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Original Article

HIV-2 drug resistance genotyping and viral load among HIV-2 infected adults in Burkina Faso, West Africa

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Abstract

HIV-2 infection although less virulent compared to HIV-1 is endemic in many parts of West Africa. In Burkina Faso, few data exist on HIV-2 genotypic resistance. The objective of this study was to assess HIV-2 genotypic resistance and viral load in adult patients infected with HIV-2 in Burkina Faso. This was a cross-sectional study that ran from February 2017 to March 2019. This study included 91 HIV-infected adult patients on ARV treatment. HIV and hepatitis B and C status were confirmed by serological tests. HIV-2 viral load and HIV-2 clusters were determined by in-house tests. The mean age was 58.99 ±8.66 years. Of the patients, 12.1% were HIV-1, 73.6% were HIV-2 and 14.3% were co-infected with HIV-1/HIV-2. Only 15% had a high viral load (more than 1000 copies/mL). Groups A and B were detected in this study with the majority being group A (23.75%). HIV-2 subtype CRF01_AB was found in 3.75% of HIV-2 patients. Of the 34 HIV-2 patients whose subtypes were determined, only 7 had reverse transcriptase and 3 had protease resistance mutations. The M184V mutation was the most detected. This study revealed recent data on the status of HIV-2 genotypic resistance in Burkina Faso. Although few HIV-2 infected patients on ARV treatment have developed resistance, it is important to establish a surveillance system for HIV-2 genotypic resistance.

Keywords: HIV-2, Viral load, Subtype, Mutations, Sequencing

1. Introduction

HIV type 1 (HIV-1) and HIV type 2 (HIV-2) are very closely related but differ in pathogenicity, natural history, and sensitivity to therapy. HIV-1 is more easily transmitted and therefore accounts for the vast majority of HIV infections worldwide [1, 2]. HIV-2 infection is endemic in West Africa, with the highest prevalence in Cape Verde, Côte d'Ivoire, Gambia, Guinea-Bissau, Mali, Mauritania, Nigeria, and Sierra Leone [3]. However, globalization has led to a significant number of cases in other parts of Africa, Europe, India, and the United States [4]. In Burkina Faso, HIV-1 infection is predominant in 97% of cases, 2% for HIV-2, and 1% for HIV-1/HIV-2 co-infection [5]. HIV-2 infection is associated with slower disease progression than HIV-1 infection due to the lower plasma viral load levels of HIV-2 [6]. Although HIV-2 is less virulent than HIV-1, individuals with HIV-2 exhibit similar clinical signs, symptoms, and opportunistic infections (OIs) as those seen with HIV-1. Furthermore, the majority of individuals with HIV-2, if left untreated, will eventually progress to AIDS and death [7]. Nowadays, there are 10 distinct groups of HIV-2 namely A, B, C, D, E, F1, F2, G, H, and I [8, 9]. Groups A and B are more endemic [10]. Only one subtype has been detected since then, namely CRF01_AB. The first circulating recombinant form (CRF) of HIV-2 was described by Ibe et al. 2010 [11]. They defined CRF from 3 genomes from Japan (NMC307, NMC716, NMC842) and the 1990 isolate 7312A (L36874) from Ivory Coast. HIV-2 viral load and resistance genotype sequencing remain limited in Africa. This test is more accessible for HIV-1 infected individuals. These weaknesses will be due to a lack of HIV-2 viral load kits but also to poor HIV-2 sequencing capabilities. These shortcomings help explain the data gap on HIV-2 viral load and resistant genotypes in low-income countries. The objective of this study was to assess HIV-2 genotypic resistance and viral load in adult HIV-2-infected patients in Burkina Faso.

