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Virological Failure among HIV Patients on the Antiretroviral Therapy (ART) in N'Djamena (Chad)

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Abstract

Virological failure is defined as any viral load greater than 1000 copies/mL (≥log3), after at least 6 months of treatment. The study focused on the assessment of the level of treatment failure in people living with HIV on antiretroviral treatment in Chad. This was an analytical and descriptive prospective study conducted between July 2021 and July 2022. The determination of the filler was carried out by the Reaction Chain Polymerization (PCR) method with kit Generic HIV Viral Load® (Biocentric, Bandol, France) and the Xpert HIV-1 Viral Load® Kit (Cepheid, Maurens-Scopont, France) on Genexpert. During the study, 4890 patients benefited from viral loads, including 3443 (70.4%) women and 1447 (29.6%) men. The majority of patients were married (60.9%), followed by single (16.6%), divorced (13.9%) and widowed (8.6%). The ratio of 2.4 in favor of women. Of all the patients included, 881 (18.0%) were in virological failure, of which 59.6% were married, 22% were single, 12.1% were divorced and 6.2% were widowed. Of these, 50.3% (444/881) were on TDF/FTC/EFV, 37.7% (333/881) were on TDF/3TC/DTG, 3.9% (35/881) on TDF/FTC/ATZ, 2.9% (26/881) were on AZT/3TC/EFV-based diet, 1.9% (17/881) were on ABC/3TC/LPV-based diet, 1.5% (14/881) were on TDF/

FTC-based diet, and 1.3% (12/881) were on ABC/3TC/ATV-based diet. The majority of patients had been on treatment for between five (05) and ten (10) years, respectively 52.7% (2578/4890) and 32.8% (1603/4890). 13.9% (680/4890) had been on treatment for fifteen (15) years and 0.6% (28/4889) had been on treatment for more than twenty (20) years. In patients with virological failure, 0.5% (4/881) of patients with treatment failure had been on treatment for more than 20 years, 11.9% (105/881) had been on treatment for more than 15 years, 54.9% (484/881) had been on treatment for less than 10 years 32.7% (288/881) had been on treatment for less than 5 years. The compliance rate was 3.7% (179/4890) in all patients. It is 4.3% (38/881) in patients with treatment failure. Treatment failure is a burden for the patient on antiretroviral therapy, as the drug fails to control the virus and key organs continue to be poisoned.

Keywords

PVVIH, Treatment Failure, HIV, ARV, Chad

1. Introduction

Human immunodeficiency virus (HIV) disease is one of the most common diseases in the world. In 2022, 33.1 to 45.7 million people were living with this disease and 29.8 million people had access to antiretroviral therapy [1]. The Central and West Africa region was home to more than 12% of these patients [2]. In 2022, Chad had more than 82.000 people who were on antiretroviral treatment (ART) [3] and many of whom do not have access to viral load [4] [5] despite the relentless efforts of the government and its partners [6]. While viral load is used to measure the effectiveness of ART [7], it is also an indicator to assess the third UNAIDS HIV performance indicator [8]. Monitoring viral load minimizes Treatment failures by adapting treatment according to the levels of treatment failure observed, which according to studies varies between 14 and 53% after 6 to 24 months of treatment initiation [9]. This makes it possible to reduce new infections as much as possible [10] or even the eradication of the disease [11] [12], because the suppression of the viral load is synonymous with non-transmission [13]. However, treatment failure is defined as any viral load greater than 1000 copies/mL after at least 6 months of antiretroviral therapy [14]. It is also the lack of control of the virus that may be due to poor compliance or resistance of HIV to one or more antiretroviral molecules [15]. It should be noted that virological failure is a double punishment for patients. Antiretroviral drugs (ARVs), which are effective drugs against HIV, can also be harmful to the kidneys and liver [16] which over time, leads patients to problems of immune deficiency, metabolic diseases (kidney failure, metabolic hepatitis, etc.), among other things.

In Chad, given the absence of the genotyping test for the diagnosis of HIV resistance, clinicians rely mainly on virological failure criteria to better manage patients therapeutically according to the national protocol.

