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*Original Article*

# Prevalence of *HBsAg* among Moroccan *HIV-1* infected patients and *APOBEC3G* variant frequencies in *HIV-1/HBV* co-infection

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## Abstract

Introduction: Human immunodeficiency virus (*HIV*) / hepatitis B virus (*HBV*) causes higher rates of liver disease compared to infection with just one virus. Co-infection can accelerate the progression to liver fibrosis or hepatocellular carcinoma and disturb the treatment response. *APOBEC3G* is a host defense factor which interferes with HIV-1 and *HBV*. We aimed to determine the prevalence of hepatitis B surface antigen (*HBsAg*) among *HIV*-infected patients and seronegative controls, and screen the *HIV/HBV* population for *APOBEC3G* variants *rs8177832*, *rs35228531* and *rs2294367*, previously associated with *HIV-1* infection susceptibility in Morocco.

Methodology: A case control study was conducted on 404 individuals (204 *HIV*-infected and 200 eligible blood donors) from April to November 2021. *HBsAg* was measured on the Roche Cobas e411 automatic analyzer (Roche Diagnostics, Basel, Switzerland) and *APOBEC3G* polymorphisms were identified using the TaqMan genotyping allelic discrimination method. Fisher Exact test, odds ratio (OR) with 95% confidence interval (CI), and haplotype frequencies were calculated.

Results: Of the 204 *HIV-1* seropositive patients and 200 controls, 4.9% (95%CI: 2.38-8.83) and 2.50% (95% CI: 0.82-5.74) were *HBsAg*-positive respectively. There was a significant association between increasing age (> 40 years) and *HBV* infection among controls ($p = 0.04$). The distribution of genotypes and alleles frequencies of *APOBEC3G* variants was heterogenous and five different haplotypes with frequencies ≥ 5% were obtained, of which *ACC* (*rs8177832*, *rs35228531*, *rs2294367*) was the most prevalent.

Conclusions: *HBV* co-infection is common among *HIV-1* infected individuals in Morocco. Efforts should be made to prevent, treat and control *HBV* transmission in this population.

**Key words:** *HIV-1/HBV* co-infection; *HBsAg*; *APOBEC3G*; polymorphism; Morocco.

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## Introduction

As of 2021, 38.4 million individuals worldwide were living with human immunodeficiency virus (HIV), including more than 25.7 million in the World Health Organization (WHO) African region [1]. In Morocco, the overall prevalence of HIV is estimated at 0.08%. A study reported that out of 18,147 seropositive subjects, 15,880 (i.e. 87.37%) were receiving antiretroviral therapy (ART) [2]. Worldwide, approximately, 10–15% of HIV-1 infected people suffer from a chronic hepatitis B virus (HBV) co-infection due to shared transmission routes [3]. With the success of anti-HIV treatment, the incidence of traditional opportunistic infections linked to acquired immunodeficiency syndrome (AIDS) has largely decreased, and liver disease has become one of the major causes of morbidity and mortality in subjects co-infected with HIV and HBV [4]. HIV-1/HBV co-infection accelerates progression from chronic infection to cirrhosis or hepatocellular carcinoma (*HCC*) compared to chronic HBV mono-infection. Thus, HIV-1/HBV co-infection alters the natural progression of hepatitis B and complicates antiviral treatment [5]. According to WHO data, Morocco was ranked among the low-prevalence countries for HBV [6] with estimated prevalences ranging from 1.5% to 2.5% [7,8]. However, given that the frequency of HIV-1/HBV co-infection varies from 0% to > 28.4% in African countries [9], no study has investigated the possible

association between HIV infection and the prevalence of HBV infection in Morocco.

Some host genetic factors (genetic mutations) such as apolipoprotein B mRNA editing enzyme catalytic polypeptide-like 3G (APOBEC3G) have been reported to affect the progression of HIV-1 infection and the chronicity of hepatitis B [10,11]. In fact, APOBEC3G (A3G) is a potent host genetic factor that has been widely reported to be associated with HIV and HBV infections [12,13]. In the absence of the *HIV-1 virion infectivity factor* (*vif*), *A3G* incorporates into newly synthesized viral particles and mutates, in HIV single-stranded DNA (ssDNA) from deoxycytidine (dC) to deoxyuridine (dU) during reverse transcription leading to a substitution of deoxyguanosine (dG) to deoxyadenosine (dA) in the plus-strand provirus DNA [14]. In the HBV viral genome, the *A3G* editing occurs in the negative DNA strand resulting in G-to-A changes in the positive strand [15]. *A3G* can inhibit both HIV and HBV viruses through the synergistic action of deaminase-hypermutation-dependent and -independent mechanisms [16].

