

Variation of biological and biochemical parameters in patients receiving antiretroviral treatment at the Maradi Regional Hospital during 2021-2022

ABSTRACT

Aims: To follow the variation of some biological and biochemical parameters in HIV-infected patients under antiretroviral treatment at the Maradi Regional Hospital.

Study design: retrospective and prospective study

Study location and duration: Maradi Regional Hospital; from August 2021 to April 2021, a duration of 9 months.

Methodology: We followed the variation of some immunological and biochemical parameters in patients living with HIV, evaluated the CD4+ T cell counts, the viral load, the leukocyte count, and carried out the measurement of haemoglobin, glycaemia, creatinemia, and ALAT levels in the blood at the follow-up visits (month 0 (M0), month 3 (M3), and month 6 (M6)), except for the viral load and CD4+ T-cell counts, which were measured at M0 and M6, and the HBsAg test at M0.

Results: 99 patients were included in this study. The sex ratio was 2.6 in favour of females. At enrolment, 63.6% of patients had a CD4+ T-cell count < 200/mm³, 56.6% had anaemia, 40.4% had hypoglycaemia and there was a significant increase in patients with an undetectable viral load from enrolment to the last visit at M6. At the end of the study, we observed an improvement in CD4+ T-cell counts, haemoglobin, glycaemia and viral load at each subsequent visit. We did not observe any significant evolution of creatinemia and alanine aminotransferase rate.

Conclusion: At the end of the study, we observed an improvement in CD4+ T-cell count, glycaemia, haemoglobin and viral load. We did not observe any particular change in the biochemical parameters of creatinemia and ALAT levels. This shows the non-toxicity of the antiretroviral treatments. Finally, we observed some difficulties in our study which deserve to be improved.

Key words: HIV, CD4, anaemia, Maradi, Niger.

INTRODUCTION

CD11a is important for normal lymphocyte development [1]. HIV activates CD4+ T lymphocytes, dendritic cells, and macrophages, resulting in immune system dysfunction [2]. Toll like receptor 2 and 4 (TLR2 and TLR4) play a considerable role in the host defense against microorganism [3]. HIV-1-infected patients, increased expression of TLR2 and TLR4 was observed in DCs, but only of TLR2 in monocytes [4]. IL-10 is an immune-regulatory cytokine [5] having a potential pathogenic role in HIV infection [6], while There is no association between HIV naive and sVCAM-1[7], as the latter is a cytokine-inducible endothelial cell adhesion molecule (CAM) [8]. PD-L1 is responsible for T cell activation, proliferation, and cytotoxic secretion to produce anti-tumor and immune responses [9]. PD-1 and HIV-specific CD4 T cell responses dysregulation are major features of HIV infection [10].

AIDS is the advanced stage of HIV infection. There are several classifications of HIV infection, developed according to the possibilities of diagnosis and follow-up in different regions of the world. In the United States, the most recent classification, revised in 1993, takes into account the clinical situation of patients as well as a biological criterion (CD4+ T-cell count) [11]. HIV remains a major public health problem of global significance, with more than 36.3 million deaths to date [27.2-47.8 million]. There is no cure for HIV infection. However, with improved access to effective prevention, diagnosis, treatment and care, including for opportunistic infections, HIV infection has become a chronic condition that can be managed with the possibility of a long and healthy life. By the end of 2020, an estimated 37.7 million [30.2-45.1 million] people will be living with HIV, with more than two-thirds (25.4 million) in the WHO African Region. In 2020, 680 000 [480 000-1.0 million] people will have died from HIV-related causes and 1.5 million [1.0-2.0 million] people will have become infected with HIV [12].

In Niger, the prevalence of HIV infection in the general population was estimated to be 0.4% in 2012 [13].

HIV treatment in Niger is based on highly active antiretroviral treatment (HAART), which suppresses the viral load. However, the triple therapy used is sometimes poorly tolerated due to its high toxicity and can lead to death in some patients.

However, strict adherence by the patients themselves by taking their medication daily, a health and social system that ensures proper monitoring of patients and, above all, biological monitoring are essential for better management of patients living with HIV.

In this context, we initiated this work to study the variations in biological parameters of patients on HAART during the period from August 2021 to April 2022 at the Maradi Regional Hospital.

