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Anti-SARS-CoV2 serological profile and associated factors in adults living with HIV followed at Departmental and Teaching Hospital of Borgou in 2022.

Cossi Angelo Attinsounon^{1,2,3*}, Comlan Albert Dovonou^{2,3}, Kazali Alidjinou⁴, Fabius Kanninkpo^{1,2}, Adébayo Alassani^{2,3}, Amos Vodounou^{1,2}, Khadidjatou Saké^{2,3}, Serge Adé^{2,3}

> ¹Infectious Diseases and Tropical Medicine Unit, University of Parakou, R. Benin. ²Faculty of Medicine, University of Parakou, R. Benin. ³Departmental and Teaching Hospital of Borgou-Alibori (DTH-BA), Parakou, R. Benin. ⁴Laboratoire de virologie, Centre Hospitalier Universitaire de Lille, Faculté de médecine de Lille, France.

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*Correspondence:

*Dr. Attinsounon Cossi Angelo, Infectious Diseases and Tropical Medicine Unit, University of Parakou, R. Benin; Email: acosange@yahoo.fr

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Abstract

Introduction: Literature data suggest that people living with the human immunodeficiency virus (PLHIV) are at increased risk of severe forms of Coronavirus 2019 (COVID-19) infection and related mortality. The aim of this study was to investigate the anti-SARS-CoV-2 serological profile in adults living with HIV followed at the Departmental and Teaching Hospital of Borgou (DTH-B) in 2022 and to identify factors associated with anti-SARS-CoV-2 seropositivity in the latter.

Methods: This was a descriptive and analytical cross-sectional study conducted in the Internal Medicine Department at DTH-B, from June 27, 2022 to July 27, 2022. PLHIV were systematically recruited after informed consent. A survey form was used to collect epidemiological, clinical, paraclinical and therapeutic data. Anti-SARS-CoV-2 antibodies (IgG and IgM) were tested using the BIOSYNEX COVID-19 BSS rapid test (Biosynex SA, France). Data were analyzed using STATA/MP14.1 software. The significance level was 5%.

Results: A total of 135 adults living with HIV were included in the study. The sex ratio was 0.34 and the mean age 45 \pm 11.03 years. Anti-SARS-CoV-2 seroprevalence was 50.37%. Only one respondent reported a confirmed COVID-19, while vaccination coverage was 37.78%. Anti-SARS-CoV-2 seroprevalence in unvaccinated patients was 40.48%. Factors significantly associated with anti-SARS-CoV-2 seropositivity in multivariate analysis were vaccination status (p=0.02) and viral load (p=0.001).

Conclusion: Anti-SARS-CoV-2 antibodies were detectable in more than half the PLHIV. Their presence was associated with the notion of vaccination and an undetectable viral load. This study therefore suggests the need to promote COVID-19 vaccination among PLHIV followed up at DTH-B, as well as the continuation of adequate management of HIV infection in order to reduce COVID-19-related morbidity and mortality in this so-called vulnerable population.

Introduction

SARS-CoV2 infection may seem like an ordinary or asymptomatic flu in some people, but in others it can be serious or even fatal. Six months after it was first detected in Wuhan, China, more than half a million deaths were recorded worldwide^[1]. Several serious risk factors have been identified, such as advanced age, diabetes mellitus, obesity, high blood pressure, cardiovascular disease and chronic lung disease². It has been reported that people living with HIV (PLHIV) have a higher risk of morbidity and mortality from SARS-CoV2 than HIV-negative people³⁻⁶. HIV infection is a risk factor both for severe COVID-19 on admission and for in-hospital mortality of hospitalized COVID-19 cases⁴⁻⁷.

Another study seems to show the protective role of antiretroviral therapy (ART) against COVID-19 in PLWH. Indeed, some antiretroviral drugs (ARVs) have been used in the management of COVID-19⁸⁻¹⁰. According to some authors, the risk of testing positive and being hospitalized for COVID-19 was significantly reduced in PLHIV receiving a combination of tenofovir and emtricitabine¹¹. Other studies have shown that there is no difference in severity or mortality in PLHIV compared with HIV-uninfected subjects or the general population¹²⁻¹⁴.