The objective of this study was to assess the level of treatment failure in person living with HIV on antiretroviral treatment who had achieved a viral load at the National Reference Laboratory for HIV and Hepatitis (LNR-HIV-Hep) in N'Djamena.

2. Material and Methods

2.1. Scope of the Study

This was a prospective descriptive and analytical study conducted at the Reference Laboratory for HIV and Hepatitis in N'Djamena (Chad) from July 2021 to July 2022 in collaboration with the Laboratory of Applied Biochemistry and Immunology (LaBIA) of the Pr Joseph Ki-Zerbo University in Ouagadougou (Burkina Faso). The study involved person living with HIV who were on ARV treatment. All patients on ART for more than six (6) months were included in the study according to WHO recommendations. Patients on ART less than 6 months of age, children under 15 years of age, and person living with HIV who refused to sign the consent form were not included.

2.2. Antiretroviral Therapy

The national protocol for the management of person living with HIV in Chad has defined the treatment regimen to be followed [17]. Since 2020, all patients on ART have been switched to the dolutegravir-based regimen, including patients with treatment failure. Thus, since this period and in accordance with the national protocol (**Table 1**), the triple therapy regimen Tenefovir/Lamuvidin/Dolutegravir has been retained as a first-line regimen, but the transition to the Dolutegravir-based regimen has been slow to be effective.

In this study, we have taken into account the old protocol and the revised protocol.

Table 1. National protocol for the management of person living with HIV in Chad.

Choice	1st line	2nd line treatment	3rd line treatment
First intention	TDF/3TC/DTG	AZT/3TC/DTG AZT/3TC/ATVr ou LPVr	ETV/DRV/RTVr
Alternative	TDF/FTC/EFV TAF/3TC/DTG TDF/3TC/RAL	AZT/3TC/DRVr AZT/3TC/ATVr ou LPVr ou DRVr AZT/3TC/DRVr	

TDF: Tenofovir; 3TC: Lamivudine; FTC: Emtricitabine; AZT: Zidovudine; EFV: Effavirenz; DTG: Dolutegravir; RAL: Raltegravir; TAF: Tenofovir-fumarate; DRV/r: Daranavir/ritonavir; LPV/r: Lopinavir/ritonavir; ATZ: Atazanir/ritonavir.

2.3. Viral Load Test

The patients in the study gave a blood sample. 5 mL of venous blood was collected in a duplicate EDTA tube per patient. Plasmas, after centrifugation, were obtained and used for the determination of the plasma viral load of HIV-1 (VL).

Viral load assay for treatment failure or success was performed by PCR (Polymerization Chain of Reaction) using two PCR platforms, the Fluorocycler XT (Hain Lifescience, Nehren, Germany) and the GeneXpert® (Cepheid, Maurens-Scopont, France).

The GeneXpert® platform (Cepheid, Maurens-Scopont, France), is a closed system using Xpert HIV-1 Viral Load® reagents (cartridges, Cepheid, Maurens-Scopont, France) that combines both extraction and amplification. The open platform used a combination of RNA extraction with automated GenoXtract® extraction (Hamilton, Bonaduz, Switzerland) and amplification on Fluorocycler® XT (Hain Lifescience, Nehren, Germany) using the Generic HIV Viral Load Kit® (Biocentric, Bandol, France).

The detection limits of the GeneXpert and Flurocycler platforms were 40 copies/1ml and 390 copies/0.25mL, respectively.

2.4. Data Collection, Analysis and Processing

The study data was collected in sociodemographic, clinical (age, sex, treatment regimens, ARV treatment lines, adherence and treatment durations) and biological data. The viral load application form standardized by the sectoral program for the fight against HIV-AIDS, hepatitis and sexually transmitted infections (PSLSH/STI) was used to collect information on patients.

The data collected was entered in Microsoft Excel 2016. Processed and analyzed on the Microsoft Office Excel 2016 SPPS Statics software version 20.0.

2.5. Ethical Considerations

The study was approved by the Ministry in Charge of Public Health, specifically by the Sectoral Programme for the Fight against AIDS, Hepatitis and IST (PSLSH/IST) through the Psycho-Medico-Social Support Centre, a structure under the supervision of the PSLSH/STI. Individual consent forms were used for each patient's consent. All patients included agreed to provide 5 mL of their blood for the study.

