Observational Study

Medicine

OPEN

Viral suppression in the era of transition to dolutegravir-based therapy in Cameroon

Children at high risk of virological failure due to the lowly transition in pediatrics

Joseph Fokam, PhD, PGD[a,b,c,d], Alex Durand Nka, PhD[a,e,f,*], Flore Yollande Mamgue Dzukam, BMLS[a,b], Jeremiah Efakika Gabisa, BMLS[a], Yagai Bouba, PhD[a,e,g], Michel Carlos Tommo Tchouaket, Msc[a,h], Aude Christelle Ka'e, Msc[a,e], Ezechiel Ngoufack Jagni Semengue, PhD[a,e,f], Desire Takou, Msc[a], Sylvie Moudourou, MD[a], Nadine Fainguem, PhD[a,e,f], Willy Pabo, Msc[a,i], Rachel Audrey Nayang Mundo, Msc[a], Aurelie Minelle Kengni Ngueko, Msc[a], Collins Ambe Chenwi, MD, Msc[a,j], Junie Flore Yimga, Bsc[a], Marie Krystel Nnomo Zam, Bsc[a], Rachel Simo Kamgaing, MD[a], Charlotte Tangimpundu, Bsc[a], Nelly Kamgaing, MD[a,d], Anne-Esther Njom-Nlend, MD[k], Paul Ndombo Koki, MD[l], Daniel Kesseng, MD[l], Suzie Ndiang Tetang, MD[m], Etienne Kembou, Msc[n], Lifanda Ebiama Lifanda, MD, MPH[g], Bouba Pamen, MPH[d,n], Alice Ketchaji, MPH, PhD[o], Edith Saounde Temgoua, MD[g], Serge Clotaire Billong, MD, PhD[c,d,g], Anne-Cecile Zoung-Kanyi Bissek, MD[c,d,p], Hamsatou Hadja, MD[g], Edie Gregory Halle, MD[b], Vittorio Colizzi, MD, PhD[a,e,f], Carlo-Federico Perno, MD, PhD[a,q], Samuel Martin Sosso, PharmD[a], Alexis Ndjolo, MD[a,d]

Abstract

This study aimed to compare viral suppression (VS) between children, adolescents, and adults in the frame of transition to dolutegravir (DTG)-based antiretroviral therapy (ART) in the Cameroonian context. A comparative cross-sectional study was conducted from January 2021 through May 2022 amongst ART-experienced patients received at the Chantal BIYA International Reference Centre in Yaounde-Cameroon, for viral load (VL) monitoring. VS was defined as VL < 1000 copies/mL and viral undetectability as VL < 50 copies/mL. Chi-square and multivariate binary logistic regression models were used to identify factors associated with VS. Data were analyzed using SPSS v.20.0 (SPSS Inc., Chicago, Illinois), with $P < .05$ considered significant. A total of 9034 patients (72.2% females) were enrolled. In all, there were 8585 (95.0%) adults, 227 (2.5%) adolescents, and 222 (2.5%) children; 1627 (18.0%) were on non-nucleoside reverse transcriptase-based, 290 (3.2%) on PI-based, and 7117 (78.8%) on DTG-based ART. Of those on DTG-based ART, only 82 (1.2%) were children, 138 (1.9%) adolescents, and 6897 (96.9%) adults. Median (interquartile range) duration on ART was 24 (12–72) months (24 months on Tenofovir + Lamivudine + Dolutegravir [TLD], 36 months on other first lines, and 84 months on protease inhibitors boosted with ritonavir-based regimens). Overall, VS was 89.8% (95% confidence interval: 89.2–90.5) and viral undetectability was 75.7% (95% confidence interval: 74.8–76.7). Based on ART regimen, VS on Non-nucleoside reverse transcriptase-based, protease inhibitors boosted with ritonavir-based, and DTG-based therapy was respectively 86.4%, 59.7%, and 91.8%, $P < .0001$. Based on ART duration, VS was respectively 51.7% (≤24 months) versus 48.3% (≥25 months), $P < .0001$. By gender, VS was 90.9% (5929) in females versus 87.0% (2183) in males, $P < .0001$; by age-range, VS moved from 64.8% (144) in children, 74.4% (169) adolescents, to 90.8% (7799) adults, $P < .0001$. Following multivariate analysis, VS was associated with adulthood, female gender, TLD regimens, and combination antiretroviral therapy duration > 24 months ($P < .05$). In Cameroon, ART response indicates encouraging rates of VS (about 9/10) and viral undetectability (about 3/4), driven essentially by access to TLD based regimens. However, ART response was very poor in children, underscoring the need for scaling-up pediatric DTG-based regimens.

