Pakistan
Journal of Biological Sciences

A Decade of Follow-up and Therapeutic Drug Monitoring in HIV-2 Immunocompromised Patients at St Camille and General Lamizana Military Medical Centers, Burkina Faso, West Africa

[1,2,3]M. Sanou, [1,5]S.T. Soubeiga, [4]F. Bationo, [1]T.R. Compaore, [1,5]T.M. Zohoncon, [2]G.N. Diatto,
[5]P. Ouedraogo, [1]V. Pietra, [1,6]B.M. Nagalo, [1,7]C. Bisseye, [3]R. Ouedraogo Traore and [1,5]J. Simpore
[1]Pietro Annigoni Biomolecular Research Center (CERBA) (LABIOGENE),
University of Ouagadougou, Burkina Faso
[2]General Sangoule Lamizana Military Medical Center, Clinical Laboratory Unit,
Ministry of Defence and Veterans Affairs, Ouagadougou, Burkina Faso, Healthcare Unit Training,
(UFR-SDS), University of Ouagadougou, Ouagadougou, Burkina Faso
[3]Charles de Gaulle University Pediatric Teaching Hospital, Ouagadougou, Burkina Faso
[4]Epidemiology and Bio statistic Pole, Clinical and Experimental Research Institute (IREC),
School of Public Health, Catholic University of Louvain, Brussels, Belgium
[5]St Camille Medical Center, 01 BP 364, Ouagadougou
[6]Endicott College, School of Arts and Sciences, Beverly, Massachusetts, USA
[7]University of Sciences and Techniques of Masuku, Franceville, Gabon

Abstract: Although, HIV-2 is generally less pathogenic than HIV-1 and its progression towards AIDS occurs less frequently. HIV-2 remains an important cause of disease in West Africa. This study aimed to evaluate HIV-1 and HIV-2 prevalence among pregnant women and to describe the demographic and clinical profile of patients with HIV-2 infection from 2003-2013 at St Camille and General Lamizana Military Medical Centers. A retrospective investigation was conducted using 12,287 medical records from patients screened for HIV. To respond to the lack of data available regarding HIV-2 treatment and also to address the approach to clinical, biological as well as therapeutic monitoring, 62 HIV-2 infected patients' medical records were studied. Seroprevalence of 10.6 and 0.14% were obtained, respectively for HIV-1 and HIV-2 among 12,287 women screened during the study period. From the sixty two (62) HIV-2 patients, the average age was 49.2 years (sex ratio was 0.65). The weight loss and diarrhea were the major clinical manifestations observed, respectively 54.8 and 25.8%. Fungi and herpes zoster (shingles) infections were reported as major opportunistic infections. Also, nearly half of the patients had more than 60 kg, less than 2% were in WHO stage IV and about 2/3 had a CD4 count bellow 250 cells mm^{-3}. AZT-3TC-IDV/LPV/R was the most prescribed combination. The gain in weight gain the Body Mass Index (BMI) improvement and the non-significant increase of the rate of CD4 between 1st (M1) and 24th month (M24) were observed after treatment with antiviral.

Key words: HIV-2, CD4, ARV, Viral load

INTRODUCTION

In 2012, the United Nations Program on HIV/AIDS (UNAIDS), estimated in his global report at 35.3 million the number of people infected with HIV worldwide with, respectively 2.3 million of new infections and 1.6 million deaths each year. Sub-Saharan Africa is so far the most affected region of the world with 25 million infections, followed by South Asia and South East Asia with 4.8 million of cases (UNAIDS., 2013). HIV prevalence in Burkina Faso at the year's end of 2013 was 1.1% according to World Health Organization (WHO) and UNAIDS. In the country a decrease of the prevalence was observed, from 7.2% in 2001 to 1.1% in 2013. This reduction in prevalance is the result of the efforts made by the geverment and Non-Government Organizations (NGOs) as well as the awareness of youth regarding HIV/AIDS (Simpore *et al.*, 2007).