3. Results

A total of 4890 patients were included in the study, of which 3443 (70.4%) were women and 1447 (29.6%) were men, for a female/male ratio of 2.4. The mean age was 38 years with extremes of (20 - 75) years.

Among of 4890 patients who achieved the viral load, 881 (18.0%) were in treatment failure (≥log3 or ≥1000 copies) according to the 2018 WHO guideline.

Table 2 describes the distribution of patients by viral load suppression, sex, and marital status.

The majority of patients were married (60.9%), followed by single (16.6%), divorced (13.9%) and widowed (8.6%). In terms of virological failure, 59.6% of patients with an unsuppressed viral load are married, 22% are single, 12.1% are divorced and 6.2% are widowed.

Table 2. Distribution of patients according to viral load suppression, sex and marital status.

Viral load	*Sex*	*Marital status*				*Total*
		Single	Divorce	Married	Widower	
Deleted	Women	110 (18.6%)	95 (15.9%)	338 (56.9%)	51 (8.6%)	594 (100%)
	Men	84 (29.2%)	12 (4.2%)	187 (65.1%)	4 (1.4%)	287 (100%)
		194 (22%)	107 (12.1%)	525 (59.5%)	55 (6.2%)	881 (100%)
No deleted	Women	354 (12.4%)	490 (17.2%)	1666 (58.5%)	337 (11.8%)	2847 (100%)
	Men	260 (22.4%)	85 (7.4%)	788 (67.8%)	29 (2.4%)	1162 (100%)
Total		808 (16.6%)	682 (13.9%)	2979 (60.9%)	421 (8.6%)	4890 (100%)

Distribution of patients according to treatment regimen, viral load suppression and gender

Table 3 describes the distribution of patients according to treatment regimen, viral load suppression and gender.

Table 3. Distribution of patients by treatment regimen, viral load suppression and gender.

Therapeutic regimen	Viral load						Cumulative number		Total
	Deleted			No deleted					
	Women	Men	Total	Women	Men	Total	Women	Men	
ABC/3TC/ATV	17 (48.6%)	18 (51.4%)	35 (100%)	9 (75.0%)	3 (25.0%)	12 (100%)	26 (55.3%)	21 (44.7%)	47 (100%)
ABC/3TC/LOPI/r	0 (0.0%)	3 (100%)	3 (100%)	———	———	———	0 (0.0%)	3 (100%)	3 (100%)
ABC/3TC/LPV	19 (51.4%)	18 (48.6%)	37 (100%)	7 (41.2%)	10 (58.8%)	17 (100%)	26 (48.1%)	28 (51.9%)	54 (100%)
AZT/3TC/EFV	39 (56.5%)	30 (43.5%)	69 (100%)	19 (73.1%)	7 (26.9)	26 (100%)	58 (61.1%)	37 (38.9%)	95 (100%)
DRV/r	1 (50.0%)	1 (50.0%)	2 (100%)	———	———	———	1 (50.0%)	1 (50.0%)	2 (100%)
TDF/3TC	1 (100%)	0 (0.0%)	1 (100%)	———	———	———	1 (100%)	0 (0.0%)	1 (100%)
TDF/3TC/DTG	1256 (69.7%)	545 (30.3%)	1801 (100%)	218 (65.5%)	115 (34.5%)	333 (100%)	1474 (69.1%)	660 (30,9%)	2134 (100%)
TDF/FTC/EFV	1419 (73.4%)	514 (26.6%)	1933 (100%)	309 (69.6%)	135 (30.4%)	444 (100%)	1728 (72.7%)	649 (27.3%)	2377 (100%)
TDF/FTC	19 (82.6%)	4 (17.4%)	23 (100%)	7 (50.0%)	7 (50.0%)	14 (100%)	26 (70.3%)	11 (29.7%)	37 (100%)
TDF/FTC/ATZ	76 (72.4%)	29 (27.6%)	105 (100%)	25 (71.4%)	10 (28.6%)	35 (100%)	101 (72.1%)	39 (27.9%)	140 (100%)
Total	2847 (71.0%)	1162 (29.0%)	4009 (100%)	594 (67.4%)	287 (32.6%)	881 (100%)	3441 (70.4%)	1449 (29.6%)	4890 (100%)

In terms of failure by regimen, 50.3% (444/881) were on TDF/FTC/EFV, 37.7% (333/881) were on TDF/3TC/DTG, 3.9% (35/881) on TDF/FTC/ATZ, 2.9% (26/881) were on AZT/3TC/EFV-based regimen, 1.9% (17/881) were on ABC/3TC/LPV-based regimen, 1.5% (14/881) were on TDF/FTC-based regimen, and 1.3% (12/881) were on ABC/3TC/ATV-based regimen.

