

Evolutionary Profile of Opportunistic Infections in People Living with Human Immunodeficiency Virus during Six Months of Dolutegravir Based Antiretroviral Treatment in Kinshasa, Democratic Republic of Congo

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Abstract

Background: Opportunistic infections (OI), which are still a major problem in the care of People Living with HIV (PLHIV), occur in situations of immunosuppression. The AntiRetroViral Treatments (ART) used allow a spectacular reduction in the frequency of Opportunistic Infections. Objective: The objective of this study is to present the evolution of Opportunistic Infections in People Living with HIV under AntiRetroViral Treatment in Kinshasa in the era of Dolutegravir. Methods: The present study is a prospective cohort to present the evolutionary profile of OIs in PLHIV on ART for 6 months in Outpatient Treatment Centers (OTC) in Kinshasa. Sixteen OTCs had been included. The population of the present work was patients over 18 years of age at inclusion, infected with HIV-1 and initiating ART in the selected OTC. Results: On inclusion, 119 patients were included of which 56.3% were women. Malaria (45.4%), tuberculosis (29.4%) and cutaneous pruritus (23.5%) were the most common Opportunistic Infections (OIs). In the third month of ART, 37 patients came for the consultation of which 70.3% were women. Non-specific STIs (97.3%), skin pruritus (37.8%) and malaria (24.3%) were the dominant OIs among patients. At the sixth month of ART, 62 patients came for the medical consultation of which 61.3% were women. Skin pruritus

(25.8%), dermatitis (22.6%) and rash (21%) were the most common OIs. **Conclusion:** The evolutionary profile is marked by the conservation of Opportunistic Infections such as dermatitis (pruritus and rashes) and malaria.

Keywords

Opportunistic Infections, ART Initiation, PLHIV, Kinshasa

1. Introduction

Human Immunodeficiency Virus (HIV) infection affects all social strata throughout the world. Nearly 2/3 of those infected are located in Sub-Saharan Africa (SSA), which bears the heavy burden of this epidemic [1] [2] [3]. The advent of AntiRetroViral Treatments (ART) has made it possible to modify the natural history of the infection. The ARTs used today allow a significant improvement in the survival of People Living with HIV (PLHIV), a slowing down of immune degradation, as well as a spectacular reduction in the frequency of Opportunistic Infections (OI) [2] [3]. They constitute the main part of the symptomatology of HIV infection responsible for a heavy mortality and morbidity of PLHIV, especially in developing countries [3]. Most OIs respond to specific treatment. The effectiveness of this treatment is closely linked to the precocity of its initiation and to immune restoration thanks to ART [4]. The control of HIV infection today has great hopes in its management.

ART can make the Viral Load (VL) permanently undetectable and maintain or restore immunity [5]. OIs occur in PLHIV in situations of immunosuppression that are often caused by late management or rupture of AntiRetroVirals (ARVs). It is in this situation that the OIs declare themselves and lead them to Acquired Immunodeficiency Syndrome (AIDS).

In the Democratic Republic of Congo (DRC), OIs are still a major problem in the management of PLHIV [6]. In different centers, this management is often limited to the treatment of OIs. Some local studies have shown that Tuberculosis, Candidiasis, Pneumonia and Malaria are the most common infections found in the population [7] [8] [9] [10] [11]. Nevertheless, knowledge about OIs throughout ART is still limited in Kinshasa, especially since the introduction of Dolutegravir (DTG) in the care of PLHIV.

Hence the objective of this study is to present the evolution of Opportunistic Infections in People Living with HIV under AntiRetroViral Treatment in Kinshasa in the era of Dolutegravir.

2. Methods

2.1. Study Design, Patient and Sample Setting

The present study is a prospective cohort to determine the evolutionary profile of Opportunistic Infections (OI) in People Living with HIV (PLHIV) who are on

ART from D0 to M6 followed in HIV Outpatient Treatment Centers (OTC) in Kinshasa. Sixteen (16) OTCs were included based on their expertise in the care of PLHIV and their accessibility [12]. The patient inclusion period was from October 04, 2021 to February 15, 2022.

Data on Opportunistic Infections (OI) were recorded on the worksheets previously tested by the study team.

2.2. Study Population

The population of interest was patients over the age of 18 years at inclusion, infected with HIV-1 and initiating ART in a selected OTC during the inclusion period (October 04, 2021 to February 15, 2022). Patients were included on the following criteria: to be diagnosed as PLHIV at the OTC, to be at least 18 years old at inclusion and naïve to ART. PLHIV were followed in the respective OTCs for 6 months.