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2. Materials and Methods

2.1. Study population and sample collection

This was a cross-sectional study that took place from February 2017 to March 2019 in Ouagadougou, Burkina Faso, West Africa. The study population consisted of diagnosed HIV-positive patients on ARV treatment followed up in hospitals. ARV treatment consisted of two nucleoside reverse transcriptase inhibitors (NRTIs) and a protease inhibitor. After inclusion, venous blood samples were taken from each patient and collected in EDTA and dry tubes. Aliquots of plasma and serum were centrifuged and shipped to BIOMEX in Germany for further testing (serology, viral load, and sequencing).

2.2. Serological tests (HIV, HBV, and HCV) and viral load

Serological tests for HIV, HBV, and HCV were performed by the BIOMEX laboratory from serum using the "Architect HIV Ag/Ab Combo", "Architect HBsAg Qualitative II" and "Architect Anti-HCV" tests on Architect 1000 SR (Abbott Laboratories, Abbott Park, IL, USA). Differentiation and confirmation of HIV-1 and HIV-2 antibodies were performed using the "Geenius HIV-1/2" assay (Bio-Rad Laboratories, Inc. France).Charge virale plasmatique du VIH-2 Plasma HIV-2 viral load was performed from plasma using the Qiagen EZ-1 automatic extractor (QIAGEN, USA). Amplification was done using an in-house test on the ABI PRISM 7500 thermocycler (Applied Biosystem, USA).

2.3. Sequencing of HIV-2 subtypes and identification of resistance mutations

Sequencing was performed on samples with a detectable HIV-2 viral load (at least 10 copies/mL) using an in-house test. The sequencing involved the protease and reverse transcriptase regions of HIV-2.

Genotypes were assessed for evidence of drug resistance using the HIV2EU web tool (http://www.hiv-grade.de/HIV2EU/deployed/grade.pl) and the Stanford HIVdb Program for HIV-2 (https://hivdb.stanford.edu/hivdb/hiv2/by-sequences/), specifically searching for known “major” substitutions to RT and PR mutations. The Fasta formatted sequences were then analyzed in the HIV basic local alignment search tool program (http://www.hiv.lanl.gov) for identification of HIV-2 groups.

3. Results

3.1. Socio-demographic characteristics and viral hepatitis B and C prevalence

The mean age was 58,99 ±8,66 years. Female was most represented with 63.7% and sex ratio (F/M) was 0.57. The prevalence of HBAgs and Anti-HCV was 9.9% and 1.1 % respectively. Among HIV-infected patients, 12.1 % were HIV-1, 73.6% were HIV-2 and 14.3% were coinfected HIV-1/HIV-2 (Table 1).

3.2. Characteristics of HIV-2 infected and HIV-1/HIV-2 coinfected patients

Among the patients, the prevalence of HBV and HCV were 8.75% and 1.25%, respectively. More than half of the HIV-2 patients had an undetectable viral load. Only 15% had a high viral load (more than 1000 copies/mL). HIV-2 group A was the most detected (23.75%). HIV-2 subtype CRF01_AB was found in 3.75% of HIV-2 patients (Table 2).

3.3. Viral load, HIV-2 subtypes, groups, and drug resistance mutations

The HIV-2 viral load ranged from 10 to 1,600,000 copies/mL. Of the 34 HIV-2 patients whose subtypes were determined, only 7 had reverse transcriptase and 3 had protease resistance mutations. The M184V mutation was the most detected (Table 3).

4. Discussion

This study revealed a high prevalence of hepatitis B among HIV-infected persons. This situation confirms that people living with HIV constitute a population at risk of viral hepatitis infections due to their common modes of transmission and the failure of their immune systems [12]. This shows the need to create integrated HIV and viral hepatitis programs in Burkina Faso. In this study, we quantified HIV-2 plasma viral load and determined HIV-2 clusters and RT and PR resistance mutations in HIV-2 infected and HIV-1/HIV-2 co-infected patients in Burkina Faso. This study reveals more recent data on HIV-2 resis-

Table 1. Socio-demographic characteristics of study patients.