Distribution of patients according to viral load suppression, gender and duration of treatment

Table 4 describes the distribution of patients by viral load suppression, gender, and duration of treatment.

Table 4. Distribution of patients by viral load suppression, gender and duration of treatment.

Viral load	Sex	Treatment time				Total
		20> year	<15 year >10 year	<10 year >05 year	<05 year	
No deleted	Women	1 (0.2%)	73 (12.3)	337 (56.7%)	183 (30.8%)	594 (100%)
	Men	3 (1.0%)	32 (11.1%)	147 (51.2%)	105 (36.6%)	287 (100%)
		4 (0.5%)	105 (11.9)	484 (54.9%)	288 (32.7%)	881 (100%)
Deleted	Women	20 (0.7)	454 (15.9)	1494 (52.5%)	879 (30.9%)	2847 (100%)
	Men	4 (0.3%)	121 (10.4)	600 (51.7%)	436 (37.6%)	1161 (100%)
		24 (0.6)	575 (14.3)	2094 (52.2%)	1315 (32.8%)	4008 (100%)
Total	Women	21 (0.6)	527 (15.3)	1831 (53.2%)	1062 (30.9%)	3441 (100%)
	Men	7 (0.5%)	153 (10.6)	747 (51.6%)	541 (37.4%)	1448 (100%)
	Total	28 (0.6)	680 (13.9)	2578 (52.7%)	1603 (32.8%)	4889 (100%)

The majority of patients had been on treatment for between five (05) and ten (10) years, respectively 52.7% (2578/4890) and 32.8% (1603/4890). 13.9% (680/4890) had been on treatment for fifteen (15) years and 0.6% (28/4889) had been on treatment for more than twenty (20) years.

In patients with virological failure, 0.5% (4/881) of patients with treatment failure had been on treatment for more than 20 years, 11.9% (105/881) had been on treatment for more than 15 years, 54.9% (484/881) had been on treatment for less than 10 years 32.7% (288/881) had been on treatment for less than 5 years.

It should be noted that all these patients should be switched to the dolutegravir-based regimen.

Allocation of patients according to viral load suppression, gender and adherence

Table 5 describes the distribution of patients according to viral load suppression, sex and adherence.

The non-compliance rate was 3.7% (179/4890) in all patients. It was 4.3% (38/881) in patients with treatment failure. 18.2% (892/4890) of all patients do not know whether they are compliant or not. Among those who failed treatment, 15.8% (139/881) did not know whether they were compliant or not.

Table 5. Distribution of patients according to viral load suppression, sex and adherence.

Viral load	Sex	Observance			Total
		Don't know	No	Yes	
No deleted	Women	88 (63.3%)	25 (65.8%)	482 (68.5%)	595 (67.5%)
	Men	51 (36.7%)	13 (34.2%)	222 (31.5%)	286 (32.5%)
	Total	139 (15.8%)	38 (4.3%)	704 (79.9%)	881 (100%)
Deleted	Women	559 (74.4%)	89 (63.1%)	2199 (70.6%)	2847 (71.0%)
	Men	194 (25.8%)	52 (36.9%)	916 (29.4%)	1162 (29.0%)
	Total	753 (18.8%)	141 (3.5%)	3115 (77.7%)	4009 (100%)
Total	Women	647 (72.5%)	114 (63.7%)	2681 (70.2%)	3442 (70.4%)
	Men	245 (27.5%)	65 (36.3%)	1138 (29.8%)	1448 (29.6%)
	Total	892 (18.2%)	179 (3.7%)	3819 (78.1%)	4890 (100%)

4. Discussion

The ratio of 2.4 shows that the number of women people living with HIV on ART in Chad was higher than men. This remark was also reported in the 2022 statistical yearbook of the Ministry of Health and Prevention. The average age was 38 years, which means that the Chadian population is very young and the disease mainly affects age groups that are very sexually active. This could explain the high percentage found among married patients (60.9%), followed by bachelors (16.6%). The low percentage found among divorced women (13.9%), followed by widowers (8.6%), and clearly confirms that HIV circulates in the sexually active young population. It is important to implement HIV eradication strategies adapted to the Chadian context within this population.

