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Evolution of Viral Load in Patients Infected with HIV-1 at Point G University Hospital

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Abstract

Introduction: HIV, the human immunodeficiency virus, is the etiological agent of acquired immunodeficiency syndrome (AIDS). The aim of this study was to assess the evolution of the viral load in patients under treatment. **Methodology**: This was a study carried out from July 2017 to June 2022 at the Point G University Hospital laboratory. The determination of the viral load of patients was carried out by PCR on the ABOTT M2000sp/rt platform. **Results**: A total of 129 patients infected with HIV-1, aged 19 to 72 years with a mean age of 40.05 years ± 10.71; all on antiretroviral chemotherapy. The female gender predominated among our patients. The most common treatment regimen was 2INTI + 1INNTI with 72.9% followed by 2INTI + 1INI with 13.2%. As for the combinations of molecules, the combination TDF + 3TC + EFV and TDF + 3TC + DTG predominated, respectively 65.1% and 13.2%. 89.9% of our patients had undetectable viremia after 12 months of treatment ($p < 0.005$) with an average viral load which had evolved from 681315.65 copies/ml ± 1616908.484 to M0 at 5742.36 copies /ml ± 35756.883 at M12 ($p < 0.005$). **Conclusion**: Generally speaking, antiretroviral treatment had contributed to controlling viral loads, however the therapeutic combination TDF + 3TC + DTG had made it possible to obtain more patients with undetectable viremia instead.

Keywords

HIV-1, Treatment, Viral Load, Point G University Hospital

1. Introduction

The human immunodeficiency virus (HIV) is part of the retroviridae family (known as retroviruses). Retroviruses have a unique replication cycle. It has an impressive diversity [1]. HIV is the etiological agent of acquired immunodeficiency syndrome (AIDS) [2]. HIV infection remains a global public health problem; at the end of 2020, 37.7 million [30.2 million - 45.1 million] people were estimated to be living with HIV, with 680,000 [480,000 - 1.0 million] people dying from AIDS-related illnesses. Access to antiretroviral therapy affected 28.2 million people in 2021 [3].

In the same year, West and Central Africa recorded 4.7 million people living with HIV, including 3.5 million people on antiretroviral treatment [3].

In Mali, the total number of people living with HIV (PLHIV) regularly receiving antiretroviral treatment (ARV) increased from 37,902 (58% in 2016) to 45,459 (58.8%) in 2018 [4]. The advent of the Malian Initiative for Access to ARVs (IMAARV) in June 2001 [5], and free ARVs since July 2004 [6], has led to a significant increase in the number of patients receiving antiretroviral treatment. Since 2015, when a person is diagnosed with HIV, the World Health Organization (WHO) has advised initiating medical care to put the patient on antiretrovirals (ARV) as soon as possible, thus limiting the risk of developing complications [7]. Especially since PLHIV on ARVs with an undetectable viral load (VL) have an almost zero risk of transmitting HIV [7]. HIV disease has become chronic and requires better monitoring of treatment by the patient. Numerous studies have been carried out in developed countries as well as in certain African countries to evaluate the effectiveness of multiple antiretroviral therapies [8] [9]. Like many medications, antiretrovirals can cause adverse effects (AEs) [10]. HIV-1 group M was more frequently associated with treatment failure [11]. Therapeutic failure includes very diverse situations, whether it is a virological failure, immunological failure, or clinical failure [12]. The complexity of HIV management with continuous multitherapy leads us to undertake this retrospective and prospective epidemiological study concerning the virological monitoring of patients under ARV treatment. This work essentially aims to analyze the viral load of patients monitored at the Point G University Hospital, and to study viral suppression and possibly virological failure of ARV treatment.

2. Methodology

We conducted a cross-sectional study including a retrospective and prospective phase ranging from July 2017 to February 2019 and from December 2020 to June 2022 at the Point G University Hospital Laboratory. This study was designed with