The data in the literature are therefore not unanimous on the actual impact of HIV infection on the severity of COVID-19¹⁵. Seroprevalence studies of SARS-CoV2 infection would be useful to assess the spread of the virus in this specific population and the possible impact of ART on the severity of infection¹⁶. But few studies have addressed these concerns in the West African sub-region in general, and in Benin in particular.

Benin, with a national HIV prevalence of 0.8%, has not been spared by the SARS-CoV2 pandemic. It recorded its first case of COVID-19 on March 16, 2020, with an estimated 27638 confirmed cases and 163 deaths as of September 22, 2022¹⁷. Vaccination against SARS-CoV2 is one of the measures being taken to contain the pandemic, and is recommended for PLHIV. Vaccine response in PLHIV varies according to the degree of immunosuppression¹⁸. The greater the degree of immunosuppression, the poorer the immune system's response to vaccine antigens. Although vaccines against COVID-19 have been recommended for these patients, it is clear that the responses obtained in terms of seroconversion will vary from one individual to another. The type of vaccine also influences the quality of the post-vaccination response, as does vaccine completeness. One study found that the Johnson-Jonhson vaccine was associated with an increased incidence of SARS-CoV2 infection compared with the PFIZER vaccine¹⁹. A seroprevalence study of COVID-19 after the introduction of vaccination is admittedly difficult to interpret, but enables us to assess the overall level of seroconversion in the population.

The aim of the present study is therefore to investigate the anti-SARS-CoV2 serological profile of adults living with HIV followed at DTH-B in 2022, and to identify the factors associated with anti-SARS-CoV2 seropositivity in the latter.

Patients and methods

Type and study population

This is a descriptive cross-sectional study with analytical aims.

The study population was made up of all PLHIV followed up on an outpatient basis in the Internal Medicine Department of DTH-B.

Inclusion criteria

Inclusion was based on three main criteria: being at least 18 years old on the day of recruitment, having given free, informed and oral consent to take part in the study, and having an up-to-date and usable medical record.

Sampling technique

All PLHIV encountered on site during the period June 27, 2022 to July 27, 2022 and meeting the inclusion criteria defined above were systematically recruited.

Study variables

The study's dependent variable was the presence or absence of SARS-CoV2 antibodies, based on the results of a rapid screening test (RDT). This was the BIOSYNEX COVID-19 BSS test. This is an immunochromatographic test with sensitivity and specificity in excess of 95%, according to the supplier²⁰. The test is considered positive when one of the immunoglobulins G or M (IgG or IgM) is positive. The test is considered negative when both IgG and IgM are negative.

The independent variables related to sociodemographic characteristics, immune status, HIV viral load, antiretroviral treatment, factors associated with occupational and family exposures to SARS-CoV2, comorbidities and pathological history, and the search for any evolving COVID-19. Data on vaccination status, type of vaccine, vaccine completeness and the time between the last vaccination dose and the time of the survey were also collected.

Data collection tools and techniques

Data were collected during a face-to-face interview using a pre-established questionnaire. A pre-test of the tools was carried out prior to data collection. This enabled the questionnaire to be corrected and validated on the one hand, and the rapid diagnosis procedure to be tested on the other. Data collection took place in three stages. Firstly, after obtaining the oral and informed consent of each respondent, the questionnaire was administered to them. Secondly, the rapid screening test for SARS-CoV2 was carried out. Finally, some additional information relating to HIV infection was collected through a review of patients' follow-up medical records. This included clinical data (initial clinical stage, nutritional status, medical history), immunological data (TCD4 lymphocyte count), virological data (HIV viral load) and therapeutic data (current antiretroviral treatment).

Data processing and analysis

At the end of data collection, the forms were manually

counted to check for completeness and consistency. Data was double-entered into the French version of Epi Data 3.1. Data were cleaned and analyzed using STATA/MP 14.1 statistical software. A descriptive analysis of the variables under study was carried out. For qualitative variables, frequencies and proportions were determined. Comparisons were made using the Chi2 test, or the ficher's exact test if the expected value is less than 5. For quantitative variables, means with standard deviation, medians, minima and maxima were described. Univariate and multivariate logistic regression models were used to determine associated factors. The significance threshold was 5%, and confidence intervals were calculated at 95%.

Ethical approvals

This study has obtained the favorable opinion of the local ethics committee for biomedical research of the University of Parakou (N°0560/CLERB-UP/P/SP/R/SA of January 31, 2022). A survey authorization was issued by the site manager. Oral and informed consent was obtained from the subjects before the questionnaire was administered. The data from this study were treated confidentially and anonymously.

