



Estimation of Clinical, Immunological and Virological Failure of First Line Antiretroviral Treatment in Kinshasa, Democratic Republic of Congo

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How to cite this paper: Kamangu, E.N. (2018) Estimation of Clinical, Immunological and Virological Failure of First Line Antiretroviral Treatment in Kinshasa, Democratic Republic of Congo. *Open Access Library Journal*, 5: e4560. <https://doi.org/10.4236/oalib.1104560>

Received: April 2, 2018

Accepted: May 19, 2018

Published: May 22, 2018

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Abstract

Background: The prevalence of Human Immunodeficiency Virus (HIV) infection was 1.2% in the Democratic Republic of Congo, according to the Demographic Health Study report in 2014. In 2012, the severe failure rate to first-line ART in Kinshasa was estimated at more than 16%. **Objective:** The objective of this study is to determine the rate of clinical, immunological and virological failure in first-line treatment in Kinshasa. **Methodology:** At the 6th month of Antiretroviral Treatment (ART), 138 patients from a follow-up cohort of 8 centers in Kinshasa were received for paraclinical evaluations and analyses. The clinical and paraclinical parameters were recorded on the individual patient sheets as well as the survey forms. Clinical parameters, viral load and CD4 were evaluated at the 6th month of ART. **Results:** One hundred and thirty-eight (138) patients had returned for follow-up treatment, 81 women and 57 men. The average age of patients is 37 ± 12 years. The dominant age groups are those of 26 to 35 years and 36 to 45 years with 39 patients (28.3%) each, followed by those of 18 to 25 years (21.7%). One hundred and twenty-five (125) patients (90.5%) were in clinical stage 3 and 13 (9.5%) in clinical stage 4 according to the WHO classification. CD4 levels ranged from 98 to 1050 cells/mm³ and a median value of 560 cells/mm³. The median value of the patients' VLs was 0.90 log₁₀ copies of RNA/ml with respective minimum and maximum values of 0 and 4.82 log₁₀ copies of RNA/ml. The virological failure rate was 24.6%. **Conclusions:** The rate of virological failure of first-line antiretroviral treatment of patients under treatment in Kinshasa is 24.6% for the year 2015.

Subject Areas

HIV

Keywords

Treatment Failure, HIV, Kinshasa

1. Introduction

To date, the Human Immunodeficiency Virus (HIV) remains a public health problem around the world. In 2014, the United Nations program to fight HIV and AIDS (UNAIDS) reports an average of 35.3 million (32.2 - 38.8 million) HIV-infected people worldwide and an average of 2.3 million (1.9 - 2.7 million) new cases for the year. Sub-Saharan Africa still bears the greatest burden of the global epidemic. Almost 2/3 (63%) of all adults and children living with HIV in the world are in Sub-Saharan Africa. Nearly 1/3 (32%) of all People Living with HIV (PLHIV) in the world are in Southern Africa and 34% of all deaths from Acquired Immune Depression Syndrome (AIDS) have occurred there [1].

The Democratic Republic of Congo (DRC) is one of the countries with stable prevalence for HIV infection. The prevalence of infection was 1.2% for the country according to the report of the Demographic Study of Health in 2014 (EDS-2014) [2].

The tri-therapy adopted since 2008 in the DRC for PLHIV is a combination of 2 Nucleoside Inhibitors of Reverse Transcriptase (NRTI) and 1 Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI) as a first-line treatment [3]. The most used first-line molecules in Kinshasa are Didanosine (ddI), Lamivudine (3TC), Stavudine (d4T) and Zidovudine (ZDV or AZT), as well as Nevirapine (NVP) and Efavirenz (EFV) [3] [4].

In 2012, the rate of primary first-line ART failure in Kinshasa was estimated at more than 16% [5]. Therapeutic failure brings together a wide range of situations; it can be clinical failure, immunological failure with persistence of an immune deficiency or virological failure resulting from persistent viral replication under treatment [6] [7] [8].

The objective of this work is to determine the clinical, immunological and virological failure rate at first-line treatment in Kinshasa.

2. Methods

The present study is a cross-sectional evaluation at the 6th month of treatment on a patient follow-up cohort. One hundred and fifty-three patients were randomly selected from 8 centers in Kinshasa from August 1, 2013 to February 28, 2014. At 6th month of antiretroviral treatment, 138 patients were received for the assessments and analyzes of the parameters. The first-line treatment used for all patients was a combination of Zidovudine (ZDV), Lamivudine (3TC) and Nevirapine (NVP) which is the most available combination in the different treatment centers in Kinshasa.

2.1. Clinical and Biological Monitoring

The clinical parameters were taken from the individual patient files in their respective centers as well as from the survey forms. The determination of the Viral Load (VL) was made at the Laboratory of Molecular Biology of the Faculty of Medicine of the University of Kinshasa (UNIKIN) using the same *in-house* assay used at inclusion [9] [10] [11]. The CD4 T-cells count was done using the Fasco-count under the same conditions as at day 0.