However, the number of people living with HIV continues to grow. The number of new infections is higher than the number of deaths (UNAIDS., 2013). The

Corresponding Author: J. Simpore, Pietro Annigoni Biomolecular Research Center (CERBA)/(LABIOGENE),
University of Ouagadougou, 01 BP 364, Ouagadougou 01, Burkina Faso
Tel: +226 70 23 07 92 Fax: +226 50 36 34 42

HIV infection persists and remains a public health problem, despite the significant decline in the prevalence in the population. Both types of HIV co-exist in Burkina Faso but with a predominance of HIV-1, 97% of patients (HDS-IV., 2010). A lot of efforts have already been done to reduce the incidence of HIV-1 in Burkina Faso (Pignatelli *et al.*, 2006; Simpore *et al.*, 2006, 2007; Kagone *et al.*, 2011; Linguissi *et al.*, 2012; Foca *et al.*, 2014). On the opposite side, few exertion have been made for HIV-2 because of it has a low virulence and prevalence compare to HIV-1. Most of the reports on HIV-2 are found in West Africa due to the fact that it is highly concentrated in this region, in countries such as Senegal, Nigeria, Ghana, Ivory Coast and Burkina Faso (Ndour *et al.*, 2006; De Mendoza *et al.*, 2014). However, people infected with HIV-2 are subjected to the same opportunistic infections as those people infected with HIV-1. The differences between HIV-1 and HIV-2 lie in their structures (HIV-2 has vrp and vpx proteins while HIV-1 has only vpr) which in turn influence the way the two viruses behave once they enter the human body regarding the treatments, the progression towards AIDS, gene polymorphisms and the resistance to antiretrovirals (De Mendoza *et al.*, 2014).

HIV-2 is also more difficult to monitor than HIV-1 in Burkina Faso, due to the fact that there is no viral load assay available. Infectious samples are shipped in Europe for viral loads and prices are often too high for patients (90% of people live under poverty line with less than 1\$ per day). This investigation was undertaken to improve our knowledge on the monitoring of HIV-2 infected patients in Burkina Faso. At first, we estimated the prevalence of HIV-2 and its progression towards AIDS stage in a group of women under treatment, from the Prevention of Mother-to-Child-Transmission program of HIV (PMTCT) at St Camille Medical Center. A dedicated institution to HIV treatment, prevention, research and surveillance. Secondly a systematic review of medical records was performed in order to describe the clinical characteristics of patients infected with HIV-2 as well as the biological and therapeutic procedure used in treatment centers. Finally, the effectiveness of clinical, biological and therapeutic management was assessed over the past ten year (2003-2013).

MATERIALS AND METHODS

A retrospective study was conducted which aimed to describe the evolution in therapeutic drug monitoring of infected patients with HIV-2 through its clinical and biological aspects from June, 2003 to September 2013.

Study design and population: A total of 12,287 pregnant women attending antenatal care were enrolled in the Prevention of Mother-to-Child-Transmission program of HIV (PMTCT) at St Camille medical center (CMSC) from 2003-2013. All of the pregnant women were tested for HIV-1 and HIV-2 antibodies following informed consent, counselling and completion of a questionnaire. Rapid tests were performed to determine serological status of patients according to WHO recommendations. First of all, a primary sensitive test was performed (Determine, Abbott, Chicago, USA). Then, a second specific and differential test was also performed in order to differentiate HIV-1 and HIV-2 (SD Bioline, Standard Diagnosis, Seoul, South Korea). HIV-positive patients underwent a regular clinical and psychological monitoring.

Sampling: Given the low prevalence of HIV-2 and to better assess the efficiency of clinical management of this infection, we have associated to our initial sampling, patients treated at the Military medical Center, General Sangoule Lamizana (CM-GSL). Characteristics such as incomplete charts, untreated, death or loss of follow-up were excluded from our analysis. Out of 77 infected patients with HIV-2, only 80.5% (62/77) were included in this study as follows 29.9% (23/77) at CMSC and 50.6% (39/77) at CM-GSL. Patients' characteristics such as age, gender, occupation, marital status were recorded. Significant clinical signs were considered for inclusion in the analysis (fever, weight loss, cough, diarrhea, anemia, pruritus, opportunistic infections). The CD4 cells count, hemoglobin level and biochemistry (glycaemia, creatinine, transaminases) parameters were also recorded.

Ethical aspects: This study was approved by the St Camille Medical Center and Ethics Review Committee and the Institutional Review Board of Pietro Annigonni Biomolecular Research Center (CERBA). Patient informed consent was not required as only routine, anonymized, monitoring data were collected and analyzed.

Statistical analysis: Data was analyzed using SPSS 17.0 and Epi Info 3.5.1 softwares. The Chi-square test was used for comparisons. The p-values bellow 0.05 were considered statistically significant.