*A3G* polymorphism is reported to be associated, in some ethnic groups, with HIV-1 infection risk and progression to AIDS and could modulate the course of HBV infection [12,16]. In Morocco, the polymorphism of *A3G* (H186R) was shown to be irrelevant in HBV acquisition in a study of 179 HBV chronic carriers and 216 healthy donors [17]. Furthermore, three *A3G* variants were the subject of two successive studies; the first was carried out on 90 HIV-1 infected patients receiving highly active antiretroviral therapy (HAART) and 68 healthy volunteers and showed that two *A3G* allelic variants, *H186R* and *rs35228531*, were not correlated to the response to HAART in the Moroccan population [18]. The second study aimed to investigate the association of three single nucleotide polymorphisms (SNPs) in the *A3G* gene (*rs8177832*, *rs35228531*, *rs2294367*) with disease outcomes in Moroccan HIV-1 infected patients, and included 194 HIV-1 seropositive individuals and 195 healthy controls. The study revealed significant associations between the studied polymorphisms in *A3G* with plasmatic viral load (pVL) variations during treatment and the susceptibility modulation to HIV-1 infection in Morocco (data submitted for publication).

Here, we aimed to investigate the prevalence of HBV in Moroccan HIV-1 infected subjects and seronegative individuals, to determine the frequency of the three SNPs that have been previously associated with susceptibility and progression of HIV-1 infection, in HIV-1/HBV coinfected patients in Morocco.

## Methodology

*Study population*

A case control study was conducted in a total of 404 individuals from April to November 2021. The study sample included 204 HIV-1 infected individuals and 200 eligible blood donors. The HIV-1 group was recruited from the Infectious Diseases Service in IBN Rochd Hospital in Casablanca, and the control group (CG) was enrolled from the National Blood Transfusion Center in Rabat. The HIV group represented HIV-1 seropositive patients receiving ART for at least more than one year and whose immunological and virological monitoring was carried out at the National Institute of Hygiene (INH). The controls had volunteered to take part in the study. To meet the requirements for blood donation and participation in the study, donors needed be free of autoimmune and malignant diseases, and be in a healthy state. Both patients and the CG were over 18 years of age. The whole blood from each participant was collected in EDTA anti-coagulant containers.

*Laboratory analysis*

All laboratory tests were performed in the National Reference Laboratory for HIV, Department of Virology in INH, Rabat. Analytical evaluation of hepatitis B surface antigen (HBsAg) serology in all subjects (patients and controls) was done using the Elecsys HBsAg II Assay at the Cobas e411 automatic analyser (Roche Diagnostics, Basel, Switzerland) that is routinely used in the Department for Infectious Disease Diagnosis. The Elecsys HBsAg II quantitative assay intended for use on Cobas e411 immunoassay analyzer allowed the quantitative detection of HBsAg in human plasma and the HBsAg levels were expressed in international units (IU)/mL. The clinical sensitivity and specificity of Elecsys HBsAg II quantitative assay were 99.90% and 99.98% respectively.

In the case of HIV-1 subjects, TCD4 counts were determined by flow cytometry using CellQuest Pro software BD Facs Calibur™ (Becton-Dickinson, Franklin Lakes, New Jersey, USA) and the HIV-1 viral load was determined using a fully automated real-time polymerase chain reaction (PCR) testing system (Abbott *m*2000sp RealTi*m*e System, USA). *A3G* genotyping was done by extracting the genomic DNA from peripheral blood for all individuals using the Maxwell® 48 RSC instrument with the Maxwell® RSC Whole blood DNA kit (Promega, Madison, Wisconsin, USA). Polymorphisms of *A3G* included *three SNPs*, *rs8177832*, *rs35228531* and *rs2294367*, previously reported to be associated with the modulation of HIV-1 infection susceptibility and AIDS progression.

Polymorphisms in HIV-1/HBV co-infected patients were identified using allele specific fluorogenic probes (TaqMan®assays *A3G*: C_2189646_10, C_16186714_10 and C_61215563_10), on the ABI 7500 FAST real time PCR platform (Applied Biosystems, Waltham, Massachusetts, USA).

*Ethics approval and consent*

The study protocol was reviewed and approved by the National Ethics Committee and local institutional review boards (Ethics Committee for Biomedical Research Mohammed V University / Rabat, and, Faculty of Medicine and Pharmacy of Rabat). The approval reference number was: 72/16. All participants provided informed consent.

