgM absent) (Figure 1).

Table 1 presents the socio-demographic characteristics in mono-infected and HIV/HBV co-infected patients. There were no significant differences between the HIV mono-infected group and the HIV/HBV co-infected group in terms of age, occupation, religion, level of studies and origin. However, the prevalence of co-infection was higher in male than female patients (12.90% vs 4.41%; $p = 0.0306$),

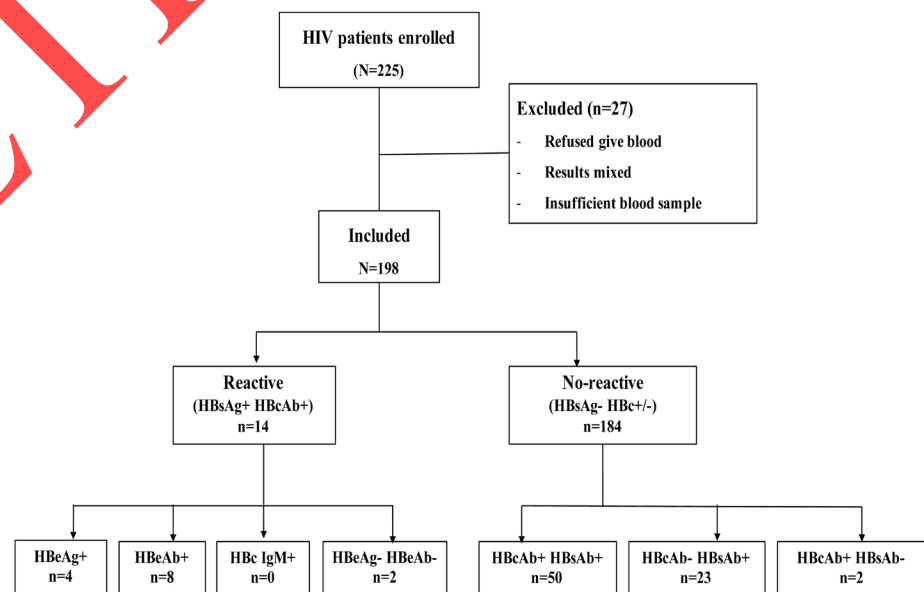


Figure 1. Testing of HBV markers in HIV-infected patients.

Table 1. Sociodemographic characteristics in mono-infected and HIV/HBV co-infected patients.

Variables	HIV+ n = 184	HIV+/HBV+ n = 14	Total	Chi-square	p-value
Sex					
Female	130 (95.59%)	6 (4.41%)	136 (68.69%)	4.673	0.0306
Male	54 (87.10%)	8 (12.90%)	62 (31.31%)		
Mean age (years)	43 ± 1 an	44 ± 3 ans	43 ± 1 an	2.7725	0.0959
Age range (years)					
15 - 34	48 (94.12%)	3 (5.88%)	51 (25.76%)	0.200	0.9048
35 - 54	103 (92.79%)	8 (7.21%)	111 (56.06%)		
>55	33 (91.67%)	3 (8.33%)	36 (18.18%)		
Marital status					
Married	88 (88.00%)	12 (12.00%)	100 (50.50%)	7.471	0.0063
Living alone	96 (97.96%)	2 (2.04%)	98 (49.49%)		
Occupation					
Private sector	45 (90.00%)	5 (10.00%)	50 (25.25%)	1.866	0.6008
Public sector	39 (90.70%)	4 (9.30%)	43 (21.72%)		
No occupation	100 (95.24%)	5 (4.76%)	105 (53.03%)		
Level of studies					
High	16 (88.89%)	2 (11.11%)	18 (9.09%)	0.506	0.7766
Medium	95 (93.14%)	7 (6.86%)	102 (51.52%)		
Low	73 (93.59%)	5 (6.41%)	78 (39.39%)		
Ethnic group					
Lega	28 (84.85%)	5 (15.15%)	33 (16.67%)	9.208	0.0100
Others	30 (85.71%)	5 (14.29%)	35 (17.68%)		
Shi	126 (96.92%)	4 (3.08%)	130 (65.66%)		
Origin					
Rural	36 (87.80%)	5 (12.20%)	41 (20.71%)	2.066	0.15
Urban	148 (94.27%)	9 (5.73%)	157 (79.29%)		

in married patients than in those living alone (12.00% vs 2.04%; $p = 0.0063$), in other ethnicities and the Lega ethnic group than in the Shi ethnic group (15.15% and 14.29% vs 3.08%; $p = 0.0100$).