METHOD

We conducted a retrospective and prospective study at the RODA Medical Department of the Magama Unit. Our study population consisted of HIV-positive adult patients with a 2-year follow-up and a usable file. They were all regularly followed up. First, we used each patient's file to record the various examinations carried out at enrolment (B1), *i.e.* the examinations carried out before the patients were put on HAART (retrospective study).

We then performed three (3) tests for each of the following parameters : haemoglobin level, creatinine level, transaminases (ALAT) and blood glucose level at M0 (B2), M3 (B3) and M6 (B4), except for the viral load and CD4 level, which were requested at M0 (B1), which corresponds to the inclusion test, and M6 (B4) (prospective study).

Analysis was performed using SPSS V.20 software.

RESULTS

A total of 99 patients were included in the study. The mean age was 42 years, with extremes of 19 and 71 years. The sex ratio was 2.6 in favour of females. The majority of patients were between 30 and 40 years of age (38.4%).

HIV1 was the majority in our sample with 96.96%. Most patients (82.8%) came from Maradi, the regional capital. Married people and housewives were the most represented with 60.6% and 59.6% respectively. TDF-3TC-EFV was the most commonly used regimen, prescribed to 68.7% of patients. (Table 1)

At enrolment, more than half of the patients had anaemia (56.6%) ; (43.4%) had normal haemoglobin levels. This frequency varied significantly between visits 2, 3 and 4, reaching 16.2% of patients with anaemia and 83.8% of patients with normal haemoglobin at visit 4 (Table 2).

The incidence of anaemia was 56.6% and 40.4% in patients with severe and moderate immunodepression, respectively, and 16.2% in patients with insignificant immunodepression. (Figure 1)

At enrolment, 63.6% of patients had a CD4+ T-cell count $< 200/\text{mm}^3$, 40.4% had hypoglycaemia and there was a significant increase in patients with an undetectable viral load from 42.4% at enrolment to 72.7% at the last visit. At the end of the study, we observed a significant improvement in CD4+ T-cell counts, haemoglobin, glycaemia and viral load over time. There was no significant change in creatinine or ALAT levels (Table 2).

At enrolment, almost half of the patients had hypoglycaemia (40.4%), with (9.1%) of the patients having hyperglycaemia. This situation varied with subsequent visits up to the fourth visit, where hypoglycaemia decreased significantly to 12.1% and hyperglycaemia to 5.1% (Table 2).

At enrolment, 37.4% of patients had an elevated ALAT level, and this frequency did not vary significantly with each examination. At the fourth visit (B4), 23.2% of patients had an elevated ALAT level (Table 2).

At baseline, 51.1% of patients had an elevated creatinine level, but this frequency varied significantly between examinations, reaching 23.2% at the third examination (B3) (Table 2).

At baseline, 63.6% of patients were severely immunocompromised, compared with 16.2% at baseline 4. 3% of patients were not significantly immunocompromised at baseline, compared to 60.6% at the fourth visit (Table 2).

At baseline, 100% of patients had a detectable viral load ; at the second and fourth visits, 42.4% and 72.7%, respectively, had an undetectable viral load (Table 3).

DISCUSSION :

We conducted a retrospective and prospective study with some limitations related to the lack of completeness of patient records, the breakage of reagents for the determination of viral load and CD4+ T-cell counts. Our sample consisted of 99 patients. The sex ratio was 2.6. These results are comparable with those of Derep Veltomtoh [14], who reported a sex ratio of 2.13 in 2021, and Diallo et al [15] in Senegal, who reported a sex ratio of 2.87 in 2021. This female predominance can be explained by the greater exposure of women compared to men due to certain socio-cultural constraints (polygamy, excision, prostitution...) or their physiological constitution, which makes them more susceptible to infection [16].

The average age of our patients is 42 years, with extremes of 19 and 71 years. The age group 30-40 years was the majority with 38.4%. This result is comparable to that of Abdoulaye et al

[13] in Maradi, Niger, who in their study found 66.86% of patients in the 20-40 age group with a mean age of 36.10 years.

This age group is the most sexually active in the population and also the most at risk of HIV/AIDS. In fact, the peak of seroprevalence in both men and women is between 30 and 35 years of age.