*Statistical analysis*

Descriptive statistics were calculated using EpiInfo software (Version 3.5.4, 2012) [19]. National prevalence of HBsAg was estimated and presented with the corresponding 95% confidence intervals (95% CIs). Odds ratio (OR) and 95% CI were calculated to estimate the associations of HBsAg carriage and gender/age. *p* values at < 0.05 level were interpreted as statistically significant.

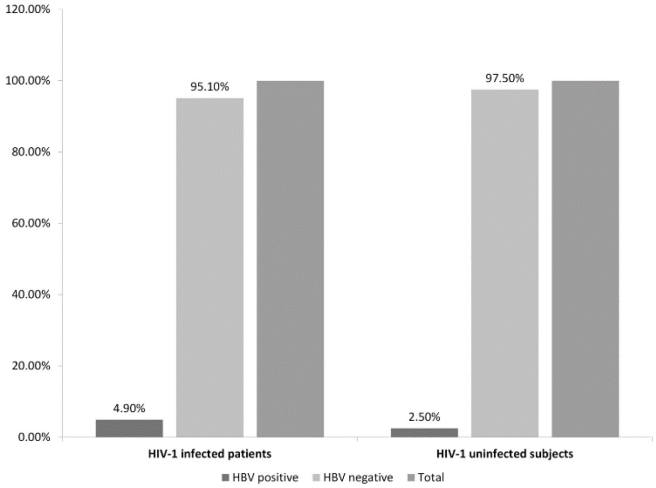
Genotype and allele frequencies in HIV-1/HBV co-infected patients were calculated using SNPstats software [20] and for each SNP, genotype frequencies were tested for Hardy-Weinberg equilibrium (HWE). Haplotypic frequencies of *A3G* polymorphisms were calculated using SNPStats software which estimates the haplotypes using the expectation maximization (EM) algorithm.

## Results

*Population characteristics*

A total of 204 HIV-1 positive patients and 200 controls were included in this study. The average age of the HIV-1 patients and controls were 80 ± 11.05 years and 35.24 ± 12.32 years, respectively. The basic characteristics of the HIV-1 patients and controls are summarized in Table 1. The frequencies of males and females in HIV-1 mono-infected and HIV-1/HBV co-infected cases were 54.12% and 45.88% vs 50.00% and 50.00% respectively. Similarly, their mean ages were 37.70 ± 10.98 years and 40 ±12.77 years. The mean TCD4 cells count in HIV-1 mono-infected and in HIV-1/HBV co-infected cases were 429.74 cells/mm$^3$ and 540.20 cells/mm$^3$ respectively. Their viral load ranged between undetectable to 3,714,211 copies/mL in mono-infected patients, and from undetectable to 1,024,147 copies/mL in co-infected patients. In the case of the CG, the frequency of males and females in HBV mono-infected individuals and seronegative subjects was 40.00% and 60.00% vs 44.61% and 55.39%, respectively; and their mean age was 49.60 ± 9.76 years and 34.87 ± 12.18 years.

**Figure 1.** Prevalence of HBV (HBs Ag) in HIV-1 infected patients and controls.




*Prevalence of hepatitis B infection in HIV-1 cases and controls*

The prevalence of HBV was 4.90% (10/204; 95% CI: 2.38% – 8.83%) in the HIV-1 positive patients while it was 2.50% (5/200; 95% CI: 0.82% – 5.74%) in the CG (Figure 1). Seropositivity was higher in HIV-1

**Table 1.** Basic characteristics of the two studied groups.

| | ***HIV-1* cases (N = 204)** | | **Controls (N = 200)** | |
|---|---|---|---|---|
| | ***HIV-1* mono-infected cases N = 194; (%)** | ***HIV-1/HBV* co-infected cases N = 10; (%)** | ***HBV* infected controls N = 5; (%)** | ***HIV-1/HBV* seronegative controls N = 195; (%)** |
| **Age group/average** | 37.80 ± 11.05 years | | 35.24 ± 12.32 years | |
| ≤ 40 | 114 (58.76) | 5 (50.00) | 1 (20.00) | 130 (66.66) |
| > 40 | 80 (41.24) | 5(50.00) | 4 (80.00) | 65 (33.34) |
| **Gender** | | | | |
| Male | 105 (54.12) | 5 (50.00) | 2 (40.00) | 87 (44.61) |
| Female | 89 (45.88) | 5 (50.00) | 3 (60.00) | 108 (55.39) |
| Mean CD4 count (cells/mm) | 429.74 (1-1684) | 540.2 (4-1319) | NA | NA |
| *HIV-1* viral load (copies/mL) | Undetectable-3714211 | Undetectable-1024147 | NA | NA |

*HIV*: human immunodeficiency virus; *HBV*: hepatitis B virus; NA: not applicable.