the systematic inclusion of all people living with the human immunodeficiency virus (PLHIV) followed at the Point G University Hospital laboratory for a biological assessment. Patients from the three departments (infectious diseases, internal medicine and pulmonology) in initiation and antiretroviral therapy were systematically included in the study during the study period. This period corresponded to the follow-up at M12 of all patients include. These are people infected with HIV-1 included at the Point G University Hospital, carrying out at least three control viral loads in the laboratory and having consented to the study. The variations studied were on the request form accompanied by another notification form with general information on the patient and the therapeutic level (initiation, follow-up at M6 and M12) and the molecules prescribed. This variables were: sociodemographic (age and sex); biological (viremia at initiation (M0), viremia at six months (M6), viremia at twelve months (M12), undetectable viremia) and therapeutic: (therapeutic regimens, therapeutic combinations). The treatment regimens were, Nucleotide reverse transcriptase inhibitors: NRTI (3TC: Lamivudine, ABC: Abacavir, d4T: Stavudine, FTC: Emtricitabine, TAF: Tenofovir Alafenamide, TDF: Tenofovir Disoproxil Fumarate, AZT: zidovudine); NNRTI: Non-nucleoside reverse transcriptase inhibitors (DRV: Doravirine, EFV: Efavirenz, NVP: Nevirapine); IP: Protease inhibitors (ATV: atazanavir, DRV: darunavir, LPV: lopinavir) and INI: Integrase inhibitors (DTG: Dolutegravir, RAL: Raltegravir). Venous blood samples were taken in the laboratory in EDTA tubes according to laboratory protocol.

Quantification of the HIV-1 viral load was carried out on the Abbott Real Time platform: M2000 sp/M2000rt, this method is based on the reverse transcription of HIV RNA into DNA using a reverse transcriptase. This DNA is then polymerized following cycles at several temperature states in the presence of labeled oligonucleotides and primers in the m2000rt thermal cycler. The fluorescence of the new hybridized strands makes it possible to quantify at the end of each cycle the number of viral RNA present in the plasma by comparison with an internal standard.

HIV RNA extraction involves four steps: lysis of viral membranes and capsids, separation of nucleic acids, purification of the RNA and finally elution of the RNA. It is during this elution phase that the plasma viral RNA is extracted according to the protocol described in the extraction kit.

Sample preparation was carried out automatically on the M2000 sp extractor and for samples with insufficient plasma volume we used the manual method with the sample preparation System reagent. The Master Mix was prepared with Abbott Real Time Amplification Reagent Kit to obtain a volume of 50 µL per sample. The amplification and detection start-up procedure was done, according to the m2000rt module.

Viral load measures the number of virus copies per milliliter (mL) of blood. It makes it possible to quantify a particular element of the virus called RNA or ribonucleic acid. The lower the number of virus copies, the less virus. There is in the

blood. Results can vary widely, from 1,000,000 copies/mL or more to undetectable.

Viral suppression is defined as a viral load below 1000 copies/mL. From 2019, UNAIDS recommends that countries adapt to lower detection thresholds.

The data was collected on the analysis requests, the individual notification forms for the viral load request and the results media of the examinations carried out. These documents were used to inform the individual patient data collection sheets designed for the purposes of this study. Data entry and analysis were carried out using Word 2013, Microsoft Excel 2016 and SPSS 25.0 software. We considered values of $p < 0.005$ significant in the variable comparisons. Our study was conducted with strict respect for patient confidentiality. The anonymity of the patients was respected for the coding of the data.

3. Results

This descriptive investigation into the evolution of viremia in people infected with the human immunodeficiency virus was carried out in 129 patients.

The female gender was more represented, *i.e.* 71.3% of patients, the age group of 37 - 42 years.

The 2INTI + 1INNTI regimen represented 94% of the therapeutic regimens of which the TDF + 3TC + EFV combination was the majority, *i.e.* 84%; followed by the 2INTI + 1INI scheme with 13.2% of which the predominant combination of molecules was TDF + 3TC + DTG with 13.2% (Table 1).

Viremia involved over months with detectable viral loads determining low-intensity failure.

The frequency of undetectable viremia at M0, M6 and M12 was 11.6%, 56.6% and 89.9%, respectively. There was a statistically significant link between the duration of treatment and the undetectability of viremia (Undetectable viremia from M0 to (M6, M12): $p < 0.005$, and Undetectable viremia M6 to M12: $p = 0.0017$ (<0.005) (Table 2).

The average viremia from M0 to M6 then M12 gradually decreased significantly ($p < 0.005$) over time with respectively 681315.65 copies/mL ± 1616908.484, 48520.67 copies/mL ± 189684.163, 5742, 36 copies/mL ± 35756.883. At M6 and M12 the median viremia was 40 copies/mL.