	Number (n=91)	Percentage (%)
Mean age (years)	58,99 ±8,66	
Sex		
M	33	36.3
F	58	63.7
HBsAg		
Positive	9	9.9
Negative	82	90.1
HCV-Ab		
Positive	1	1.1
Negative	90	98.9
HIV status		
HIV-1	11	12.1
HIV-2	67	73.6
HIV-1/HIV-2	13	14.3

Table 2. Characteristics of HIV-2 infected and coinfected HIV-1/2 patients.

	HIV-2 and HIV-1/HIV-2 (n= 80)
Sex	
Male	28 (35)
Female	52 (65)
HBAg	
Positive	7 (8.75)
Negative	73 (81.25)
HCV-Ab	
Positive	1 (1.25)
Negative	79 (98.75)
HIV-2 viral load (copies/mL)	
Not detected	44 (55)
≤ 1000	24 (30)
> 1000	12 (15)
HIV-2 Groups and sub-types	
Group A	19 (23.75)
Group B	12 (15)
CRF01_AB	3 (3.75)
Not detected	46 (57.5)

Table 3. Viral load, HIV-2 subtypes, and resistance mutations.

N°	Patient ID	Viral load (copies/mL)	HIV-2 subtypes	RT resistance mutations	PR resistance mutations
1	BF00056	380	HIV-2 Groupe B	No resistance	No resistance
2	BF00058	23 000	HIV-2 Groupe B	No resistance	No resistance
3	BF00068	2 400	HIV-2 Groupe B	No resistance	No resistance
4	BF00073	270 000	HIV-2 Groupe A	No resistance	No resistance
5	BF00093	2600	HIV-2 Groupe B	No resistance	No resistance
6	BF00097	620	CRF01_AB	No resistance	No resistance
7	BF00130	180	HIV-2 Groupe A	M184V	No resistance
8	BF00143	11 000	HIV-2 Groupe A	No resistance	No resistance
9	BF00163	440	HIV-2 Groupe B	No resistance	No resistance
10	BF00164	230	HIV-2 Groupe A	No resistance	No resistance
11	BF00175	5 900	CRF01_AB	No resistance	No resistance
12	BF00194	60 000	HIV-2 Groupe A	No resistance	No resistance
13	BF00022	5 000	HIV-2 Groupe A	No resistance	No resistance
14	BF00033	20 000	HIV-2 Groupe A	No resistance	No resistance
15	BF00091	7 000	HIV-2 Groupe A	No resistance	No resistance
16	BF00044	13 000	HIV-2 Groupe A	No resistance	No resistance
17	BF00053	10	HIV-2 Groupe A	No resistance	No resistance
18	BF00059	100	HIV-2 Groupe B	K65R	I50V
19	BF00060	900	HIV-2 Groupe A	No resistance	No resistance
20	BF00063	750	HIV-2 Groupe B	No resistance	No resistance
21	BF00066	670	HIV-2 Groupe B	No resistance	No resistance
22	BF00072	1 600 000	HIV-2 Groupe B	No resistance	No resistance
23	BF00081	2 100	HIV-2 Groupe A	No resistance	No resistance
24	BF00105	110	HIV-2 Groupe A	M184V	No resistance
25	BF00115	110	HIV-2 Groupe A	No resistance	No resistance
26	BF00106	100	HIV-2 Groupe B	No resistance	No resistance
27	BF00122	2 700	HIV-2 Groupe B	No resistance	No resistance
28	BF00109	7 000	HIV-2 Groupe B	M184V	No resistance
29	BF00127	1 900	HIV-2 Groupe A	M184V	V47A, I84V
30	BF00140	1 800	HIV-2 Groupe A	M184V	No resistance
31	BF00151	2 700	HIV-2 Groupe A	No resistance	No resistance
32	BF00144	5 000	CRF01_AB	No resistance	No resistance
33	BF00153	80	HIV-2 Groupe A	No resistance	No resistance
34	BF00235	1 470 000	HIV-2 Groupe A	K65R, Q151M, M184V	I54M, I82F