**Table 2.** Seroprevalence of HBsAg in HIV-1 cases and controls according to age groups and gender.

| | % of *HBs Ag* in *HIV-1* cases | | | | Total N; (%) | Odds ratio (95% CI) | *p-value* | % of *HBsAg* in Controls | | | | Total N; (%) | Odds ratio (95% CI) | *p-value* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Positive | | Negative | | | | | Positive | | Negative | | | | |
| | N | (%) | N | (%) | | | | N | (%) | N | (%) | | | |
| **Age group** | | | | | | | | | | | | | | |
| ≤ 40 | 5 | 4.2 | 114 | 95.8 | 119 (58.3%) | 1.42 (0.39 - 5.08) | 0.58 | 1 | 0.8 | 130 | 99.2 | 131 (65.5%) | 8 (0.87 - 73.03) | **0.04*** |
| > 40 | 5 | 5.9 | 80 | 94.1 | 85 (41.7%) | | | 4 | 5.8 | 65 | 94.2 | 69 (34.5%) | | |
| **Gender** | | | | | | | | | | | | | | |
| Male | 5 | 4.5 | 105 | 95.5 | 110 (53.9%) | 0.23 (0.23 - 3.02) | 0.80 | 2 | 2.20 | 87 | 97.8 | 89 (44.5%) | 0,82 (0.13 -5.06) | 0.84 |
| Female | 5 | 5.3 | 89 | 94.7 | 94 (46.1%) | | | 3 | 2.7 | 108 | 97.3 | 111 (55.5%) | | |

***** *p-value:* Fisher test; *HBV*: hepatitis B virus; *HBsAg*; hepatitis B surface antigen.

infected patients but there was no significant difference when compared to CG (OR = 2.01; 95% CI 0.67–5.99, $p = 0.202$).

*Seroprevalence of HBsAg by gender and age*

Table 2 shows HBsAg seroprevalences and odds ratios by age and gender. Among 110 male and 94 female HIV-1 infected patients, 4.54% and 5.31% had tested positive for HBsAg, respectively. HBsAg prevalences in 89 male and 111 female controls were slightly similar (2.20% and 2.70%, respectively). There was no significant difference between males and females in HIV-1 infected individuals regarding HBsAg seropositivity (OR = 0.23; 95% CI 0.23–3.02; $p = 0.80$), nor in controls (OR = 0.82; 95% CI 0.13–5.06; $p = 0.84$).

As shown, the majority of the patients and seronegative controls were in the ≤ 40 years age group, representing 58.30% of patients with HIV-1 alone and 65.50% of controls. Furthermore, 4.2% were HIV-1/HBV co-infected while only 0.8% of controls were HBV mono-infected. However, in the > 40 years age group, HBsAg seroprevalences were similar among HIV-1/HBV co-infected cases and HBV mono-infected controls (5.9% vs 5.8%), respectively. No significant difference was found regarding the % of HBsAg (OR = 1.42, 95% CI 0.39–5.08; $p = 0.58$) between the two age groups, in HIV-1 patients. However, a significant difference was observed in the HBsAg seropositivity, 0.8% in ≤ 40 years age vs 5.8% in > 40 years age; (OR = 8; 95% CI 0.87–73.03; $p = 0.04$) in the controls.

*Alleles and genotypes frequencies of A3G variants in HIV-1/HBV co-infected cases*

*A3G* variants *rs8177832*, *rs35228531*, and *rs2294367* genotypes and alleles in HIV-1/HBV co-infected cases, are summarized in Table 3. The three SNPs were in HWE in the patients. Given the small number of HIV-1/HBV co-infected individuals (N = 10), the interpretation of the genotypic and allelic distribution of the *A3G* polymorphisms, as well as the evaluation of such polymorphisms and their association with co-infection is difficult. Thus, for our study, we have limited ourselves to the description of the genotyping results obtained. Indeed, the distribution of genotypes and alleles was heterogeneous. For both variants, *rs8177832* and *rs2294367*, the wild genotypes AA and CC were frequent (40%), and the heterozygous AG and CG genotypes were present in 60% and 40%, respectively. However, we noted the total absence of the minor GG *rs8177832* genotype, and the minor GG *rs2294367* genotype was present in 20% HIV-1/HBV co-infected cases. Regarding the *rs35228531* genotyping, the major CC genotype was the most prevalent (90%), followed by the CT genotype (10%), while the minor TT genotype was absent (0%). Haplotype analysis revealed a total of five different haplotypes with frequencies ≥ 5%. ACC (*rs8177832*, *rs35228531*, *rs2294367*) was the most frequent haplotype (38.81%) followed by the ACG haplotype (26.19%), (Table 4).