Abbreviations: 3TC = lamivudine, ART = antiretroviral therapy, CIRCB = Chantal BIYA International Reference Centre for research on HIV/AIDS prevention and management, DTG = dolutegravir, IQR = interquartile range, NNRTI = non-nucleoside reverse transcriptase, RLS = resource-limited settings, SSA = Sub-Saharan Africa, TDF = tenofovir disoproxil fumarate, TLD = Tenofovir + Lamivudine + Dolutegravir, UNAIDS = joint united nations programme on HIV/AIDS, VL = viral load, VS = viral suppression, WHO = World Health Organization.

Keywords: ART duration, Cameroon, dolutegravir, HIV, viral suppression

This work was supported by the "Chantal Biya" International Reference Centre for research on HIV/AIDS prevention and management (CIRCB), under the Annual Budget 2021–2022.

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

[a] Chantal BIYA International Reference Centre for research on HIV/AIDS Prevention and Management, Yaoundé, Cameroon, [b] Faculty of Health Sciences, University of Buea, Buea, Cameroon, [c] National HIV Drug Resistance Working Group, Yaoundé, Cameroon, [d] Faculty of Medicine and Biomedical Sciences, University of Yaounde I, Yaounde, Cameroon, [e] The University of Rome Tor Vergata, Rome, Italy, [f] Evangelic University of Cameroon, Bandjoun, Cameroon, [g] Central Technical Group, National AIDS Control Committee, Yaounde, Cameroon, [h] School of Health Sciences, Catholic University of Central Africa, Yaounde, Cameroon, [i] Faculty of Sciences, University of Buea, Buea, Cameroon, [j] Mvangan District Hospital, Mvangan, Cameroon, [k] Higher Institute of Medical Technology, Yaounde, Cameroon, [l] Mother-Child Centre, Chantal BIYA Foundation, Yaounde,

1. Introduction

HIV infection remains a global health concern, especially in Sub-Saharan Africa (SSA) where about 2/3 of the world's epidemiological burden is concentrated.[1] Despite efforts made to fight the disease, AIDS has caused over 35 million deaths, with SSA being highly affected (about 27 million deaths) according to the world health organization.[2] To reduce the global incidence of HIV and its associated morbidity/mortality, World Health Organization consolidated guidelines on the use of antiretroviral drugs for HIV treatment and prevention are recommended for resource-limited settings (RLS) such as SSA.[3] In these settings, combination antiretroviral therapies (ART) are available as first, second and third-line regimens, with a transition to dolutegravir (DTG)-based therapy as a first-line regimen in several countries, including Cameroon where the transition was launched in 2020.[4]

The ambitious 95-95-95 target of the Joint United Nations Programme on HIV/AIDS (UNAIDS) to eliminate AIDS calls for 95% of all people living with HIV to know their HIV status, 95% of all people with diagnosed HIV infection to receive sustained ART, and 95% of all people receiving ART to have viral suppression (VS) by 2025.[2,5] Achieving these targets remains challenging for most RLS like Cameroon due to the suboptimal healthcare systems, characterized by frequent drug stockouts, use of drugs with a poor genetic barrier to resistance, poor viral load coverage, and high rate of attrition or nonadherence to ART.[6] Of note, at the end of 2020, 81% of infected people knew their HIV status, 67% of those diagnosed were receiving ART, and 73% of patients on ART had achieved VS.[7] Despite the progress recorded by then, the performance was below the expected targets of 90-90-90 for 2020.[7]