RESULTS

Data on HIV prevalence: Out of 12,287 pregnant women enrolled in PMTCT of HIV prevention and control programme from 2003-2013 at CMSC, 10.8% (1332/12287) were infected with HIV as follows 10.6% (1302/12287) and 0.14% (17/12287), respectively for HIV-1 and HIV-2 (Table 1). The HIV prevalence lowered significantly from 2003 (19.5%) to 2013 (4.5%) ($p < 0.0001$, Table 1 and Fig. 1). Due to the very low prevalence of HIV-2 and in order to

Table 1: Evolution and distribution of HIV-1/2 among women from 2003 to 2013

Serology	Years											Total	HIV positives	
	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013		No.	%
HIV1	101	112	132	215	119	108	106	130	83	81	115	1302	1302/1332	97.75
HIV2	0	0	2	4	1	1	2	3	1	2	1	17	17/1332	1.28
HIV1+2	0	0	2	3	2	1	0	0	3	1	1	13	13/1332	0.98
Positives	101	112	136	222	122	110	108	133	87	84	117	1332	12287/1332	10.8
Negatives	416	491	607	564	530	643	945	1081	1576	1647	2485	10985	12287/10985	89.2
Total	517	603	739	779	649	751	1051	1211	1659	1728	2600	12287		100
(%) HIV+	19.5*	18.6	18.4	28.5	18.8	14.6	10.3	11.0	5.2	4.9	4.5*	10.8		

*p<0.00001

Table 2: Socio-demographic characteristics of infected patients at the time of enrollment in PMTCT

Characteristics (n = 62)	Frequency rate means	Percentage
Age	49.2±8.3	
<40	10	16.1
40-49	15	24.1
50-55	26	42.0
≥56	11	17.8
Occupation		
Housewives	26	41.9
Civil servants	30	48.4
Others	6	9.7
Marital status		
Married	45	72.6
Widows	12	19.3
Singles	5	8.1

PMTCT: Prevention of Mother-to-Child-Transmission program of HIV

Fig. 1: HIV frequency evolution from 2003-2013

Fig. 2: Overall weights from M1-M24 (M: Month), Weight m1 vs Weight m24, *p<0.046

obtain a representative cohort statistically significant, HIV-2 infected patients from CM-GSL were added to initial sample.

Socio-demographic and epidemiological characteristics of patients infected with HIV-2: The average age of HIV-2 infected patients was 49.2±8.3, aged from 16 to 68 years. It was noticed a dominance of adult patients aged from 40-55 years with a sex ratio 0.65. Most of the infected women were married (living with a partner) and were housewives, respectively 72.5 and 42% (Table 2).

Clinical, biological and therapeutic data of infected patients at inclusion: The loss of weight as well as diarrhea were the dominant clinical signs at the enrollment
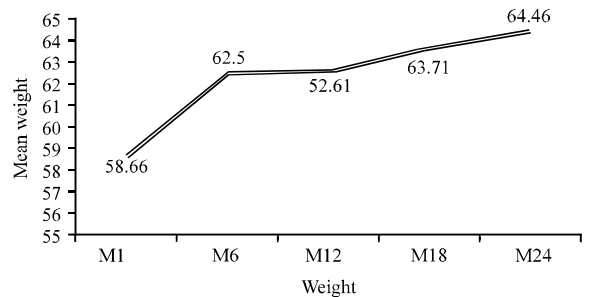
of infected patients into the treatment centers of both medical facilities, with respectively 54.8 and 25.8%. Out of 42.6% of opportunistic infections reported, 80.1% were results of combination between fungi infection (*Candida* sp.) and *Herpes zoster*. Patients with over 60 kg accounted for 54.8% of the cohort and 1.6% were in stage 4 of WHO (progression from HIV to AIDS). Patients had a weight gain from the 1st month to the 24th month of follow-up (Fig. 2). Furthermore, it was noticed that from the first month of inclusion to the 24th month, patients moved from a thin to a normal state and then from a normal to an overweight state (Fig. 3).

Anemia was present at about 37.1% among patients and 2/3 had CD4 count level below 250 cells mm^{-3}.

Table 3: Clinical, biological and therapeutic data of infected patients with HIV-2

Clinical and biological characteristics	Frequency rate	Percentage
Clinical signs (n = 82)		
Weight loss	28	34.1
Persistent cough	12	14.6
Watery diarrhea	16	19.5
Fungi infection	14	17.1
Pruritus	12	14.7
HIV clinical stage (n = 62)		
I	18	29.0
II	23	37.1
III	20	32.3
IV	1	1.6
Presence of OI (n = 61)		
Yes	26	42.6
No	35	57.4
ART (n = 62)		
AZT-3TC-IDV	19	30.6
AZT-3TC-IPV/R	9	14.5
3TC-D4T-IPV	8	12.9
AZT-D4T-LPV/R	5	8.1
Other	21	33.9
CD4 count (n = 61)		
≤50	6	9.8
50-250	34	55.7
>250	21	34.4
BMI (n = 62)		
Below normal range	12	19.4
Normal range	35	56.5
Above normal range	15	24.2