tance to antiretroviral drugs in Burkina Faso. Only 15% of patients had a high viral load (more than 1000 copies/mL). This demonstrates the effectiveness of the ARV treatment received by the patients. Indeed, the ARV treatment contributes to a considerable reduction in virus replication. This low proportion also confirms the fact that HIV-2 infection has a slow progression and reaches lower plasma viral load levels compared to HIV-1 [6]. However, it is useful for patients to have their HIV-2 viral load monitored because the development of major resistance mutations can lead to high viral loads. In this study, we found HIV-2 groups A and B with a majority of group A. This confirms that HIV-2 group A is responsible for the majority of HIV-2 infections and is predominant in Africa and Europe [13, 14]. The geographical distribution of the two HIV-2 groups is different in West Africa: group A is widely present in all regions, while Group B is mainly located in Côte d'Ivoire, Ghana, Burkina Faso, and Mali [10, 13]. In addition to groups A and B, our study revealed the presence of the recombinant form CRF01_AB in 3 HIV-2 patients. This is the first HIV-2 CRF confirmed by Los Alamos National Laboratory by whole genome sequencing in 2010 from samples of Japanese and Nigerian patients infected with HIV-2 in their home countries [11]. The CRF01_AB subtype is confirmed to be identical to the first single recombinant form (URF) 7123A detected in 1994 in a patient in Côte d'Ivoire [15] and to the second URF (510-03) identified in Cameroon in 2003 [16]. The existence to date of only these HIV-2 subtypes and CRFs demonstrates the recombination mechanism of HIV-2. This could be due to two factors: i) the low prevalence and low transmissibility of the virus and ii) the large genetic distance between HIV-2 groups which reduces recombination events [14]. Indeed, few patients with resistance mutations were detected in our study. Among those identified, the M184V mutation was the most common. Other reverse transcriptase mutations such as K65R, and Q151M were also detected. The three resistance mutations M184V, K65R, and Q151M have been reported as the most common mutations detected in HIV-2 cases and also common to HIV-1 [17, 18]. The K65R and Q151M mutations have been reported to induce high levels of resistance to most NRTIs [19]. Protease mutations I50V, V47A, I84V, I54M, and I82F were identified in our study. The same mutations were also detected in other studies in Senegal [20], Spain [21]. V47A, I82F, and I54M mutations have been identified as causing high phenotypic resistance to Lopinavir, and I54M to Darunavir [22].

5. Conclusion

This study revealed recent data on the status of HIV-2 genotypic resistance in Burkina Faso. Although few HIV-2 infected patients on ARV treatment showed resistance, major RT and PI resistance mutations and high viral loads were detected. It is therefore important that the management of HIV-2 infected patients is strengthened and that surveillance for HIV-2 genotypic resistance is implemented.

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Interests conflicts

The authors declare that there are no conflicts of interest.

Consent for publications

The author read and approved the final manuscript for publication.

Ethics approval and consent to participate

This study was performed in line with the principles of the Declaration of Helsinki. Informed voluntary consent was obtained from each of the participants. This study received approval from the Ethics Committee for Health Sciences of the Ministry of Health (Deliberation n°2016-04-75).

Availability of data and material

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Authors' contributions

STS supervised the data and sample collection. AN performed the serological tests and sequencing. ATY and STS drafted the manuscript. JS and ATY designed the study. All authors read and approved the final manuscript.