Furthermore, 104 of the patients were classified as HIV WHO clinical stage I/II (52.56%). The prevalence of co-infection was higher in patients classified as HIV WHO clinical stage III/IV (10.64% vs 3.85%; $p = 0.0301$). Patients in severe immunodepression were more likely to be co-infected than patients who were minimally and moderately immunodepressed (50.00% vs 2.63% and 6.10%).

Clinical signs such as hepatomegaly and jaundice were very highly associated

with co-infection ($p < 0.0001$). Similarly, fever and splenomegaly were highly significantly associated with co-infection ($p < 0.001$). Also, ascites was significantly more common in patients with HIV/HBV co-infection ($p < 0.05$). Mono and co-infected patients did not differ in prevalence of acute diarrhea, rash and lymphadenopathy ($p > 0.05$).

Viral encephalitis was strongly associated with co-infection ($p < 0.0001$), while, all other opportunistic infections observed in this study did not differ between those with and without co-infection (**Table 2**).

4. Discussion

We found in HIV-infected patients, HBV prevalence of 7.07% in our study setting, which is in agreement with HIV/HBV co-infection prevalence reported

Table 2. Clinical and biological characteristics of mono-infected and HIV/HBV co-infected patients.

Parameters	HIV+ n (%)	HIV+/HBV+ n (%)	Chi-square	p-value
Clinical signs				
Hepatomegaly	5 (2.72)	3 (21.43)	17.3	<0.0001
Icterus	1 (0.54)	3 (21.43)	45.742	<0.0001
Splenomegaly	2 (1.09)	2 (14.29)	24.476	0.0007
Fever	21 (11.41)	5 (35.71)	15.955	0.0095
Acute diarrhea	8 (4.35)	0 (0.00)	0.634	0.4252
Rashes	9 (4.89)	1 (7.14)	0.234	0.6284
Lymphadenopathy	2 (1.09)	0 (0.00)	0.154	0.6950
Ascites	4 (2.17)	1 (7.14)	5.667	0.0173
WHO clinical stages				
Stage I/II	100 (96.15)	4 (3.85)	4.985	0.0301
Stage III/IV	84 (89.36)	10 (10.64)		
Immunodepression degree				
Mild	74 (97.37)	2 (2.63)	9.019	0.0110
Moderate	77 (93.90)	5 (6.10)		
Severe	33 (17.93)	7 (50.00)		
Opportunistic infections				
Digestive candidiasis	33 (17.93)	5 (35.71)	2.652	0.1034
Tuberculosis	35 (19.02)	5 (35.71)	2.249	0.1337
Pneumocystis	3 (1.63)	1 (7.14)	1.997	0.1576
Cryptococcosis	3 (1.63)	1 (7.14)	1.997	0.1576
Viral encephalitis	1 (0.54)	2 (14.29)	16.465	<0.0001
Kaposi's disease	1 (0.54)	0 (0.00)	0.076	0.7821
Cerebral toxoplasmosis	1 (0.54)	0 (0.00)	0.076	0.7821

from some African countries [14] [15] [16] [17]. However, other studies did document higher prevalence rates beyond 8% [16] [18]-[29]. Indeed, in a meta-analysis by Barth *et al.*, data on the prevalence of HIV-HBV co-infection in some sub-Saharan African countries show very high rates with an average prevalence of 15% [30]. Other studies had reported lower prevalences of HIV/HBV co-infection than reported in this study [29] [31] [32]. The reason for this discrepancy (high/low) in HIV/HBV prevalences is multifactorial: differences in background HIV burden, decreased immunity related to HIV, risky sexual behavior, poor diagnostic capacity, HBV vaccination coverage, small sample size in selected studies showing low prevalence, selection bias (e.g. referral bias) etc. Of note, HIV infected people have long been considered as a group to be at high risk of HBV infection because these two viruses share the same modes of transmission and because of HIV-induced immunosuppression. There is an alteration of innate anti-HBV immune response responsible for the decrease in clearance of HBsAg and sero-conversion HBe and HBs. But this immune response contributes to increasing the risk of chronic HBV infection with a possibility to progress to cirrhosis and hepatocellular carcinoma [3].

In this cohort, the HBV contact marker (HBc antibody) was prevalent in 33.33% and 3.03% of the participants had isolated anti HBcAb. This result was higher than what was reported by others authors [33] [34] [35]. However, this prevalence was lower than that described in Rwanda by Rusine *et al.* [29]. The prevalence of isolated HBc antibody in HIV-infected patients ranges from 17% to 81% and depends on the prevalence of HBV infection [34] [35] [36] [37]. We specify that 3.03% of the participants had isolated anti HBcAb. It is likely that this would be related to either to the loss of the post-contact immunization marker or the presence of the occult HBV described as the appearance of replication, HBV DNA in the liver with surface antigen of hepatitis B negative as shown by some authors [25]. A major limitation in this study is that we could not investigate occult HBV infections in participants who were HBsAg-negative but anti HBc-positive by HBV DNA PCR testing. Occult active HBV infections are thought to be common among HIV patients, with reported prevalence rates ranging from 10% - 14% [38] [39] [40] and up to 89% in one study in South Africa [41]. Further research is needed to determine the prevalence of occult HBV in this group.