HIV1 is the predominant type in our work 96.7% of cases, in addition we have in our sample an association of HIV1 and HIV2 of 2%. HIV1 is the predominant type in sub-Saharan Africa.

These results are comparable to those of Bedji Tchenin [17] in 2012 in Côte d'Ivoire, who found 95% of patients with HIV1 and 2.89% of patients with HIV 1 and 2. Lozès et al [18] in Togo in 2012 found 95.1% for HIV1 and 4.9% for the combination of HIV 1 and 2.

The majority of patients were on TDF-3TC-EFV (68.7%), which is the first-line regimen recommended by the Medical Technical Committee according to the WHO 2015 recommendations. TDF-3TC-DTG (14.1%) was the second most commonly used regimen, followed by AZT-3TC-LPV/r (13.1%) and TDF-3TC-LPV/r (4.05%).

Diallo Cheickna [19] in his study showed a predominance of the TDF-3TC-EFV combination (84.62%) and Makougoum Njidie in Mali [20] reported the same combination (75.4%).

56.6% of patients had anaemia at enrolment (B1), a result comparable to that of Kanté et al [21] in Guinea in 2020, who found 68%, and Djibrilla Almoustapha et al [22] in Niamey, Niger in 2019, who found 71.6% of patients with anaemia at enrolment, which can be explained by the destructive effect of HIV on blood cells, but also by the issue of underdevelopment of the country.

In our study, we found a significant change in haemoglobin level from 56.6% at enrolment to 16.2% at the last visit.

This evolution was observed by Karfo et al [23] in Burkina in 2019, who found 47.1% at enrolment and 16.7% at the last examination after one year of follow-up.

At inclusion, more than half of the patients had hypoglycaemia (50.5%), compared to 12.1% at the fourth visit (B4). These results are comparable to those of Meminta [16] in Mali in 2014, who found 57.47% at inclusion and 54.45% at the last visit.

37.4% of patients had elevated ALAT at enrolment compared to 23.2% at last follow-up (B4). This result is comparable to that of Kalimira Kachelewa et al [24] in Congo, who found 47.4% at enrolment and 33.5% at the last examination.

At enrolment all our patients had a detectable viral load, this result had a clear evolution at B2 and B4 respectively 42.4% and 72.7% of patients with an undetectable viral load. This evolution of viral load was observed in the Dollo study [25] in Mali in 2021, where all patients had a detectable viral load at enrolment, 30.2% of patients had an undetectable viral load at the first visit and 66.9% at the last visit.

63.6% of patients were severely immunosuppressed at baseline, 16.2% at last visit (B4). Patients with non-significant immunosuppression : 3% at baseline and 60.6% at last visit (B4). These results are comparable to those of Lozès et al [18] in Togo in 2012, who found 69.9% of patients in the stage of severe immunosuppression at baseline compared to 18.9% at last follow-up, and 12.3% of patients in the stage of non-significant immunosuppression at baseline compared to 79.7% at last follow-up.

Table 1. Sociodemographic and therapeutic characteristics	
Variables	Number (%)
Gender	
Men	27 (27,3)
Women	72 (72,7)
Sex ratio	2,6
Age (years)	
Average	
Extremes	19 – 71
15 – 30	17 (17,2)
30 – 40	38 (38,4)
40 – 55	29 (29,3)
> 55	15 (15,1)
Marital status	
Married	60 (60,6)
Widow/widower	19 (19,2)
Divorced	12 (12,1)
Singles	8 (8,1)
Profession	
Households	59 (59,6)
Merchants	17 (17,2)
Cultivators	8 (8,1)
Drivers	5 (5,1)
Teachers	3 (3,03)
Retired	3 (3,03)
Other	4 (4,04)
Place of residence	
Maradi**	82 (82,8)
Periphery	17 (17,2)
The type of HIV	
HIV 1	96(96,97)
HIV 2	2(2,02)
HIV 1 & HIV 2	1(1,01)
Therapeutic scheme	
TDF-3TC-EFV	68 (68,7)
TDF-3TC-DTG	14 (14,1)
AZT-3TC-LPV/r	13 (13,1)
TDF-3TC-LPV/r	4 (4,05)
* tailors, carpenter, worker ** regional headquarter	