Results

In all, 135 of the 137 registered patients were included in this study. Two (02) registered subjects were excluded because their follow-up medical records could not be found.

Table 1: Socio-demographic	characteristics	of PLHIV	surveyed	by
vaccination status at DTH-B in	2022			

	Vaccina	ted	Unvaccinated	
	Numbers	%	Numbers	%
Age (N=135)				
< 50 years	32	23.71	55	40.74
≥ 50 years	19	14.07	29	21.48
Gender (N=135)				
Female	38	28.15	63	46.67
Male	13	9.63	21	15.55
Occupation (N=135)				
Liberal	30	22.22	48	35.55
Housewife	8	5.93	18	13.33
Civil servant	9	6.67	5	3.70
Cultivator	4	2.96	10	7.41
Unemployed/unemployed	0	0	2	1.48
Student	0	0	1	0.75
Marital status (N=135)				
In couple	32	23.70	55	40.74
Single	20	14.82	28	20.74
Level of education (N=135)				
Out of school	13	9.63	38	28.15
Primary	15	11.11	25	18.52
Secondary	20	14.82	17	12.59
University	3	2.22	4	2.96

 Table 2: Characteristics relating to the retroviral terrain of PLHIV surveyed at DTH-B in 2022

	Numbers	%
Length of time in cohort (N=135)		
<60 months	45	33.33
≥ 60 months	90	66.67
HIV serotype (N=135)		
HIV1	134	99.26
HIV2	1	0.74
Number of TCD4 lymphocytes (N=128)		
≥500 / mm³	73	57.03
<500/ mm ³	55	42.97
Current viral load (N=118)		
Undetectable (≤ 40 copies)	85	72.03
Detectable (> 40 copies)	33	27.97
WHO clinical stage at treatment initiation (N=	135)	
Late stage (WHO stage III and IV)	86	63.70
Early (WHO Stage I and II)	49	36.30
Duration of ARV treatment (N=135)		
<60 months	45	33.33
≥ 60 months	90	66.67
Treatment regimen (N=135)		
TDF+3TC+DTG	100	74.07
TDF+3TC+EFV	25	18.52
TDF+3TC+ATV	4	2.96
ABC+3TC+DTG	2	1.48
AZT+3TC+EFV	1	0.74
AZT+3TC+ATV	1	0.74
TDF+3TC+LPV/r	1	0.74
ABC+TDF+3TC+LPV/r	1	0.74

TDF: Tenofovir Disoproxil Fumarate; **3TC**: Lamivudine; **DTG**: Dolutegravir; **EFV**: Efavirenz; **ATV**: Atazanavir; **ABC**: Abacavir; **AZT**: Zidovudine; **LPV/r**: Lopinavir/ritonavir

Socio-demographic characteristics

The median age of the subjects surveyed was 44, with extremes of 23 and 72. There was a clear predominance of women among the PLHIV in this study (74.81%). The sex ratio was 0.34. **Table 1** presents the socio-demographic characteristics of the respondents.

Characteristics of HIV infection

These were HIV1-infected subjects (134; 99.26%), 90 (66.67%) of whom had been on antiretroviral therapy for more than 60 months. The TCD4 lymphocyte count was above 500 cells/mm³ in 73 (54%) and the viral load was undetectable in 85 (63%). **Table 2** shows data on the HIV status of the respondents.

Anti-SARS-CoV2 seroprevalence

Of the 135 PLHIV surveyed, 68 showed anti-SARS-CoV-2 antibodies, giving an overall anti-SARS-CoV-2 seroprevalence of 50.37%. These included 67 cases with an IgG+/IgM- profile and one with an IgG+/IgM+ profile. No patient had an IgG-/IgM+ profile.