The frequencies of undetectable viremia from M0 to M6 then to M12 were significant ($p < 0.005$) in both sexes with respectively 8.1%, 54.1% and 94.6% in men and 13.0%, 57.6% and 88.0% among women. We did not find a significant link between sex and viremia (T-test: $p = 0.157$); as well as between the average ages of 47.6 years ± 9.58 at M0, 41.21 years ±10.89 at M6 and 41.09 ± 10.69 at M12 and viremia (Age and undetectable viremia from M0 vs M6: $p = 0.4581$; from M0 to M12: $p = 0.4581$; from M6 to M12: $p = 1$).

The suppression of viremia was progressive for the majority of our patients regardless of the treatment regimen. We noted that at M6, 56.6% of our patients monitored had already suppressed their viremia (73/129) (Table 3).

The 2INTI + 1INNTI and 2INTI + 1IP regimens made it possible to signifi-

cantly ($p < 0.05$) obtain undetectable viremia from M0 to M6 then M12 and from M6 to M12 in the respective frequencies of 10.6%; 55.3%; 91.5% then 12.5% and 43.8% and 93.6%. As for the 2INTI + 1INI scheme from M0 (11.8%) to M6 (82.4%) and M12 (88.2%), the differences were significant ($p < 0.05$) (Table 4).

Table 1. Socio-demographic characteristics of the patients.

Sex	Frequency	Percentage (%)
Male	92	71.3
Female	37	28.7
Age range (an)	Frequency	Percentage (%)
19 - 24	4	3.1
25 - 30	23	17.8
31 - 36	25	19.4
37 - 42	28	21.7
43 - 48	20	15.5
49 - 54	17	13.2
55 - 60	8	6.2
≥61 - 66	4	3.2
Average age: 40.05 ± 10.71 ans		

Therapeutic profiles								
Combinations (n, %)	**Therapeutic treatment (n, %)**							
	2INTI + 1INNTI		2INTI + 1IP		2INTI + 1INI		2INTI + 1IP + 1INI	
TDF + 3TC + EFV	84	65.1	0	0	0	0	0	0
AZT + 3TC + ATV	0	0	2	1.6	0	0	0	0
TDF + 3TC + DRV + RAL/r	0	0	0	0	0	0	2	1.6
TDF + 3TC + DTG	0	0	0	0	17	13.2	0	0
AZT + 3TC + LPV/r	0	0	4	3.1	0	0	0	0
AZT + 3TC + NVP	7	5.4	0	0	0	0	0	0
TDF + 3TC + ATV	0	0	2	1.6	0	0	0	0
ABC + 3TC + LPV/r	0	0	3	2.3	0	0	0	0
FTC + TDF + EFV	1	0.8	0	0	0	0	0	0
D4T + 3TC + NVP	1	0.8	0	0	0	0	0	0
TDF + 3TC + LPV/r	0	0	5	3.9	0	0	0	0
AZT + 3TC + EFV	1	0.8	0	0	0	0	0	0
Total	**94**	**72.9**	**16**	**12.4**	**17**	**13.2**	**2**	**1.6**
	Triple therapy = 127 (98.4%)						Quadrupletherapy **2 (1.6%)**	

Table 2. Evolution of qualitative viremia depending on the duration of treatment.

Viremia	Duration			P
	Initiation M0	Follow up M6	Follow up M12	
Average (copies/mL) (Standard deviation)	681315.65 ± 616908.484	48520.67 ± 189684.163	5742.36 ± 35756.883	<0.05
Median (copies/mL) (Extremes)	87640.00 (40.10000000)	40.00 (40.1478109)	40.00 (40. 352693)	
Undetectable (N, %)	15 (11.6)	73 (56.6)	116 (89.9)	<0.05
Detectable (N, %)	114 (88.3)	56 (43.4)	13 (10.1)	
Total	129 100	129 100	129 100	

Table 3. Distribution of undetectable viremia according to sex and age.

Sociodemographic variables		Undetectable viremia			P
		M0 (%)	M6 (%)	M12 (%)	
Sex, n (%)	Male	3 (8.1)	20 (54.1)	35 (94.6)	<0.05
	Female	12 (13.0)	53 (57.6)	81 (88.0)	<0.05
Age Average		47.6± 9.58	41.21 ± 10.89	41.09 ± 10.69	>0.005

Table 4. Distribution of undetectable viremia according to treatment regimens.