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References

1. Harries K, Zachariah R, Manzi M, Firmenich P, Mathela R, Drabo J, Onadja G, Arnould L, Harries A. (2010) Baseline characteristics, response to and outcome of antiretroviral therapy among patients with HIV-1, HIV-2 and dual infection in Burkina Faso. Trans R Soc Trop Med Hyg 104(2): 154-61. https://doi.org/10.1016/j.trstmh.2009.08.012
2. Soubeiga ST, Yonli AT, Bazie BVEJT, Ouedraogo HG, Simpore J. (2022) Prevalence of anemia and associated factors in HIV-1 infected children before and after initiation of antiretroviral therapy in Burkina Faso: A retrospective study. Afr J Microbiol Res 16(4): 140-6. https://doi.org/10.5897/AJMR2022.9622
3. Gottlieb GS, Raugi DN, Smith RA. (2018) 90-90-90 for HIV-2? Ending the HIV-2 epidemic by enhancing care and clinical management of patients infected with HIV-2. Lancet HIV 5(7): e390-e9. https://doi.org/10.1016/S2352-3018(18)30094-8
4. Campbell-Yesufu OT, Gandhi RT. (2011) Update on human immunodeficiency virus (HIV)-2 infection. Clin Infect Dis 52(6): 780-7. https://doi.org/10.1093/cid/ciq248
5. SP-CNLS 2020. Rapport Enquête de sérosurveillance au Burkina Faso. p36-38
6. Van der Loeff MFS, Larke N, Kaye S, Berry N, Ariyoshi K, Alabi A, van Tienen C, Leligdowicz A, Sarge-Njie R, da Silva Z, Jaye A, Ricard D, Vincent T, Jones SR, Aaby P, Jaffar S, Whittle H. (2010) Undetectable plasma viral load predicts normal survival in HIV-2-infected people in a West African village. Retrovirology 7(1): 1-10. https://doi.org/10.1186/1742-4690-7-46
7. Esbjörnsson J, Månsson F, Kvist A, da Silva ZJ, Andersson S, Fenyö EM, Isberg PE, Biague AJ, Lindman J, Palm AA, Rowland-Jones SL, Jansson M, Medstrand P, Norrgren H; Sweden and Guinea-Bissau Cohort Research Group. (2019) Long-term follow-up of HIV-2-related AIDS and mortality in Guinea-Bissau: a prospective open cohort study. Lancet HIV 6(1): e25-e31. https://doi.org/10.1016/S2352-3018(18)30254-6
8. Ayouba A, Akoua-Koffi C, Calvignac-Spencer S, Esteban A, Locatelli S, Li H, Li H, Li Y, Hahn BH, Delaporte E, Leendertz FH,

Peeters M. (2013) Evidence for continuing cross-species transmission of SIVsmm to humans: characterization of a new HIV-2 lineage in rural Côte d'Ivoire. AIDS 27(15): 2488-91. https://doi.org/10.1097/01.aids.0000432443.22684.50