The treatment failure rate in person living with HIV in this study is 18.0% (881/4890). Similar results were reported by Endalamaw *et al.* 2020 [18], Wadonda *et al.* 2012 [9], and Lailulo *et al.* (2020) [4]. This could explain the high percentage found among married patients (60.9%), followed by bachelors (16.6%). The low percentage found among divorced women (13.9%), followed by widowers (8.6%) and clearly confirms that HIV circulates in the sexually active young population. It is important to implement HIV eradication strategies adapted to the Chadian context within this population. Inadequate overall management and neglect of the patients themselves could explain this high percentage. It should be noted that comprehensive management of HIV is based on an approach that combines blocking the development of the virus, strengthening the immune system and regular monitoring of viremia (viral load). This approach is difficult and costly for countries with limited resources and fewer qualified personnel. This is sometimes compounded by insufficient availability of drugs and reagents for immunological and virological (viral load) monitoring.

The main factors of treatment failure reported in the studies are age, adherence, anemia, treatment interruptions, education level, low CD4 count, treatment in-

terruptions and virus resistance [19]-[22].

The 59.6% virological failure in married patients is worrying, as it increases the risk of HIV transmission in married women when they become pregnant and has been very well monitored.

It should be noted that the treatment failure observed in patients on second-line treatment and in patients who observe could be due to a phenomenon of resistance of HIV-1 to treatment, which has also been reported in several studies [23] [24]. A recent study reported by Keita *et al.* 2020, established the existence of HIV1 virus resistance genes against non-nucleotide reverse transcriptase inhibitors (NNRTIs) and reverse transcriptase nucleotides (NRTIs) in Chad [25].

However, the treatment failure observed in non-compliant patients could be explained by patient negligence or poor therapeutic education. This observation has also been reported by other studies [26]. Patients who do not know whether they are compliant or not may be classified as careless or in poor therapeutic education. With a non-compliance rate of less than 5%, Chad could achieve the 95% target of eliminating the patient burden if patient support and retention strategies are strengthened. It is therefore necessary to develop therapeutic education strategies for these patients and to provide psychological support.

Virological failure in patients on ART based on DTG 37.7% (333/881) for more than a year of treatment needs to be investigated and shed more light on the reasons, because in recent years, studies have reported resistance of the virus to integrase inhibitor molecules [27] [28].

The rate of treatment failure observed in persons living with HIV on ART for more than 10 years is very worrying [6], as these patients should be switched to the dolutegravir-based regimen. While virological failure is observed in patients on this regimen. Virological failure in person living with HIV on ART for more than 10 years is a catastrophe from a physiological point of view [29], because liver or kidney poisoning is a real disorder for the body. This most often leads patients to other metabolic diseases with disastrous consequences.

5. Conclusion

The study showed that many of the patients have been on treatment for several years, but the treatment does not respond. The study of the resistance of the HIV1 virus to the molecules used in Chad and the implementation of resistance tests are necessary. It is also necessary to develop therapeutic education strategies and provide psychological support for non-compliant patients and patients who do not even know whether they are compliant or not.

Author's Contributions

Study conception and design: Hassan Mahamat Ali (HMA) and Seid Idriss Ahmat (SIA). Data collection and analysis: HMA. Coordination of the survey and correction of the manuscript: Chatté Adawaye, Tapsoba François and Savadogo Aly. All authors have corrected the final version.

Conflicts of Interest

The authors do not declare any conflict of interest regarding this work.

Study Limitations

The study was unable to determine the number of previous viral loads achieved by each patient in treatment failure, in order to understand whether the patient had already experienced a previous treatment failure. It was also unable to identify the factors contributing to virological failure.

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