Protocols therapeutic		Undetectable viremia			P
		M0	M6	M12	
		N (%)	N (%)	N (%)	
Treatment regimens	2INTI + 1INNTI (n = 94)	10 (10.6)	52 (55.3)	86 (91.5)	<0.05
	2INTI + 1IP (n = 16)	2 (12.5)	7 (43.8)	15 (93.6)	<0.05
	2INTI + 1INI (n = 17)	2 (11.8)	14 (82.4)	15 (88.2)	<0.05
	2INTI + 1INI + 1IP (n = 2)	1 (5.0)	0 (0.00)	0 (0.00)	0.317
Therapeutic combinations	TDF + 3TC + EFV (n = 84)	9 (10.7)	47 (55.9)	79 (94.0)	<0.05
	TDF + 3TC + DTG (n = 17)	2 (11.7)	14 (82.3)	15 (88.2)	<0.05
	Others (n = 28)	4 (14.3)	12 (42.8)	12 (42.8)	

NRTI: Nucleoside reverse transcriptase inhibitors, NNRTI: Non-nucleoside reverse transcriptase inhibitors, PI: Protease inhibitors, NII: Integrase inhibitors, 3TC: lamivudine, TDF: tenofovir disoproxil fumarate, EFV: efavirenz, DTG: dolutegravir.

4. Discussion

Work on the therapeutic monitoring of VIH-infected patients on antiretroviral drugs is certainly numerous in the literature, but it would be a major contribution to assess the role of therapeutic regimens and combinaisons with particular interest in two aspects which remain little explored. In our context, namely: the evaluation of quadruple therapy and the level of prescription of therapeutic lines based on dolutegravir.

In our study, the female gender was predominant with 71.3% compared to 28.7% for men with a sex ratio (M/F) of 0.40. Our study confirms that of Diawara in Mali [13] with (60.90%) women and (39.1%) men. In our African context this situation could be attributed to polygamy and the frequency of heterosexual transmission. Another factor is the vulnerability of women on a biological level with the mucosa of the transition zone which is that of the female genital tract which contains the most immune cells. As a result, this area is considered the most susceptible to infection by HIV and papillomaviruses (HPV) [14]. Likewise, the socioeconomic vulnerability of women exposes them much more to the sexual risk of transmission. More than a third of women worldwide have experienced physical and/or sexual violence by an intimate partner or sexual violence by a non-partner at some point in their lives. They then have 1.5 times more risk of contracting HIV than women who have not suffered such violence. In sub-Saharan Africa, women and girls accounted for 63% of all new HIV infections [15].

The work of CAZEIN and colleagues in France revealed different results with a majority of 67% men in their studies [16]. This high prevalence among men in northern countries could be explained by the role of homosexuality and the use of injecting drugs.

The average age of the patients was 40.05 ± 10.71 years with extremes of 19 and 72 years. The most represented age group was 37 - 42 years old. These results are close to studies carried out in Cotonou [17] which noted an average age of 38 and 41 years. The differences could be explained by the size of our larger samples and by the period of the studies being quite distant from each other.

Generally speaking, we observe in all studies that it is the sexually active young population, between 20 and 45 years old, who are most affected by this disease. This observation is consistent with that of the Samaké 2019 study in Mali [18]. The most frequent combination of molecules in prescriptions was TDF + 3TC + EFV with 60.7%. As for the TDF + 3TC + DTG combination it was 64.7%. This is confirmed by the observations made concerning the frequency of patients in these services.

In addition, the life expectancy of PLHIV differs greatly depending on the stage in which the patient is at the time of ARV initiation. The use of the 2INTI + 1INNTI scheme was very significant in our study with 72.9% ($p < 0.005$). This observation is confirmed with the work of Sidibé [19] with 88.5%. The other associations in decreasing order of frequency were 13.2% for 2INNTI + 1INI, 2INNTI + 1IP represented 12.4%, and 1.6% for 2INTI + 1IP + 1INI. A goal has

been set by the Joint United Nations Program on HIV/AIDS (UNAIDS) to end the AIDS epidemic. It is a care cascade for HIV of 90-90-90 for the year 2020 and set at 95-95-95 for 2030 [20]. The place attributed to the 2INNTI + 1INI regimen in our study compared to previous ones would be due to the introduction of Dolutegravir in the first line of HIV treatment in Mali [21] and the transition to this molecule, an integrase inhibitor which appears today to be essential in therapeutic success, the relatively low frequency of the 2INNTI + 1IP combination is due to the fact that this regimen is a 2nd line prescription for HIV1, recommended in the event of failure of the first line or in cases of infection or co-infection with HIV-2 [22]. We found quadruple therapy in 1.6% of cases. This was a scheme under experimentation, but the advent of other molecules reinforcing triple therapy caused this scheme to be abandoned. Other plans are in progress where the patient can take their treatment four or five days a week instead of seven days a week [23]. This is another therapeutic relief strategy consisting of reducing the number of days taken of treatment, per week.