2.3. Parameters of Interest

The parameters of interest followed for the present study were: age, sex, clinical state and opportunistic infections found in PLHIV on ART at D0, M3 and M6.

2.4. Operational Definitions

An Opportunistic Infection is an infection due to germs that are usually not very aggressive but whose pathogenicity is amplified by the patient's deficient immune system, his sensitivity to infections.

2.5. Ethical Consideration

This study has been approved as a whole by the research ethics committee of the School of Public Health, Faculty of Medicine, University of Kinshasa (ESP/CE/115/2021). Authorization to enter the OTCs has been taken from the managers of the various centers included. Prior to inclusion, fully informed consent was obtained from each participant.

2.6. Statistical Analyzes

The analyzes were carried out using SPSS version 26 software (Statistical Packaging for Social Sciences, IBM). Only available data were analyzed, missing data were considered completely random. Correlations were sought using Pearson's correlation test.

3. Results

3.1. At Inclusion (D0)

One hundred and nineteen (119) patients were included in this study respecting the inclusion criteria. Fifty-two (52) patients, or 43.7%, included in the study are men while 67 patients (56.3%) are women; thus giving a sex ratio of 1.29 in favor of women.

The average age of patients included on D0 is 39.87 ± 12.36 years with extremities of 18 to 69 years. The most represented age group is that of 36 to 45 years with 37 patients (31.9%) followed by that of 26 to 35 years with 24 patients (20.7%), that of 46 to 55 years with 22 patients (19.0%) and that of 18 to 25 years with 19 patients (16.4%). These data are presented in **Table 1**.

Forty-nine patients (49), or 41.5%, were at WHO clinical stage 3; followed by 40 patients (33.9%) who were at clinical stage 1, 18 patients (15.3%) at clinical stage 2 and 11 patients (9.3%) at clinical stage 4. Fifty-five (55) patients, or 47.0%, had a normal clinical condition; followed by 39 patients (33.3%) who had a good clinical state, 22 patients (18.8%) a bad clinical state and 1 patient (0.9%) a pre-moribund clinical state. **Table 2** presents the clinical aspects of the patients.

Demonstrations	Patients (%)					
Parameters	J0 (N = 119)	M3 (37)	M6 (62)			
	Sex					
Women	56.3	70.3	61.3			
Men	43.7	29.7	38.7			
Age Interval (years)						
18 - 25	16.4	13.5	13.3			
26 - 35	20.7	24.3	18.3			
36 - 45	31.9	27.1	26.7			
46 - 55	19.0	32.4	25.0			
56 - 65	9.5	9.5 2.7				
>65	2.5	0	0			

Table 1. Distribution of the population by sex and age group.

Table 2. Clinical parameters of PLHIV from D0 to M6.

Parameters	Patients (%)							
	J0 (n = 119)	M1 (n = 42)	M3 (n = 37)	M6 (n = 62)				
Clinical stage according to WHO								
Stage 1	33.9	48.7	38.9	29.1				
Stage 2	15.3	2.7	19.4	9.1				
Stage 3	41.5	45.9	41.7	61.8				
Stage 4	9.3	2.7	0	0				
Clinical state								
Normal	47	65.8	67.6	67.9				
Good	33.3	34.2	32.4	28.3				
Bad	18.8	0	0	3.8				
Moribund	0.9	0	0	0				
Pre-Moribund	0	0	0	0				

The Opportunistic Infections most found in PLHIV initiating ART were: Malaria with 54 cases (45.4%), Tuberculosis (29.4%), cutaneous pruritus (23.5%), Urinary tract infections (21.8%), Oral candidiasis and skin eruptions (20.2%). **Table 3** and **Figure 1** present the exhaustive list of OIs found.

Some correlations were observed between the clinical stages of patients and certain OIs such as Oral Candidiasis (0.215; p = 0.023), Vaginal Pruritus (0.188; p = 0.044), Diarrhea (0.221; p = 0.017), Tuberculosis (0.422; p < 0.000) and Dermatitis (0.198; p = 0.033).

Deremeters	Patients (%)			
Farameters	J0 (N = 119)	M3 (N = 37)	M6 (N = 62)	
Oral candidiasis	20.2	13.5	4.8	
Vaginal mycosis	10.9	8.1	6.5	
Vaginal pruritus	13.4	10.8	9.7	
Cutaneous pruritus	23.5	37.8	25.8	
Shingles	3.4	2.7	3.2	
Rash	20.2	18.9	21.0	
Dermatosis	15.1	21.6	22.6	
Diarrhea	14.3	2.7	3.2	
Intestinal parasitosis	10.1	5.4	3.2	
Rhinitis	9.2	13.5	9.7	
Tuberculosis	29.4	2.7	6.5	
Malaria	45.4	24.3	11.3	
Urinary tract infection	21.8	8.1	9.7	
Non-specific STI	4.2	2.3	0	
Others	9.2	8.1	11.3	

Table 3. Opportunistic infections encountered in patients on inclusion.