Table 3. Factors associated with the presence of anti-SARS-CoV-2 antibodies in PLHIV surveyed at DTH-B in 2022

Features Results		Detection of anti-SARS-CoV-2 antibodies				
	Desults	Univariate analysis		Multivariate and	te analysis	
	Results	RC _{brut} [¶] [IC] [‡] (95%)	p⁺	¶ [IC] [‡] _{RCadjusted}	p⁺	
Initial WHO stage of HIV infe	ction			()		
Tardif	38/86(44.19)	1	0.00	1	0.430	
Early	30/49(61.22)	1.99[0.06 - 0.98]	0.06	1.61[0.49 - 5.22]		
Current viral load						
< 40 copies/ml	54/85(63.53)	4.65[1.92 - 11.26]	<10-3	4.82[1.94 - 11.97]	<0.001	
> 40 copies /ml	9/33(27.27)	1	<10-3	1		
TCD4 lymphocyte count						
<500/ mm3	22/55(40.00)	1	0.07	1	0.205	
≥500/ mm3	41/73(56.16)	1.92[0.94 - 3.91]	0.07	1.86[0.59-4.25]		
Duration of ARV treatment						
<60 months	17/45(37.78)	1	0.04	1	0.197	
≥60 months	51/90(56.67)	2.15[1.04 - 4.48]		2.28[0.65 - 7.94]		
Vaccination status						
Unvaccinated	34/84(40.48)	1	0.003	1	0.02	
Vaccinated	34/51(66.67)	2.94[1.42 - 6.09]		2.63[1.14 - 6.06]		

According to vaccination status, anti-SARS-CoV-2 seroprevalence was 40.48% among unvaccinated PLHIV and 66.67% among those who had received at least one dose of COVID-19 vaccine.

Anti-SARS-CoV2 vaccine coverage and history of COVID-19

Only one person (0.74%) of the 135 PLHIV surveyed reported having had a confirmed COVID-19. Two subjects (1.49%) reported having been in contact with a confirmed case of COVID-19.

Of the 135 PLHIV surveyed, 51 (37.78%) had received at least one dose of COVID-19 vaccine, while 84 (62.22%) had not received any dose. Complete vaccination had been noted in 45 (88.24%) vaccinated respondents. The vaccines used were Johnson & Johnson in 36 cases (70.59%), Sinovac in 11 cases (21.57%), Pfizer in 3 cases (5.88%) and only 1 respondent had received the Astra Zeneca vaccine. Of the 51 respondents who had been vaccinated, 20 (39.22%) had received their last dose less than six months before the survey date and 31 (60.78%) more than six months before. The average time between vaccination and the survey date was 9 \pm 6 months.

Factors associated with SARS-CoV2 antibody positivity

In univariate analysis, undetectable viral load (p<0.001), duration of antiretroviral treatment greater than or equal to 5 years (p=0.04) and vaccination against COVID-19 (p=0.003) were statistically significantly associated with the presence of anti-SARS-CoV-2 antibodies.

In multivariate analysis, only undetectable viral load (OR = 4.82 [1.94-11.97], p<0.001) and a vaccination

against COVID-19 (OR = 2.63 [1.14-6.06], p = 0.002) remained associated with the presence of anti-SARS-CoV-2 antibodies (**Table 3**).

When the analysis was reduced to the subgroup of unvaccinated patients, the detection of anti-SARS-CoV-2 antibodies was associated with an undetectable viral load OR= 11.55[2.34-54.03], p=0.003 and a CD4 count greater than 500 cells/µL OR= 4.033[1.16-13.99], p=0.028.

Discussion

The aim of the present study was to assess the anti-SARS-CoV-2 serological status of adults living with HIV and correlate it with their COVID-19 vaccination status.

Seroprevalence of COVID-19 among people living with HIV varies from study to study²¹⁻²⁴. Wolter et *al.* in South Africa (2022) had in a case-control study, an anti-SARS-CoV-2 seroprevalence of 48.10% among PLHIV²².

Anti-SARS CoV-2 seroprevalence among unvaccinated PLHIV was 40.48%. This result is close to that of Kaboré et *al.* in Burkina Faso in 2023 which was $31.0\%^{23}$. Shalaka et *al.*, in Libya (2021)²⁴ and Dutschke et *al*,²¹ also found high anti-SARS CoV-2 seroprevalence in unvaccinated PLHIV, at 28.70% and 27.70% respectively. These high seroprevalences in unvaccinated patients reflect a significant circulation of SARS-CoV-2 in this vulnerable population.