Based on evidence from pretreatment HIV drug resistance surveillance surveys (i.e., critical threshold of 10%), current first-line ART regimens in most RLS consist of tenofovir disoproxil fumarate (TDF), lamivudine (3TC) and efavirenz combination referred to as Tenofovir + Lamivudine + Efavirenz,[8] and/or TDF, 3TC and DTG combination referred to as Tenofovir + Lamivudine + Dolutegravir (TLD).[9,10] Furthermore, TLD is also recommended for use as a second-line regimen for patients failing on efavirenz- or nevirapine-containing first-line regimens or any other non-DTG-containing first-line regimen. Of note, supportive evidence underscore the use of TLD as preferred first-line ART due to its high potency (rapid tailoring of viral load [VL]),[9] its higher genetic barrier to resistance (requires 3–4 the emergence of drug resistance mutations) compared to non-nucleoside reverse transcriptase (NNRTIs) (1 drug resistance mutation) and first-generation integrase-strand transfer inhibitors. Regarding drug intake, TLD appears more convenient and associated with fewer drug interactions.[9] Thus, the ongoing transition to TLD may represent a game changer in the ART paradigm of RLS, thereby suggesting the need for investigations in real-life conditions, in order to design interventions for ART optimization in the entire target population (children, adolescents and adults) living in these settings.

In Cameroon, a study conducted in 2019 revealed challenges in achieving the third UNAIDS target (about 80% overall VS), with very poor response in the population of adolescents (about 50% VS rate only).[4] This highlights gaps in achieving the previously set 90% target by 2020 in Cameroon, which might constraint programmatic efforts in reaching the expected 95% targets by 2025.[2,5] This prompts the need to closely monitor response to treatment in the course of transitioning to TLD at country level. Since the transition to TLD in 2020, little is known about the use of TLD in different target populations and the response to TLD as compared to other recommended regimens used in the national ART program in Cameroon. Data availability on patients who are virally suppressed and those who had attained viral undetectability are scarce. As such, strides aimed at achieving the 3rd 95% UNAIDS target by 2025 to curb the transmission of HIV infection at population-level cannot be adequately assessed. With the advent of DTG-containing regimens and the frame of wide transition to these new regimens, we sought to investigate the proportions of VS and viral undetectability among HIV-infected children, adolescents, and adults receiving ART in Cameroon, and to determine factors associated with virological response taking into account age-range, gender, ART regimens, and duration on ART.

2. Methods

2.1. Study design

A comparative cross-sectional study was conducted among, children (0–9 years), adolescents (10–19 years), and adults (≥ 20 years) routinely monitored for viral load at the Chantal BIYA International Reference Centre for research on HIV/AIDS prevention and management (CIRCB) in Yaounde, Cameroon. Data was queried from the institutional database from January 2021 to May 2022. This study period was purposely selected to match with the effective scale-up of "TLD" as the preferred first-line regimen at national-level."

2.2. Description of the study site

CIRCB is one of the main national reference laboratories designated by the Ministry of Public Health on the management and prevention of HIV/AIDS, with a focus on, but not limited to, HIV confirmatory diagnosis, viral load measurements, CD4 count, HIV DR genotypic testing, HIV early infant diagnosis, as well as complementary HIV/AIDS biochemical and haematological analyses. CIRCB participates in HIV/AIDS external quality assurance programs (http://circb.cm/btc_circb/web/).

Cameroon, [m] Essos Health Centre, National Social Welfare Centre, Yaounde, Cameroon, [n] World Health Organisation Afro, Country Office, Yaounde, Cameroon, [o] Division of Disease, Epidemic and Pandemic Control, Ministry of Public Health, Cameroon, [p] Division of Health Operational Research, Ministry of Public Health, Yaounde, Cameroon, [q] Bambino Gesu Pediatric Hospital, Rome, Italy.