Figure 1. Overview of opportunistic infections by period.

3.2. At Month 3 of ART (M3)

The total number of patients who respected the appointment of the third month of follow-up was 37 patients with a predominance of the female sex of the order of 26 Women (70.3%) against 11 Men (29.7%), with a sex ratio of 2.36 in favor of women.

The most found age group was that of 46 to 55 years with 12 cases (32.4%), followed by 36 to 45 years with 10 cases (27%), 26 to 35 years with 9 cases (24. 3%), 18 to 25 years old with 5 cases (13.5) and finally 56 to 65 years old with 1 case or 2.7% (Table 1).

Fifteen (15) patients were at WHO stage 3 (41.67%), followed by 14 patients at stage 1 (38.89%), 7 patients at stage 2 (19.44%) and no patients on stage 4. Twenty-three patients (23), 67.65%, had a normal clinical condition, followed by 11 patients (32.35%) had a good clinical condition and 3 patients (8.1%) had a poor clinical condition (**Table 2**).

The most common Opportunistic Infections found in patients in the third months of ART were: non-specific STIs with 36 out of 37 cases (97.3%), skin pruritus 14 out of 37 cases (37.8%), malaria with 9 out of 37 cases (24.3%), dermatitis 8 out of 37 cases (21.6%) and rashes 7 out of 37 patients (18.9%). Table 3 and Figure 1 present the exhaustive list of OIs found.

3.3. At the Sixth Month of ART (M6)

The total number of patients who respected the appointment of the sixth month of follow-up was 62 patients with a predominance of the female sex of the order of 38 women (61.3%) against 24 men (38.7%), with a sex ratio of 1.58 in favor of women.

The most found age group is that between 36 to 45 years with 16 cases (26.7), followed by the age group from 46 to 55 year with 15 cases (25%), 26 to 35 years with 11 cases (18.3), followed by 56 to 65 years with 10 cases (16.7%) and finally the age group from 18 to 25 years with 8 cases (13.3%) (Table 1).

Thirty-four (34) cases or 61.82% were at WHO stage 3, 16 cases (29.09%) were at stage 1 and 5 cases (9.09%) were at stage 2. Thirty-six (36) patients, or 67.92%, had a normal clinical condition, 15 patients (28.3%) had a Good clinical condition and 2 patients (3.77%) had a poor clinical condition (Table 2).

The most common Opportunistic Infections found in patients in the sixth month of ART are: skin pruritus with 16 out of 62 patients (25.8%), dermatitis with 14/62 patients (22.6%), skin rash with 13 of 62 patients (21%). Table 3 and Figure 1 present the exhaustive list of OIs found.

4. Discussion

The objective of this study was to present the evolution of Opportunistic Infections (OI) in People Living with HIV (PLHIV) on ART in the OTC from D0 to M6 in Kinshasa during the era of Dolutegravir. According to the criteria, 119 PLHIV were included on D0 in 16 OTCs scattered in the four districts of Kinshasa. OIs were recorded in patients according to the frequency of patient consultation appointments published by the national program; appointment for the first month (M1), third month (M3) and sixth month (M6) after initiation of ART on inclusion (D0) [13].

One hundred and nineteen (119) patients were included respecting the inclusion criteria. Fifty-two (52) patients (43.7%) were male while 67 patients (56.3%) were female; thus giving a sex ratio of 1.29 in favor of women. At the third month, 37 patients responded to the appointment with a predominance of the female sex (70.3%) and a sex ratio of 2.36. At the sixth month, 62 patients responded to the appointment with a predominance of the female sex (61.3%) and a sex ratio of 1.58. Through the various meetings, the sex ratio in favor of women is always present. The female sex remains dominant in the population of PLHIV in the various OTCs. This feminization of HIV infection is presented by various authors in the literature for Kinshasa and even for the country [8]-[19].