In our study, the undetectability of the viral load changed significantly ($p < 0.005$) from M0 to M6 and M6 to M12 with respectively 11.6%, 56.6% and 89.9%. After six months of treatment, more than 50% of our patients had suppressed their viremia, as also shown in the study by Abdelli in Algeria (2015) [24]. The median viral load was 87640.00 at M0, 40 at M6 and 40 at M12 with a significant difference from M0 to M6 then M12. This median viremia at M6 in our study was lower than the 200 copies per milliliter declared by Landman and colleagues [23] to express viral suppression. It was also lower than that of Abdelli with 156,387 (copies/ml) [24]. An essential aspect lies in the fact that the median viremia at M6 and M12 was 40 copies/µl, which allows us to see that the majority of patients had suppressed their viral load although at M12 the average and extreme viremia could suggest possible failure in some of our patients.

The frequency of undetectability of patients increased significantly ($p < 0.005$) both in men from M0 (8.1%) to M6 (54.1%) and M12 (94.6) and from M6 to M12 than among women from M0 to M6 and M12 and from M6 to M12 with respectively 13.0%, 57.6% and 88.0%. However, the difference in the evolution of viremia between the two sexes was not significant ($p = 0.157$). This result is similar to that of Abdelli who found 59% of patients undetectable after 6 months of treatment [24].

Age also did not have a significant influence on the development of viremia. However, the frequencies of undetectability of viremia from M0 to M6 and M12 increased in both sexes, as in the study by Sanogo, 2014 in Mali at CESAC [25].

In our study, the use of the 2INTI + 1INNTI, 2INTI + 1 IP and 2INTI + 1INI regimens increased undetectable viremia significantly ($p < 0.005$) from M0 to M6 then M12 with 10.6%, 55.3% respectively. , 91.5%; 12.5%, 43.8% 93.6% and 11.8%, 82.4% 88.2%. The frequencies of deletions under 2INTI + 1INNTI at M6 and M12 evolve in the same direction as in the Sanogo study [25]. It should be noted that the 2INTI + 1INNTI combination was the preferred regimen for antiretroviral treatment in Mali. As for the 2INTI + 1IP protocols, its relatively low

prescription (16/129) would be attributed to a preferential substitution use of the regimen in the event of failure or HIV-2 [21]. Quadritherapy, uncommon in this study (2/129) due to the large number of tablets to take and its therapeutic effectiveness which can be superimposed on triple therapy, was quickly abandoned.

The frequencies of undetectable viremia from M0 to M6 then to M12 were significant ($p < 0.005$) with respectively 10.7%, 55.9% then 94.0% for TDF + 3TC + EFV and 11.7%, 82.3%, then 88.2% for TDF + 3TC + DTG. The majority combination TDF + 3TC + EFV with 55.9% of undetectable viremia at M6 in our patients, is higher than that of Dolo in 2013 in Mali [26] which obtained 30.6% for the same treatment duration. Although the frequencies were different, viremia evolved in the same logic as the results of Dokekias in Brazzaville in 2008 [8]. Our results also showed that the frequency of viremia from M6 under the TDF + 3TC + DTG combination was 82.3% higher than 55.9% observed with the TDF + 3TC + EFV combination. This could be explained by the presence of dolutegravir in the combination. Intermittent antiretroviral treatment (ART) (4 days per week) for HIV-1 patients may be more convenient, better tolerated and less expensive than continuous treatment [23].

The limits of the study: the size of the sample, certainly sufficient, would have benefited from being enlarged. We were unfortunately held back by time and shortages of reagents and consumables. It therefore seems necessary to us that a larger study be undertaken a better support the results of our preliminary study.

We were unable to demonstrate the influence of factors such as sex and age on viremia although women and young people predominated in our study.

5. Conclusion

The results could be used to enrich the literature but also to help design a more advanced research protocol on the therapy of a virus with high genetic diversity. It therefore seems necessary to us that a larger study be undertaken to better support the results of our preliminary study.

Contributed

All authors contributed to this work.

Conflicts of Interest

The authors have no conflicts of interest to report.

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