BMI: Body mass index, OI: Opportunistic infection
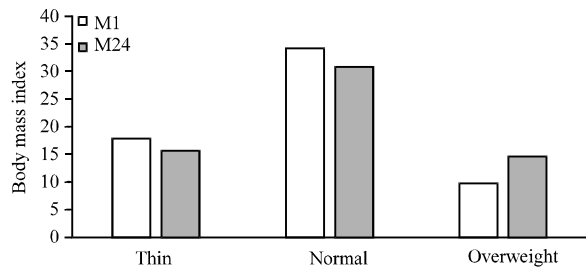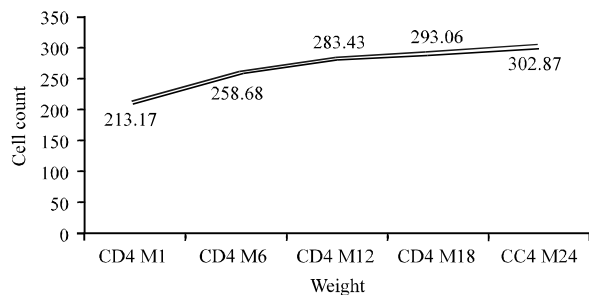

Fig. 3: BMI M1-M24

Fig. 4: CD4 count from M1-M24

There was an increase in CD4 cell counts from the first month of follow-up to the 24th month (Fig. 4).

The combination, AZT-3TC-IDV was the most prescribed treatment to patients. The changes in the treatment due to the failure of prior treatment used represented 14.5% (Table 3).

DISCUSSION

From 2003-2013, out of the 12,287 pregnant women attending antenatal care at CMSC, 10.8% were detected positive for HIV as follows 97.7, 1.3 and 1.0%, respectively positives for HIV-1, HIV-2 and co-infection HIV-1/2 (Table 1). There is a significant decrease in the distribution of the infected pregnant women with rates of 19.5% in 2003 to 4.8% in 2013 (p<0.0001). Those findings are in agreement with the rate of 2.9% (2.1- 4.0) reported in the National Survey conducted in Ouagadougou among pregnant women (HDS-IV., 2010).

To evaluate efficiently the clinical management of infected patients with HIV-2 as well as factors associated to the progress of the infection towards AIDS stage, we conducted a retrospective study of monitoring of HIV-2 infected patients at CMSC and CM-GSL both located in Ouagadougou, capital city of Burkina Faso.

Over 62 infected patients with HIV-2 were included in the present analysis with an average age of 49.2±0.8 (16-69 years). The sex ratio was 0.67 which is in agreement with the value found in Ivory Coast in the study of (Eholie *et al.*, 1998). Married and housewives patients were represented respectively with 41.9 and 72.5%. Weight loss as well as diarrhea was the most common clinical signs found in more than 54.8% cases studied. The similar values were found in the study among Senegalese women by Ndour *et al.* (2006). In contrast of the results found in several investigations in the

surroundings countries, opportunistic infections and malignancies resulting from depletion of the immune system were presents at a higher rate (42%), essentially fungi infection caused by *Candida* sp. and *Herpes zoster* (Ndour *et al.*, 2006; Eholie *et al.*, 1998). At the time of the enrollment in the PMTCT of HIV, 70% of infected patients were treated using the combination of AZT+3TC+IDV/LPV/R. Contrary to several studies conducted in Sub-Saharan Africa most of the patients in our investigation were at a lower stage of HIV infection (I and II) according to WHO. Also, all patients enrolled in the PTMTC of HIV in antenatal care clinics had received medical and social assistance as well as psychological care. The majority of patients were provided with antiretroviral drugs and medical monitoring as soon as the biological parameters of the diseases progression were known. However, we reported 9 changes in the antiretroviral drugs initially prescribed to the patients due to a failure in the treatments (low/unchanged CD4 count, poor health). Several drop-outs of patients were recorded as follows, due to two laboratory errors (cross reaction with HIV-1 and HIV-2), four loss of follow-up, one co-infection with hepatitis B and one unknown reason. In overall it was observed a weight gain from M1 (58.66±15.90) and M 24 (64.46±15.56) (p = 0.046), essentially after a changes in HIV medicines prescribed (Fig. 2). The increase in a weight as well as improvement in Body Mass Index (BMI) appears as good predictors of disease progression. In the Fig. 3 from M1 to M24, BMI is showed as predictor of gain of CD4+T-lymphocyte in women receiving antiretroviral treatment which is in agreement with previous studies (Palermo *et al.*, 2011; Ndour *et al.*, 2006; Matheron *et al.*, 2006). Anti-HIV treatment combined to parameters such as weight gain and BMI will improve the clinical management in low income countries. Furthermore, increasing access to viral load testing for HIV-2 as well as HIV-1, will dramatically improve the quality of HIV treatment services in disadvantaged countries (Matheron *et al.*, 2006; Delarue *et al.*, 2013).