** Correspondence: Alex Durand NKA, Chantal BIYA International Reference Centre for Research on HIV/AIDS Prevention and Management, 3077 Yaounde-Melen, Yaoundé, Cameroon (e-mail: nkaalexdurand@yahoo.com).*

Copyright © 2023 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

How to cite this article: Fokam J, Nka AD, Mamgue Dzukam FY, Efakika Gabisa J, Bouba Y, Tommo Tchouaket MC, Ka'e AC, Ngoufack Jagni Semengue E, Takou D, Moudourou S, Fainguem N, Pabo W, Nayang Mundo RA, Kengni Ngueko AM, Ambe Chenwi C, Flore Yimga J, Nnomo Zam MK, Simo Kamgaing R, Tangimpundu C, Kamgaing N, Njom-Nlend A-E, Ndombo Koki P, Kesseng D, Ndiang Tetang S, Kembou E, Ebiama Lifanda L, Pamen B, Ketchaji A, Saounde Temgoua E, Billong SC, Zoung-Kanyi Bissek A-C, Hadja H, Halle EG, Colizzi V, Perno C-F, Sosso SM, Ndjolo A. Viral suppression in the era of transition to dolutegravir-based therapy in Cameroon: Children at high risk of virological failure due to the lowly transition in pediatrics. Medicine 2023;102:20(e33737).

Received: 10 February 2023 / Received in final form: 4 April 2023 / Accepted: 20 April 2023

http://dx.doi.org/10.1097/MD.0000000000033737

Table 1

Population characteristics according to ART combination.

Variable	Overall† N = 9034	TDF + 3TC + DTG‡ N = 7117 (78.8)	Other 1st line ARV‡ N = 1627 (18.0)	ATVr or LPVr Based ARV‡ N = 290 (3.2)	*P* value*
Gender, n (%)					
Male	2508 (27.8)	2003 (79.9)	386 (15.4)	119 (4.7)	<.0001
Female	6526 (72.2)	5114 (78.4)	1241 (19.0)	171 (2.6)	
Age in yr, median (IQR)	39 (32–48)	40 (32–48)	37 (29–46)	38 (17–48)	<.0001
Age groups, n (%)					
Children	222 (2.5)	82 (36.9)	85 (38.3)	55 (24.8)	
Adolescents	227 (2.5)	138 (60.8)	58 (25.5)	31 (13.7)	<.0001
Adults	8585 (95.0)	6897 (80.3)	1484 (17.3)	204 (2.4)	
Duration on cART in month, median (IQR)	24 (12–72)	24 (12–72)	36 (12–72)	84 (24–156)	<.0001
Duration on cART in mo					
6–12	4013 (44.4)	3271 (81.5)	672 (16.7)	70 (1.7)	<.0001
13–24	655 (7.3)	522 (79.7)	123 (18.8)	10 (1.5)	
25–36	672 (7.4)	553 (82.3)	105 (15.6)	14 (2.1)	
≥ 48	3694 (40.9)	2771 (75.0)	727 (19.7)	196 (5.3)	

Other first-line ARV [ABC + 3TC + EFV (n = 13), ABC + 3TC + NVP (n = 2), AZT + 3TC + EFV (n = 36), AZT + 3TC + NVP (n = 14), TDF + 3TC + NVP (n = 51), TDF + 3TC + EFV (1511)], dLopinavir based (n = 173) and atazanavir based (n = 117).

3TC = lamivudine, ART = antiretroviral therapy, ARV = antiretroviral, ATVr = ritonavir boosted atazanavir, cART: combined antiretroviral therapy, EFV = efavirenz, IQR = interquartile range, LPVr = ritonavir boosted lopinavir, TDF = tenofovir disoproxil fumarate.

* *P* value for virological success at < 1000 copies/M.

† Percentages in this column represent column percentage.

‡ Percentages in this column represents row percentage.