2.2. Comparison of Variables

The clinical and laboratory parameters of the 6th month of treatment were compared with those collected at the beginning of the cohort at baseline [12] [13] to determine the outcome of patients on the treatment. For compliance, the clinical endpoints were evaluated according to the World Health Organization (WHO) classification; and paraclinical examinations were performed in the same laboratories and the same conditions.

2.3. Statistics

Pearson correlation test was used to analyze the data. The probability value $p < 0.05$ was considered as significant. The Viral Load was expressed in logarithmic decimal RNA copies/ml.

2.4. Operational Definitions [6] [7] [8]

Clinical failure to treatment is based on the reoccurrence of opportunistic infections and/or progression to a higher clinical stage (as recommended by the WHO) after the start of treatment, as well as the lost of weight of patient in a context without stress problem and reconstruction syndrome.

Immunological failure to treatment is defined by the absence of increased CD4 T-cells count despite effective ARV therapy for at least 6 months. This is seen more frequently in patients with initially low CD4 cell counts. As a general rule, a CD4 count below 200 cells/mm³ is an indicator of immunological failure.

Virological failure to treatment is defined as a persistence VL greater than 200 copies of RNA/ml (2.30 log₁₀ RNA copies/ml) 6 months after the start of treatment. Three definitions are presented for virological failure: 1) minimal failure (200 < VL < 5000 or 2.30 log₁₀ < VL < 3.70 log₁₀ RNA copies/ml), 2) moderate failure (5000 < VL < 30,000 or 3.70 log₁₀ < VL < 4.48 log₁₀ RNA copies/ml) and 3) major or severe failure (VL > 30,000 or VL > 4.48 log₁₀ RNA copies/ml).

3. Results

One hundred and thirty-eight (138) patients returned for follow-up treatment control at the 6th month. Eighty-one patients were women (**Table 1**), giving here a sex-ratio M/F of 0.70. The age of the patients ranged between 18 and 65 years with an average of 37 ± 12 years (**Table 1**). The dominant age groups are those aged 26 to 35 and 36 to 45 years old, with 39 patients (28.3%) each, followed by

those aged 18 to 25 (21.7%), aged 46 to 55 (16.7%) and 56 to 65 years (5.1%).

3.1. Clinical and Biological Data at Baseline (D0)

At baseline, 140 patients (91.5%) were in clinical stage 3 and 13 (8.5%) in clinical stage 4 for HIV infection according to the WHO classification [13]. CD4 T-cells counts were between 8 and 915 cells/mm³ with 69 patients (86.8%) with CD4 count below 500 cells/mm³ [12] [13]. The median VL value of the included patients was 5.68 log₁₀ RNA copies/ml [12] [13]. The minimum and maximum VL values were respectively 0.37 log₁₀ and 7.95 log₁₀ RNA copies/ml with 97 patients (63.4%) having a VL greater than 100,000 RNA copies/ml or 5.0 log₁₀ copies RNA/ml [12] [13].

3.2. Clinical and Biological Data at 6th month (M6)

At 6th month, 125 patients, or 90.5%, were in clinical stage 3 and 13 (9.5%) in clinical stage 4 according to the WHO classification. CD4+ T-cell counts, which were performed on 113 patients (71%), ranged from 98 to 1050 cells/mm³ with 52 patients (46.02%) with CD4 counts greater than 500 cells/mm³ and median of 560 cells/mm³ (Table 1). The median VL value of the patients was 0.90 log₁₀ RNA copies/ml. The minimum and maximum values were respectively 0 and 4.82 log₁₀ RNA copies/ml with 104 patients (75.4%) having a VL less than 200 RNA copies/ml or 2.3 log₁₀ RNA copies/ml thus giving a virological failure rate of 24.6% (Table 2). Of the 34 patients with virological failure, 8 (23.5%) were in minimal failure (2.30 log₁₀ < VL < 3.70 log₁₀ RNA copies/ml), 23 (67.7%) had moderate failure (3.70 log₁₀ < VL < 4.48 log₁₀ copies of RNA/ml) and 3 (8.8%) in severe failure (VL > 4.48 log₁₀ RNA copies/ml) (Table 2).

Table 1. Characteristics of patients.

Characteristics	Patients
Sex (n = 138)	
Male	57 (41.3%)
Female	81 (58.7%)
Age (years) (n = 138)	
Interval	18 - 65
Mean	37 ± 12
18 - 25	30 (21.7%)
26 - 35	39 (28.3%)
36 - 45	39 (28.3%)
46 - 55	23 (16.7%)
56 - 65	7 (5.1%)
Viral Load (log₁₀ RNA copies/ml) (n = 138)	
Interval	0 - 4.82 log ₁₀

Continued

Median	0.90 log ₁₀
CD4 T-cells count (Cells/ml) (n = 113)	
Interval	98 - 1050
Median	480

Table 2. Virological failure.