Table 2: Biological tests according to frequency

Biological check-up	Frequency of assessment			
	Balance sheet 1 (B1)	Balance sheet 2 (B2)	Balance sheet 3 (B3)	Balance sheet 4 (B4)
haemoglobin				
Normal	43 (43,4%)	69 (69,7%)	59 (59,6%)	83 (83,8%)
anemia	56 (56,6%)	30 (30,3%)	40 (40,4%)	16 (16,2%)
Blood glucose				
Hypoglycemia	40 (40,4%)	42 (42,4%)	38 (38,4%)	12 (12,1%)
Normoglycemia	50 (50,5%)	51 (51,5%)	56 (56,5%)	82 (82,8%)
hyperglycemia	9 (9,1%)	6 (6,1%)	5 (5,1%)	5 (5,1%)
Creatinine levels				
Normal	48 (48,5%)	76 (76,8%)	79 (79,8%)	69 (69,7%)
High	51 (51,5%)	23 (23,2%)	20 (20,2%)	30 (30,3%)
Transaminasemias ALAT				
Normal	62 (62,6%)	60 (60,6%)	71 (71,7%)	76 (76,8%)
High	37 (37,4%)	39 (39,4%)	28 (28,3%)	23 (23,2%)
Viral load				
DVL	99 (100%)	57 (57,6%)	-	27 (27,3)
NDVL	0	42 (42,4%)	-	72 (72,7)
ALAT : alanine aminotransferase DVL : detectable viral load, NDVL : non detectable viral load				

Table 3 : Distribution of patients by CD4 count and immune stage

		TCD4	
		Number	Percentage
BALANCE SHEET1 (B1)	severe	63	63,6
	advance	26	26,3
	moderate	7	7,1
	Not significant	3	3
	Total	99	100
BALANCE SHEET2 (B2)	severe	24	24,2
	advance	20	20,2
	moderate	19	19,2
	Not significant	36	36,4
	Total	99	100
BALANCE SHEET4 (B4)	Severe	16	16,2
	Advance	8	8,1
	Moderate	15	15,2
	Not significant	60	60,6
	Total	99	100

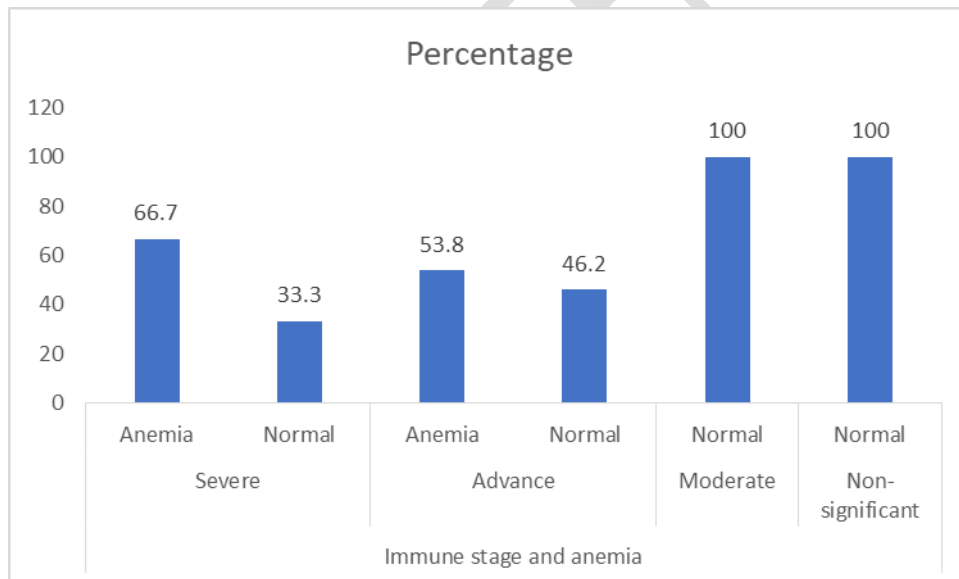


Figure 1 : Variation in haemoglobin levels as a function of immune status at workup 4 (B4)

CONCLUSIONS :

Both sexes were affected by the infection, but there was a female predominance, married people were mostly infected, the age group 30-40 years was most affected. Housewives and shopkeepers were most infected. HIV type 1 was in the majority. The immune status, haemoglobin levels and blood sugar levels of the patients improved significantly from the time of enrolment to the last examination. There was no significant increase in ALAT or creatinine levels, demonstrating the effectiveness of HAART in HIV patients.