**Table 3.** Genotype and allele frequencies of *A3G* SNPs in HIV-1/HBV co-infected patients.

| Genotypes/ Alleles | *rs8177832* N = 10 | % | Genotypes/ alleles | *rs35228531* N = 10 | % | Genotypes/ alleles | *rs2294367* N = 10 | % |
|---|---|---|---|---|---|---|---|---|
| *AA* | 4 | 40 | *CC* | 9 | 90 | *CC* | 4 | 40 |
| *AG* | 6 | 60 | *CT* | 1 | 10 | *CG* | 4 | 40 |
| *GG* | 0 | 0 | *TT* | 0 | 0 | *GG* | 2 | 20 |
| A | 14 | 70 | C | 19 | 95 | C | 12 | 60 |
| G | 6 | 30 | T | 1 | 5 | G | 8 | 40 |
| HWE | 0.48 | | HWE | 1 | | HWE | 0.57 | |

*HBV*: hepatitis B virus; *HBsAg*; hepatitis B surface antigen; *SNP*: single nucleotide polymorphism; HWE: Hardy Weinberg Equilibrium.

**Table 4.** Haplotype frequencies of *A3G* variants among HIV-1/HBV co-infected patients.

| | *rs8177832* | *rs35228531* | *rs2294367* | Frequencies |
|---|---|---|---|---|
| 1 | A | C | C | 0.3881 |
| 2 | A | C | G | 0.2619 |
| 3 | G | C | C | 0.2119 |
| 4 | G | C | G | 0.0881 |
| 5 | A | T | G | 0.05 |

*HIV:* human immunodeficiency virus*; HBV*: hepatitis B virus.

## Discussion

The prevalence of HBV exposure in HIV-infected individuals varies by geographic area and the risk exposure of the study population [21]. HIV-HBV co-infection is variable in different regions of the world. The overall rates appear to be highest in parts of west and south Africa such that the highest carriage is observed in sub-Saharan African populations [22]. Morocco is classified as a low HBV endemic area and the prevalence of co-infection among the cohort of HIV-infected individuals in our study (4.90%) was almost twice as high as in the general population [23]. The prevalence of HBV was 2.5% in our CG, which confirms previous Moroccan findings (1.5% among blood donors and 2.5% through patients referred to the Ibn Sina University Hospital Center of Rabat) [8,17] and those reported by countries with a low endemicity *for HBV*.

This was the first report to describe the epidemiology of HIV-1/HBV in Moroccan co-infected patients receiving ART. The HBV prevalence identified in our study is in line with the findings of other studies conducted in Netherlands (5%) and Spain (3.5%) [2,25]; higher compared to those in Japan, Brazil, Latin America and North America (< 2%, 2.5%, 2.8%, and 4.2%, respectively) [3,21,26]; and much lower in comparison to that reported among west and south Africans (> 20%) and east Asians (15.4%) [4,27] (Table 5). Indeed, in low HBV endemicity areas such as Australia, western Europe and North America, estimated co-infection rates are from 1% to 14% among young people who inject drugs or engage in unprotected sex [5]; while in high endemicity areas for HBV (8% to 20 % of HBsAg) such as sub-Saharan Africa and East Asia, the prevalence of co-infection of HIV and HBV varies between 10% and 28 %, and was reported to be strongly linked to close family contact and certain African cultural traditions during childhood [4]. Additionally, the low prevalences of HBsAg reported among individuals co-infected with HIV and HBV could be result of deployment of HBV vaccination drives from a young age, and in some cases, HBV vaccination of HIV-positive individuals may result in a moderately lower response rate than the general population [28].

Our results suggest that individuals infected with HIV are exposed to HBV at a higher rate, compared to controls and thus confirm the existing data on the main routes of HBV infection transmission [22]. Additionally, some vulnerable populations such as sex workers, men who have sex with men, and injecting drug users are at even greater risk of being co-infected with HBV and HIV viruses [37].