Characteristics	Frequencies	
Treatment success $CV < 2.30 \log_{10}$	104 (75.4%)	
Treatment failure $CV > 2.30 \log_{10}$	34 (24.6%)	
Failure by age group (years)		
	<2.30 log₁₀	>2.30 log₁₀
18 - 25	18 (17.3%)	12 (35.3%)
26 - 35	31 (29.8%)	8 (23.5%)
36 - 45	31 (29.8%)	8 (23.5%)
46 - 55	19 (18.3%)	4 (11.8%)
56 - 65	5 (4.8%)	2 (5.9%)
Total	104	34
Type of virological failure		
Minimal failure ($2.30 < CV < 3.70 \log_{10}$)	8 (23.5%)	
Moderate failure ($3.70 < CV < 4.48 \log_{10}$)	23 (67.7%)	
Severe failure ($CV > 4.48 \log_{10}$)	3 (8.8%)	

4. Discussion

The aim of this work was to determine the clinical, immunological and virological failure rate at treatment in Kinshasa.

After 6 months of ART, of the 138 patients (90.2%) who returned for their control, 81 (58.7%) patients were women and 57 (41.3%) were men, which give a sex ratio M/F of 0.70. Various studies in our community have also published similar M/F sex ratios that tend to feminize HIV infection in adults in Sub-Saharan Africa [10] [14] [15] [16].

According to WHO recommendations, 125 patients, or 90.5%, were in clinical stage 3 and 13 (9.5%) in clinical stage 4 after 6 months of treatment. Whereas at the inclusion, 91.5% were in clinical stage 3 and 8.5% in clinical stage 4 [13]. This difference is not significant. Clinically, the clinician did not register much sign of deterioration of the state on the different patients during the different visits. Clinical stages are a function of the clinical signs recorded by clinicians during different visits to the patient [3].

CD4 T-cells counts were performed in 113 patients (71%). The minimum and maximum CD4 T-cells counts were 98 and 1050 cells/mm³, respectively. The median CD4 value is 560 cells/mm³ of which 52 patients (46.02%) with CD4

counts greater than 500 cells/mm³. It was not possible to determine immunological failure based on CD4 count because of the irregularity of this parameter in patients. Nevertheless, of all the patients who have the results at baseline and at the 6th month, none were in immunological failure because CD4 values have increased for all. The median difference in CD4 levels at month 6 from baseline (Δ CD4) was 247.5 cells/mm³. This brings us back to the issue of tracking people living with HIV/AIDS (PLHIV) in our environment [4] [16]. The biological parameters, not being supported in the free treatment, are the responsibility of the patients. This implies that these parameters are very often neglected and not present in patient records [4] [16].

The median VL value of the included patients was 0.90 log₁₀ RNA copies/ml. The minimum and maximum values were respectively 0 and 4.82 log₁₀ RNA copies/ml with 104 patients (75.4%) having a VL less than 200 RNA copies/ml or 2.3 log₁₀ RNA copies/ml thus giving a virological failure rate of 24.6%. Of the 34 patients with virological failure, 8 (23.5%) had minimal failure (2.30 log₁₀ < VL < 3.70 log₁₀ RNA copies/ml), 23 (67.7%) had moderate failure (3.70 log₁₀ < VL < 4.48 log₁₀ copies of RNA/ml) and 3 (8.8%) in severe failure (VL > 4.48 log₁₀ RNA copies/ml). Most failed patients (67.7%) have moderate virological failure. In the past, the virological failure was estimated at 14.6% in 2011 by Muwonga and all [17] and 16% in 2012 by Kamangu and all [14] for Kinshasa, taking into account 3 clinics of referenced structure of the time. The difference in numbers lies in the criteria for inclusion of patients and selection of centers; as well as the scale of determination of treatment failure. Indeed, treatment failure was redefined as a VL > 200 copies of RNA/ml (2.3 log₁₀ RNA copies/ml) in 2013 [8] as opposed to a VL > 1000 copies of RNA/ml (3.0 log₁₀ RNA copies/ml) from previous years [6]. In this work, 8 centers that meet the criteria according to WHO recommendations were randomly selected in order of 2 per district in Kinshasa [4]. Eight treatment and PLHIV monitoring centers participated in this work. For Kinshasa, according to the updated criteria, the virological failure rate was estimated at 24.6% for 2015.

5. Conclusion

The virological failure rate of first-line antiretroviral treatment of patients on treatment in Kinshasa is estimated at 24.6% for the year 2015.

Conflict of Interest

The author declares that there was no conflict of interest.

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Abbreviation

3TC: Lamivudine, **RNA**: Ribose Nucleic Acid, **ARV**: AntiRetroViral, **VL**: Viral Load, **dAT**: Stavudine, **ddI**: Didanosine, **EDS**: Demographic Health Study, **EFV**: Efavirenz, **NNTRI**: Non-Nucleoside Transcriptase Reverse Inhibitor, **NTRI**: Nucleoside Reverse Transcriptase Inhibitor, **PI**: Protease Inhibitor, **NVP**: Nevirapine, **WHO**: World Health Organization, **UNAIDS**: United Nations Organization for the Fight against HIV/AIDS, **PLHIV**: Person Living with HIV, **DRC**: Democratic Republic of Congo, **AIDS**: Acquired Immune Deficiency Syndrome, **ART**: AntiRetroViral Treatment, **UNIKIN**: University of Kinshasa, **HIV**: Human Immunodeficiency Virus, **ZDV**: Zidovudine.