This study shows that the biological disturbances observed before the start of HAART have progressively regressed, demonstrating the effectiveness of triple antiretroviral therapy on the infection, leading to an improvement in the quality of life of people living with HIV.

CONSENT

As per international standard or university standard, patient(s) written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

REFERENCES

- [1] Abdel Hameed MR, Nafady HA, Mostafa MI, Sayed D, Obiedallah AA. Possible Role of CD11a in Primary Immune Thrombocytopenia Patients on Immunosuppressive Therapy. *J Blood Med.* 2021 ;12 :197-205 <https://doi.org/10.2147/JBM.S300717>
- [2]. Xue W., Zhang Y., Wang H., Zhang Y., Hu X. Multicenter study of controlling nutritional status (CONUT) score as a prognostic factor in patients with HIV-related renal cell carcinoma. *Frontiers in Immunology* . 2021 ;12 doi: 10.3389/fimmu.2021.778746.778746
- [3] Abdel Hamed MR, Elgendy SG, El-Mokhtar MA, Sayed D, Mansour SM, Darwish AM. T-lymphocytes Expression of Toll-like Receptors 2 and 4 in Acute Myeloid Leukemia Patients with Invasive Fungal Infections. *Mediterr J Hematol Infect Dis.* 2022 Mar 1;14(1):e2022022. doi: 10.4084/MJHID.2022.022. PMID : 35444773 ; PMCID : PMC8992612.
- 4 Hernández JC, Stevenson M, Latz E, Urcuqui-Inchima S. HIV type 1 infection up-regulates TLR2 and TLR4 expression and function in vivo and in vitro. *AIDS Res Hum Retroviruses.* 2012 Oct;28(10):1313-28. doi: 10.1089/aid.2011.0297. Epub 2012 Mar 12. PMID: 22280204; PMCID: PMC3482876.
- 5 Iyer SS, Cheng G. Role of interleukin 10 transcriptional regulation in inflammation and autoimmune disease. *Crit Rev Immunol.* 2012;32(1):23-63. doi: 10.1615/critrevimmunol.v32.i1.30. PMID: 22428854; PMCID: PMC3410706.
- 6 Stylianou E, Aukrust P, Kvale D, Müller F, Frøland SS. IL-10 in HIV infection: increasing serum IL-10 levels with disease progression--down-regulatory effect of potent anti-retroviral therapy. *Clin Exp Immunol.* 1999 Apr;116(1):115-20. doi: 10.1046/j.1365-2249.1999.00865.x. PMID: 10209514; PMCID: PMC1905221.

7 Syed SS, Balluz RS, Kabagambe EK, Meyer WA 3rd, Lukas S, Wilson CM, Kapogiannis BG, Nachman SA, Sleasman JW. Assessment of biomarkers of cardiovascular risk among HIV type 1-infected adolescents: role of soluble vascular cell adhesion molecule as an early indicator of endothelial inflammation. *AIDS Res Hum Retroviruses*. 2013 Mar;29(3):493-500. doi: 10.1089/AID.2012.0086. Epub 2012 Dec 3. PMID: 23062187; PMCID: PMC3581064.

8 Milošević N, Rütter M, David A. Endothelial Cell Adhesion Molecules- (un)Attainable Targets for Nanomedicines. *Front Med Technol*. 2022 Apr 7;4:846065. doi: 10.3389/fmedt.2022.846065. PMID: 35463298; PMCID: PMC9021548.

9 Han Y, Liu D, Li L. PD-1/PD-L1 pathway: current researches in cancer. *Am J Cancer Res*. 2020 Mar 1;10(3):727-742. PMID: 32266087; PMCID: PMC7136921.

10 Porichis F, Kaufmann DE. Role of PD-1 in HIV pathogenesis and as target for therapy. *Curr HIV/AIDS Rep*. 2012 Mar;9(1):81-90. doi: 10.1007/s11904-011-0106-4. PMID: 22198819; PMCID: PMC3731769.