2.3. Viral load quantification and results interpretation

Briefly, 4 mL of whole blood was collected in Ethylenediaminetetraacetic acid (EDTA)-containing tubes. Centrifugation of 1 EDTA tube was performed to obtain plasma, which was then divided into two (2) 700 µL aliquots and stored at – 20°C before analysis for viral load by Real Time PCR on the ABBOTT m2000rt platform, as per the manufacturer's instructions (http://www.abbottmolecular.com/products/infectious-diseases/realtime-pcr/hiv-1-assay). A protocol using 0.6 mL of plasma was used for RNA extraction, with < 40 copies/mL and > 10,000,000 copies/mL as the lower and higher detection limits, respectively.

2.4. Eligibility criteria

Patients with complete information; age, date of sample collection, date of ART initiation, and ART regimen together with VL result (s) were enrolled. Patients on ART for <6 months or those reported to be non-adherent to treatment were excluded.

2.5. Operational definitions

Virological response was interpreted as thus; VS (VL < 1000 copies/mL),[11] virological failure, VF (VL ≥ 1000 copies/mL),[11] and undetectable viral load as VL < 50 copies/mL.[11,12]

2.6. Data analysis

Data analysis was done using SPSS version 20.0 (SPSS Inc., Chicago, Illinois), with a statistical significance set at $P < .05$. Confidence intervals, proportions, and frequencies were computed, and data were summarized using Tables. The chi-square test was used to evaluate association between categorical variables.

Multivariable logistic regression was used to control for potential confounders, taking into consideration age, gender, ART regimen, and duration on ART. The independent variables included in the model were those with a P value ≤ .2 with the dependent variable in bivariate analysis.

2.7. Ethics approval and consent to participate

This study was approved by the ethics institutional review board of the faculty of health sciences of the University of Buea as part of academic research project (ref. No:2022/026). Administrative approval was provided by the CIRCB Directorate General (ref. No: 0736/022), in collaboration with the National AIDS Control Committee and the Ministry of Public health. Data were collected from the laboratory records and confidentiality/privacy of all sample identities were duly observed using specimens identified numbers.

3. Results

3.1. Participants characteristics

A total of 9034 patients were enrolled, with the majority being females (6526; 72.2%). The median (interquartile range [IQR]) age, year of ART initiation, and duration on treatment was 39 (IQR: 32–48), 2014 (IQR: 2011–2016), and 24 (IQR: 12–72) months, respectively. Most patients were adults (8585; 95.0%). A significant proportion of the study participants, 78.8% (7117/9034) were on TDF + 3TC + DTG, $P < .0001$. Children showed a lower treatment coverage with TLD (82; 36.9%), followed by adolescents (138; 60.8%), $P < .0001$. Additionally, more men (79.9%) were on TLD and the median (IQR) duration under this regimen was 24 (12–72) months, $P < .0001$ (Table 1).

3.2. Viral suppression in different study participants

The overall VS proportion (VL < 1000 copies/mL) obtained was 89.8% (8112/9034) with an optimal viral undetectability (<50 copies/mL) of 75.7% (6840/9034), $P < .0001$ (Table 2). According to gender, VS proportion was higher among females, 90.9% (5929/6526) against 87.0% (2183/2508) in males; similarly, the proportion of viral undetectability was equally higher in females, 77.9% (5082/6526) against 70.1% (1758/2508) in males, $P < .0001$ (Table 2). According to age distribution, VS was statistically significantly different, ranging from 64.8% in children, 74.4% in adolescents to 90.8% among adults, $P < .0001$ (Table 2). According to ART regimens, VS was

significantly higher among patients on TDF + 3TC + DTG at 91.8% (6533/7117) as compared to those on other first-line regimens, 86.4% (1406/1627).

Of note, patients on protease inhibitors boosted with ritonavir-based therapy presented the lowest proportion of VS, 59.7% (173/290), $P < .0001$ (Table 2). According to duration on ART, VS was 90.4% (3626/4013) at 12 months (M12), 87.6% (574/655) at 24 months (M24), 87.9% (591/672) at 36 months (M36), and 89.9% (3321/3694) from 48 months and above (≥ M48), $P < .0001$ (Table 2).

It should also be noted that, taking in to consideration gender and age group, the best viral suppression performance was observed among patients on TLD (92.7% and 89.5% among females and males, respectively, and 73.2%, 80.4% and 92.3% among children, adolescents and adults respectively; $P < .05$) (Table 3).