9. Smith SM, Christian D, de Lame V, Shah U, Austin L, Gautam R, Gautam A, Apetrei C, Marx PA. (2008) Isolation of a new HIV-2 group in the US. Retrovirology 5:103. https://doi.org/10.1186/1742-4690-5-103
10. Visseaux B, Damond F, Matheron S, Descamps D, Charpentier C. (2016) HIV-2 molecular epidemiology. Infect Genet Evol 46: 233-40. https://doi.org/10.1016/j.meegid.2016.08.010
11. Ibe S, Yokomaku Y, Shiino T, Tanaka R, Hattori J, Fujisaki S, Iwatani Y, Mamiya N, Utsumi M, Kato S, Hamaguchi M, Sugiura W. (2010) HIV-2 CRF01_AB: first circulating recombinant form of HIV-2. J Acquir Immune Defic Syndr 54(3): 241-7. https://doi.org/10.1097/QAI.0b013e3181dc98c1
12. WHO. WHO guidelines on hepatitis B and C testing. 2017; https://apps.who.int/iris/bitstream/handle/10665/254621/9789241549981-eng.pdf (Accessed 10/09/2022)
13. Abana CZ, Sagoe KW, Bonney EY, Maina EK, Aziati ID, Agbosu E, Mawuli G, Styer LM, Ishikawa K, Brandful JAM, Ampofo WK. (2019) Drug resistance mutations and viral load in human immunodeficiency virus type 2 and dual HIV-1/HIV-2 infected patients in Ghana. Medicine 98(6): e14313. https://doi.org/10.1097/MD.0000000000014313
14. Ceccarelli G, Giovanetti M, Sagnelli C, Ciccozzi A, d'Ettorre G, Angeletti S, Borsetti A, Ciccozzi M. (2021) Human immunodeficiency virus type 2: the neglected threat. Pathogens 10(11): 1377. https://doi.org/10.3390/pathogens10111377
15. Gao F, Yue L, Robertson DL, Hill SC, Hui H, Biggar RJ, Neequaye AE, Whelan TM, Ho DD, Shaw GM. (1994) Genetic diversity of human immunodeficiency virus type 2: evidence for distinct sequence subtypes with differences in virus biology. J Virol 68(11): 7433-47. https://doi.org/10.1128/JVI.68.11.7433-7447.1994
16. Yamaguchi J, Vallari A, Ndembi N, Coffey R, Ngansop C, Mbanya D, Kaptué L, Gürtler LG, Devare SG, Brennan CA. (2008) HIV type 2 intergroup recombinant identified in Cameroon. AIDS Res Hum Retroviruses 24(1): 86-91. https://doi.org/10.1089/aid.2007.0190
17. Cavaco-Silva J, Aleixo MJ, Van Laethem K, Faria D, Valadas E, Gonçalves MdF, Gomes P, Vandamme AM, Cunha C, Camacho RJ; Portuguese HIV-2 Resistance Study Group. (2013) Mutations selected in HIV-2-infected patients failing a regimen including atazanavir. J Antimicrob Chemother 68(1): 190-2. https://doi.org/10.1093/jac/dks363
18. Charpentier C, Camacho R, Ruelle J, Eberle J, Gürtler L, Pironti A, Stürmer M, Brun-Vézinet F, Descamps D, Obermeier M. (2015) HIV-2EU—Supporting Standardized HIV-2 drug-resistance interpretation in Europe: An update. Clin Infect Dis 61(8): 1346-7. https://doi.org/10.1093/cid/civ572
19. Descamps D, Damond F, Matheron S, Collin G, Campa P, Delarue S, Pueyo S, Chêne G, Brun-Vézinet F; French ANRS HIV-2 Cohort Study Group. (2004) High frequency of selection of K65R and Q151M mutations in HIV-2 infected patients receiving nucleoside reverse transcriptase inhibitors containing regimen. J Med Virol 74(2): 197-201. https://doi.org/10.1002/jmv.20174
20. Raugi DN, Nixon RS, Leong S, Faye K, Diatta JP, Sall F, Smith RA, Sall EI, Malomar JJ, Seydi M, Gottlieb GS. (2020) HIV-2 drug resistance genotyping from dried blood spots. J Clin Microbiol 59(1): e02303-20. https://doi.org/10.1128/JCM.02303-20
21. Treviño A, de Mendoza C, Caballero E, Rodríguez C, Parra P, Benito R, Cabezas T, Roc L, Aguilera A, Soriano V; HIV-2 Spanish Study Group. (2011) Drug resistance mutations in patients infected with HIV-2 living in Spain. J Antimicrob Chemother 66(7): 1484-8. https://doi.org/10.1093/jac/dkr164
22. Raugi DN, Smith RA, Ba S, Toure M, Traore F, Sall F, Pan C, Blankenship L, Montano A, Olson J, Dia Badiane NM, Mullins JI, Kiviat NB, Hawes SE, Sow PS, Gottlieb GS; University of Washington-Dakar HIV-2 Study Group. (2013) Complex patterns of protease inhibitor resistance among antiretroviral treatment-experienced HIV-2 patients from Senegal: implications for second-line therapy. Antimicrob Agents Chemother 57(6):2751-60. https://doi.org/10.1128/AAC.00405-13