CONCLUSION

Due to coordinated actions in HIV prevention and treatment by the government, financial partners and local populations, there is a decrease in HIV prevalence, since 2003. Despite the fact that, clinical and biological parameters such as weight gain and BMI can be used to monitor the progression of the disease among infected patients. Increasing the availability and affordability of viral load testing is fundamental to improve the clinical management of patients infected with HIV-2.

REFERENCES

De Mendoza, C., E. Caballero, A. Aguilera, M. Piron and R.O. de Lejarazu *et al.*, 2014. HIV-2 and HTLV-1 infections in Spain, a non-endemic region. AIDS Rev., 16: 152-159.

Delarue, S., E. Didier, F. Damond, D. Ponscarme and K. Brengle-Pesce *et al.*, 2013. Highly sensitive plasma RNA quantification by real-time PCR in HIV-2 group A and group B infection. J. Clin. Virol., 58: 461-467.

Eholie, S.P., E. Ehui, E. Aoussi, A. Kakou, P.A. Assemien, E. Bissagnene and A. Kadio, 1998. [Epidemiologic and clinical features of HIV-2 infection in Abidjan, Ivory Coast]. Medecine Tropicale, 58: 204-205, (In French).

Foca, E., S. Odolini, G. Sulis, S. Calza and V. Pietra *et al.*, 2014. Clinical and immunological outcomes according to adherence to first-line HAART in a urban and rural cohort of H IV-infected patients in Burkina Faso, West Africa. BMC Infect. Dis., Vol. 14. 10.1186/1471-2334-14-153

HDS-IV., 2010. Multipara meters health and demographic survey (EDS-IV). http://www.insd.bf/fr/IMG/pdf/rapport_preliminaire_EDS_IV_BF_2010.pdf

Kagone, T.S., H. Hien, N. Meda, P.S. Diagbouga and A. Sawadogo *et al.*, 2011. Characterization of HIV-1 genotypes and antiretroviral drug-resistance mutations among patients in Burkina Faso. Pak. J. Biol. Sci., 14: 392-398.

Linguissi, L.S.G., C. Bisseye, T. Sagna, B.M. Nagalo and D. Ouermi *et al.*, 2012. Efficiency of HAART in the prevention of mother to children HIV-1 transmission at Saint Camille medical centre in Burkina Faso, West Africa. Asian Pac. J. Trop. Med., 5: 991-994.

Matheron, S., F. Damond, A. Benard, A. Taieb and P. Campa *et al.*, 2006. CD4 cell recovery in treated HIV-2-infected adults is lower than expected: Results from the French ANRS CO5 HIV-2 cohort. AIDS, 20: 459-462.

Ndour, C.T., G. Batista, N.M. Manga, N.F.N. Gueye, N.M.D. Badiane, M. Fortez and P.S. Sow, 2006. [Efficacy and tolerance of antiretroviral therapy in HIV-2 infected patients in Dakar: Preliminary study]. Medecine Maladies Infectieuses, 36: 111-114, (In French).

Palermo, B., R.J. Bosch, K. Bennett and J.M. Jacobson, 2011. Body mass index and CD4$^+$ T-lymphocyte recovery in HIV-infected men with viral suppression on antiretroviral therapy. HIV Clin. Trials, 12: 222-227.

Pignatelli, S., J. Simpore, V. Pietra, L. Ouedraogo and G. Conombo *et al.*, 2006. Factors predicting uptake of voluntary counselling and testing in a real-life setting in a mother-and-child center in Ouagadougou, Burkina Faso. Trop. Med. Int. Health, 11: 350-357.

Simpore, J., V. Pietra, A. Savadogo, S. Pignatelli and J.B. Nikiema *et al.*, 2006. Reduction of mother-to-child transmission of HIV at Saint Camille medical centre in Burkina Faso. J. Med. Virol., 78: 148-152.

Simpore, J., V. Pietra, S. Pignatelli, D. Karou and W.M. Nadembega *et al.*, 2007. Effective program against mother-to-child transmission of HIV at Saint Camille Medical Centre in Burkina Faso. J. Med. Virol., 79: 873-879.

UNAIDS., 2013. Global report: UNAIDS report on the global AIDS epidemic 2013. Joint United Nations Programme on HIV/AIDS (UNAIDS), Geneva, Switzerland.