11 Cherabi K, Faucher JM, Landman R. HIV infection and AIDS (1998). 1998th ed. 1998. 272 p. (HIV/AIDS).

12 World Health Organization. Main landmarks on HIV/AIDS [Internet]. 2021 [cited 2022 Jan 9]. Available at: <https://www.who.int/en/news-room/fact-sheets/detail/hiv-aids>

13 Abdoulaye O, Harouna Amadou ML, Biraima A, Amadou O, Douchi M, Alhousseyni Maiga D et al. Frequency of tuberculosis and the impact of immunosuppression in people living with HIV (PLHIV) followed at the regional hospital center of Maradi, Niger. *Mali medical*. 2021;36(3):20-23

14 Derep Veltomtoh L. Evaluation of the nutritional status of PLHIV hospitalized in the infectious diseases department [Pharmacy thesis]. USTTB ; 2021.

- 15 Diallo K, Wembulua BS, Sarr G, Badiane A, Pudence BBN, Diatta A, Coumé M, et al. HIV infection in the elderly: epidemiological and clinical profile in the region of Ziguinchor in southern Senegal. *RAFMI*. 2021 ;8(1) :19-24.
- 16 Meminta B. Dynamics of some biological parameters in patients on antiretroviral treatment at the SOMINE DOLO hospital in MOPTI [Pharmacy thesis]. USTTB ; 2014.
- 17 Bedji Tchenin L. Evaluation of micronutrients (vitamins A, E), hematological and biochemical profiles in people living with human immunodeficiency virus [functional and molecular biology]. Felix Houphouët Boigny University; 2014.
- 18 Lozès E, Ahoussinou C, Agassounon Tchibozo Djikpo M, Dahouegnon E, Ahossouhe N. Variability of CD4 lymphocyte count and viral load in people living with HIV on antiretroviral treatment: case of Saint Jean De Dieu hospital in Tanguieta (Benin). *Int J Biol Chem Sci*. 2012 ;6(2) :650-6p.
- 19 Diallo Cheickna M. Late HIV screening in the delivery room at the Fousseyni Daou hospital in Kayes : clinical and epidemiological aspects [medical thesis]. USTTB ; 2019
- 20 Makougoum Njidié CF. Cardiovascular damage during HIV : epidemio-clinical aspects [medical thesis]. University of Sciences, Techniques and Technologies of Bamako ; 2021
- 21 Kante AS, Diakite M, D Kaba, Ly BM, Dembélé DT, Sako FB. Blood count abnormality in people living with HIV in the oncology hematology department of the Donka National Hospital. *Jaccr Africa* 2020 ; 4(4): 99-103
- 22 Djibrilla Almoustapha A, Chefou M, Maman Brah M, Moussa Ounteini A, Brah S, Daou M et al. Blood count abnormalities correlated with CD4 count in HIV-positive subjects followed at the Ambulatory Treatment Center (CTA) in Niamey. *J. Rech. Science. Univ. Lome (Togo)*, 2020, 22(1-2) : 229-235
- 23 Karfo R, Kabré E, Coulibaly L, Diatto G, Sakandé J, Sangaré L. Evolution of biochemical and hematological parameters in people living with HIV/AIDS on antiretroviral treatment at the Medical Center of Camp General Aboubacar Sangoule Lamizana. *Pan Afr Med J*. 2018 Mar 19 ;29 :159. English. doi : 10.11604/pamj.2018.29.159.13659. PMID : 30050623 ; PMCID : PMC6057560.

24. Kalimira Kachelewa B, Lunjwire Mulemangabo PP, Kyambikwa Bisangamo C. Elevated transaminases and associated factors in people living with HIV - AIDS (PLHIV) at the PHARMAKINA - BUKAVU Ambulatory Treatment Center (CTA). International Journal of Innovation and Scientific Research. 2016 ; 26(1) :341-46.

25. Dollo MD. Evolution of plasma viral load and TCD4 lymphocyte level in a cohort of 930 patients on ARVs followed over 18 months at the Private ALGI laboratory in Bamako (Mali). [Pharmacy thesis]. University of Bamako ; 2011

UNDER PEER REVIEW