The average age of patients included on D0 was 39.87 ± 12.36 years with extremities of 18 to 69 years. The age group most represented at inclusion is that of 36 to 45 years with 37 patients (31.9%) followed by that of 26 to 35 years with 24 patients (20.7%), that of 46 to 55 years with 22 patients (19.0%) and that of 18 to 25 years with 19 patients (16.4%). In the third month, the most found age group was that of 46 to 55 years with 12 cases (32.4%), followed by 36 to 45 years with 10 cases (27%), 26 to 35 years with 9 cases (24.3%), 18 to 25 years with 5 cases (13.5) and finally 56 to 65 years with 1 case (2.7%). At the sixth month, the most common age group was that between 36 and 45 years with 16 cases (26.7), followed by the age group from 46 to 55 year with 15 cases (25%), 26 to 35 years with 11 cases (18.3%), followed by 56 to 65 years with 10 cases (16.7%) and finally the age group from 18 to 25 years with 8 cases (13.3 %). The interval of 26 to 55 years remains the dominant age group across the cohort. These data corroborate those of the various Kinshasa studies [8] [9] [10] [11] [14] [15] [18] [19], those of the 2014 Demographic Health Study [13], and other studies of the country [16] [17].

At inclusion, 49 patients (41.5%) were at WHO clinical stage 3, followed by 40 patients (33.9%) who were at clinical stage 1, 18 patients (15.3%) at clinical stage 2 and 11 patients (9.3%) at clinical stage 4; 55 patients (47.0%) had a normal clinical condition, followed by 39 patients (33.3%) who had a good clinical condition, 22 patients (18.8%) a poor clinical condition and 1 patient (0.9%) a pre-moribund clinical state. At the third month, 15 patients were at stage 3 (41.67%), followed by 14 patients at stage 1 (38.89%) and 7 patients at stage 2 (19.44%); 23 patients (67.65%) had a normal clinical condition, followed by 11 patients (32.35%) had a good clinical condition and 3 patients (8.1%) had a poor clinical condition. At the sixth month, 34 cases (61.82%) were at stage 3, 16 cases (29.09%) were at stage 1 and 5 cases (9.09%) were at stage 2; 36 patients (67.92%) had a normal clinical condition, 15 patients (28.3%) had a good clinical condition, and 2 patients (3.77%) had a poor clinical condition. This evolutionary profile of the clinic is justified by the taking of ART of the different patients

in their respective OTC. These data corroborate those of the literature for Kinshasa which affirm the evolution of the clinical states of patients under ART [19] [20].

On inclusion, the Opportunistic Infections (OIs) most commonly found in PLHIV initiating ART were: Malaria (45.4%), Tuberculosis (29.4%), cutaneous pruritus (23.5%), urinary tract infections (21.8%), oral candidiasis and rashes (20.2%). In M3, the most common OIs found in patients were: non-specific STIs (97.3%), cutaneous pruritus (37.8%), malaria (24.3%), dermatitis (21.6%) and rashes (18.9%). In M6, the most common OIs were: skin pruritus (25.8%), dermatitis (22.6%), and rash (21%). Despite taking ART, some OIs persist over time. OIs such as cutaneous pruritus, rashes, dermatitis and malaria were maintained throughout the treatment from inclusion to the sixth month of treatment. These infections are generally linked. The appearances of the different OIs through the different periods are similar to those presented in different studies [7] [8] [9] [11]. The persistence of these OIs despite ART calls into question the therapeutic support of PLHIV in our various care structures.

Some correlations were observed between the WHO clinical stages of patients and certain OIs such as Oral Candidiasis (0.215; p = 0.023), Vaginal Pruritus (0.188; p = 0.044), Diarrhea (0.221; p = 0.017), Tuberculosis (0.422; p < 0.000) and Dermatitis (0.198; p = 0.033). These correlations can be explained by the fact that these infections are generally linked to a balance of the microbial flora which, once disturbed by immunosuppression, gives way to a multiplication of infectious germs.

Limitation of the Study

This present study was limited to some centers of Kinshasa. Therefore, generalization of the results should be done carefully. However, this does not take any value out of the findings.

5. Conclusion

The profile of Opportunistic Infections is different at inclusion, at the third and at the sixth month. The evolutionary profile is marked by the maintenance of Opportunistic Infections such as Dermatitis (pruritus and rashes) and Malaria. Despite treatment with AntiRetroViral, Opportunistic Infections persist; which calls into question the therapeutic support of patients in care centers.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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List of Abbreviations and Acronyms

AIDS: Acquired Immune Deficiency Syndrome; **ART:** AntiRetroViral Treatment; **ARV:** AntiRetroViral; **DRC:** Democratic Republic of Congo; **DTG:** Dolutegravir; **HIV:** Human Immunodeficiency Virus; **OI:** Opportunistic Infection; **PLHIV:** Person Living with HIV; **VL:** Viral Load.