A history of vaccination against COVID-19 was significantly associated with anti-SARS-CoV-2 seroprevalence in PLHIV. Vaccinated PLHIV were more likely to have positive SARS-CoV-2 serology than unvaccinated PLHIV. Several factors influence the response to vaccination against COVID-19, and these vary from one study to another, sometimes with controversy. These include the number of TCD4 lymphocytes and therefore the level of immunosuppression²⁵, the number of vaccine doses received and young age²⁶⁻²⁸. In the present study, PLHIV with a TCD4 lymphocyte count above 500 cells/ μ L seemed more likely to have positive anti-SARS-CoV-2 serology than those with a TCD4 lymphocyte count below 500 cells/ μ L. This difference was not statistically significant (p= 0.07) in the overall population, but becomes so when the analysis is restricted to unvaccinated patients. This observation also testifies to the association between the quality of immune restoration and the anti-SARS-CoV-2 response.

Viral load was significantly associated with anti-SARS-CoV-2 serological status among PLHIV. PLHIV surveyed with an undetectable viral load were more likely to have a positive anti-SARS-CoV-2 serology than those with a detectable viral load. The same finding has been reported in several studies, reflecting a good overall immune response in patients with controlled viral replication²².

PLHIV managed at an early initial clinical stage tended to have anti-SARS-CoV-2 antibodies more frequently (about twice as likely), but this difference was not statistically significant (p=0.06). Indeed, PLHIV who started antiretroviral treatment at a late stage often fail to restore their immunity properly, which could affect the vaccine response.

It should also be noted that none of the respondents in this study received a booster vaccination. Some received only a single dose of Sinovac vaccine, whereas at least two doses are required for a complete initial vaccination. These aspects should not be overlooked when analysing the results of this study. Several studies have shown that a good vaccine response is maintained by two or three booster doses in immunocompromised patients^{29, 30}.

Another factor to be taken into account when interpreting seroprevalence results is the time between vaccination and the survey period. In over 60% of cases, this is more than six months. Studies have shown a decrease in the quantity of antibodies over time, which suggests booster vaccinations^{31, 32}.

In the present study, it should also be noted that more than 62% of respondents had not received any dose of vaccine against COVID-19. Several factors may explain this finding. The anti-vaccination campaign promoted by the media and social networks certainly played a role in the decision whether or not to be vaccinated. Several studies have looked at the reluctance to vaccinate against COVID-19 and have identified several factors associated with this reluctance. These include age, level of education, fear of side effects, doubts about the efficacy of the vaccine, and the speed with which vaccines were introduced³³⁻³⁶. Some patients were not enthusiastic about the COVID-19 vaccine because of a perceived lack of effort to develop an HIV vaccine³³.

Study strengths and limitations

Limits

The use of a qualitative rather than quantitative test for IgG and/or IgM antibodies against SARS-CoV-2 in the subjects surveyed did not enable us to assess the degree of immunization. We are also unable to determine the relationship between exposure to the virus and vaccination in vaccinated respondents.

Forces

This study has many strengths that deserve to be highlighted. The fact that it was carried out in the era of vaccination means that we can assess the efforts made by the authorities to ensure the effectiveness of vaccination among PLHIV, and its actual impact on anti-SARS-CoV2 seroconversion. It will also serve as a benchmark for future serological monitoring study. This study provides further evidence of anti-SARS-COV2 seroconversion in the absence of any vaccination in a particular target population.

Conclusion

Anti-SARS-CoV-2 seroprevalence in adults living with HIV was not negligible, while only one history of confirmed COVID-19 was reported, and low COVID-19 vaccination coverage was noted. The main factor significantly associated with anti-SARS-CoV-2 seropositivity was an undetectable viral load. This study indicates a significant spread of SARS-CoV-2 infection among PLHIV and suggests the need for promotion of COVID-19 vaccination and adequate management of the retroviral terrain in order to reduce COVID-19-related morbidity and mortality in this population.

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Authors' contributions: KF developed the research protocol, conducted the data collection and participated in writing the first draft of the article. ACA, AK coordinated the drafting of the protocol, supervised data collection and wrote the first draft of the article. DCA, AA, VA, SK and ASS reviewed the article

Ethics approval and consent to participate

The research protocol has also been approved by the local ethics committee for biomedical research of the University of Parakou (N°0560/CLERB-UP/P/SP/R/SA of January 31, 2022).

All data from this survey were treated anonymously and with strict confidentiality.

Competing interests: The authors declare that there are no competing interests.

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