HBV infection in several studies was reported to be associated with the male gender [21,38,40], while other studies found that females were at higher risk [28,41,42]. In contrast, our study did not show any association between HBV infection and gender in both studied groups; however, a significant increase in the seroprevalence of HBsAg was observed among controls who were over 40 years old. Indeed, our finding was in line with previous studies which reported a significant correlation between older age and a higher risk of HBV exposure [39,43,44]. Such result was not observed in

**Table 5.** Prevalence of hepatitis B virus in HIV-1 infected subjects from different countries.

| Country | HBV prevalence in HIV-1 subjects | Author, publication year, reference |
|---|---|---|
| Brazil | 2.5% | Freitas *et al.,* 2014 *[*21] |
| Spain | 3.5% | Latorre *et al*., 2021 [25] |
| Morocco | 4.90 % | Imane *et al.* (the present study) |
| The Netherlands | 5% | MK Mason *et al.,* 2019 [24] |
| Switzerland., | 6% | Wandeler *et al*., 2013 [29] |
| Indonesia | 7% | Fibriani *et al*., 2014 [30] |
| Canada | 8% | Urvi *et al.,* 2019 [31] |
| Côte d'Ivoire | 9% | Kouamé *et al*., 2021 [32] |
| India | 11.3% | Saha *et al*., 2013 [33] |
| Mozambique | 11.4% | Augousto *et al*., 2019 [34] |
| Nigeria | 11.5% | Adewole *et al*., 2009 [35] |
| Burkina Faso | 56.7% | Compaore *et al*., 2016 [36] |

*HIV:* human immunodeficiency virus*; HBV*: hepatitis B virus.

the seropositive population in our study and this may be due to the multidisciplinary management of the newly diagnosed HIV-positive patient (vaccination against HBV; monitoring of the vaccine response; prevention program against co-infections with HCV, HBV and HPV; and meticulous biological monitoring).

A3G is an intrinsic antiviral protein that is able to diminish or block HIV-1 replication [45] and it is considered to be one of the most active deaminases with an inhibitory effect on HBV DNA editing and replication in vivo [46]. In Burkina Faso, HIV-1 infection is strongly associated with the high prevalence of HBV infection (56.7%), and Compaore *et al.* investigated the association of *A3G* restriction factor polymorphism with HBV/HIV co-infection. They demonstrated that the T minor allele of *rs35228531* is protective against HBV/HIV co-infection [36]. In this study, we described the occurrence of three SNPs of *A3G* in HIV-1/HBV co-infected patients. As mentioned in the results section, the genotypes and alleles frequency distribution of all *A3G* variants were heterogenous, but it did not reflect the reality of the entire HIV-1/HBV co-infected population, given the very small size of our sample. Moreover, five different haplotypes were identified with important frequencies among cases but we need a larger sample in order to look for haplotype-specific associations in the HIV-1/HBV co-infected group compared to control individuals.

## Conclusions

Our study demonstrates a higher HBV co-infection prevalence of 4.90% in HIV-1 infected patients in Morocco compared to controls.

However, there were some limitations in our study. First, as a prospective study, we were unable to determine the time of risk of co-infection and subsequent infections, (i.e., time from the presumed start of the risk behavior leading to co-infection and time of diagnosis). Second, in order to have more reliable data, our CG should have been recruited from the same population from which the cases originated because the population from blood donors represent a very controlled population, in which the risk of both HIV and HBV infections could be reduced. However, we have shown that HIV-1/HBV co-infection occurs in our environment at a rate that is comparable with other communities, but higher compared to healthcare workers, who are also at risk of the hepatitis B virus. Furthermore, increasing age could play an important role in the transmission of hepatitis B virus among controls and this finding should prompt the immediate implementation of a strategy that could manage both the burden of HIV/HBV co-infection and prioritize co-infected patients according to their therapeutic needs. In addition, screening for HBsAg must be ensured and included in the armamentarium of investigations among HIV-1 infected subjects before administration of HAART

On the other hand, regarding the polymorphism of *A3G* and HIV-1/HBV co-infection in Morocco, given the very small sample size of co-infected cases in our study, we could not extend our analysis to verify the association of such polymorphism with co-infection. Thus, to precisely understand the role of *A3G* variants or other genetic variants in HIV-1/HBV co-infected subjects, there is a need for additional studies with a larger sample size and with the involvement of various infectious units from diverse cities, caring for HIV-1 patients around Morocco.

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