All patients with HBV infection were in hepatitis chronic phase (defined as being HBsAg+ and HBcAb+). Of the 14 patients, 4 subjects (28.57%) had chronic replicative hepatitis infection and more than half were non-replicative. Two patients (14.29%) were inactive carriers of HBsAg and none subject had an acute viral B infection. The absence of acute hepatitis infection in HIV-infected patients and the observation that all patients have chronic viral B infection suggests that the mode of HBV infection was during infancy and from mother to child which is the most common mode of contamination in our setting as for other developing countries would be the same mode in this group of people considered at risk as the entire general population. This hypothesis suggests that these patients

were infected with HBV long before HIV infection. The prevalence of chronic replicative hepatitis infection is similar to that reported in Ghana by Geretti *et al.* [26] and in Zambia by Wandeler *et al.* [16] but higher than the 15% prevalence that was described in a study conducted in Uganda [17]. It was lower than the 62% reported in a second Ghana study [42]. The prevalence of chronic non-replicative infection of 57.19% in co-infected patients found in this study, the latter is higher than that of 47.9% reported in Ghana [26] and in 33.3% reported in Zambia [16].

We observed that 36.87% of subjects were HBV immunization marker carriers (defined as HBsAb positive) and in those, 68.49% had obtained immunization after HBV infection (HBcAb positive). This prevalence was similar to that reported by Boyd *et al.* [43]. However, it was slightly higher than the 14% to 50% prevalence in other cohorts of co-infected treated patients [10] [14] [24] [44] but similar to that between 50% and 71% in patients infected with HBV alone [31] [45] [46]. Also, these prevalences data are higher than those reported from Maputo, where less than 1% of co-infected subjects carried the marker for HBV immunization [23]. This loss of immunity against hepatitis B was explained by the fact that HIV infection leads to immunosuppression which would reduce the reaction.

Male sex was associated to co-infection significantly with co-infection as has been reported in Benin [28], Nigeria [31], South Africa [27], Rwanda [29] and Cameroon [19]. Other authors have reported a female predominance in Mozambique and Zambia [16] [23], Uganda [17], and in South Kivu [12]. In observing our study population, there were a large number of female than male patients. But by observing HIV/HBV co-infection, female subjects were less infected than male subjects. The higher proportion of women in our setting may be due to the higher accessibility of primary health care to women compared to men or other undocumented factors in our study.

In this study, the average age of co-infected patients was 44 ± 12 years. The 2008 South African study reported a similar average age of 41 years [27]. However, studies in Uganda, Kenya, Rwanda and Mozambique reported a much lower average age [14] [16] [17] [29]. These differences in average age could be due on the one hand to the introduction of the HBV vaccination program in some countries which would have significantly reduced the disease in younger age groups; and on the other hand to a recent introduction in the expanded immunization in children as is the case of our country or the absence of that program.

We also found that the majority (52.53%) of the patients in our study were in the WHO clinical I/II stage, but WHO clinical stage III/IV patients were more likely to be HIV/HBV co-infected (10.64%). Similarly, we observed that the degree of immunosuppression was more severe in co-infected subjects (50.00%) than in non-co-infected subjects (17.93%). Contrasting results were reported by Chambal *et al.* in Mozambique where the distribution of CD4 cell levels was similar in HIV/HBV-coinfected and uninfected patients, however which majority

(75%) of the subjects were in WHO clinical stage I and II [22], which could account for the differences of findings. Regarding the impact of HBV on the progression of HIV infection, our data showed that CD4+ T cell counts were very low in co-infected patients than in HIV-infected patients alone. Previous studies have failed to demonstrate that HBV may accelerate or aggravate the natural history of HIV infection [47]. However, due to the cross-sectional design of our study, our data are subject to reverse causation limitation preventing us to assess the impact of HBV on HIV disease progression. Well-designed prospective studies are needed to derive these conclusions.

5. Conclusion

We found that the prevalence of HIV/HBV co-infection was 7.07% and all patients had chronic HBV infection. This study reinforces the importance of integrating HBV screening programs into HIV routine care to reduce morbidity and mortality levels caused by HIV/HBV co-infection.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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