3.3. Factors associated with viral suppression

After adjusting gender, age categories, ART combination (TLD and other ART), and ART duration (considering 24 months

Table 2

Participants characteristics and viral suppression levels.

Variable	Overall† N = 9034	<50 copies/mL‡ N = 6840 (75.7%)	50–999 copies/mL‡ N = 1272 (14.1%)	<1000 copies/mL‡ N = 8112 (89.8%)	≥1000 copies/mL‡ N = 922 (10.2%)	*P* value*
Gender, n (%)						
Male	2508 (27.8)	1758 (70.1)	425 (16.9)	2183 (87.0)	325 (13.0)	*P* < .0001
Female	6526 (72.2)	5082 (77.9)	847 (13.0)	5929 (90.9)	597 (9.1)	
Age in yr, median (IQR)	39 (32–48)	40 (32–48)	39 (31–48)	40 (32–48)	37 (27–45)	*P* < .0001
Age groups, n (%)						
Children	222 (2.5)	104 (46.8)	40 (18.0)	144 (64.9)	78 (35.1)	*P* < .0001
Adolescents	227 (2.5)	138 (60.8)	31 (13.7)	169 (74.4)	58 (25.5)	
Adults	8585 (95.0)	6598 (76.9)	1201 (14.0)	7799 (90.8)	786 (9.1)	
Duration on cART in month, median (IQR)	24 (12–72)	24 (12–72)	12 (12–60)	18 (12–66)	24 (12–72)	*P* < .0001
Duration on cART in mo						
6–12	4013 (44.4)	2957 (73.7)	669 (16.7)	3626 (90.4)	387 (9.6)	*P* < .0001
13–24	655 (7.3)	478 (73.0)	96 (14.7)	574 (87.6)	81 (12.4)	
25–36	672 (7.4)	501 (74.6)	90 (13.4)	591 (87.9)	81 (12.1)	
≥48	3694 (40.9)	2904 (78.6)	417 (11.3)	3321 (89.9)	373 (10.1)	
ART combination, n (%)						
TDF + 3TC + DTG	7117 (78.8)	5538 (77.8)	995 (14.0)	6533 (91.8)	584 (8.2)	*P* < .0001
Other 1st line ARV	1627 (18.0)	1180 (72.5)	226 (13.9)	1406 (86.4)	221 (13.6)	
ATVr or LPVr based ARV	290 (3.2)	122 (42.1)	51 (17.6)	173 (59.7)	117 (40.3)	

3TC = lamivudine, ART = antiretroviral therapy, ARV = antiretroviral, ATVr = ritonavir boosted atazanavir, cART = combined antiretroviral therapy, DTG = dolutegravir, EFV = efavirenz, IQR = interquartile range, LPVr = ritonavir boosted lopinavir, TDF = tenofovir disoproxil fumarate.

Other first-line ARV [ABC + 3TC + EFV (n = 13), ABC + 3TC + NVP (n = 2), AZT + 3TC + EFV (n = 36), AZT + 3TC + NVP (n = 14), TDF + 3TC + NVP (n = 51), TDF + 3TC + EFV (1511)], Lopinavir based (n = 173) and atazanavir based (n = 117).

* *P* value for virological success at < 1000 copies/M.

† Percentages in this column represent column percentage.

‡ Percentages in this column represents row percentage.

Table 3

Viral suppression according to TLD coverage by age.

Variables		Overall† N = 9034	Viral load‡ <1000 copies/mL; N = 8112 (89.8%)	Viral load‡ ≥1000 copies/mL; N = 822 (10.2%)	OR (95% CI)	*P* value*
Gender						
Male	TDF + 3TC + DTG	2003 (79.9)	1794 (89.5)	210 (10.5)	1	<.0001
	Other ART	505 (20.1)	389 (77.2)	115 (22.8)	0.39 (0.30–0.50)	
Female	TDF + 3TC + DTG	5114 (78.4)	4743 (92.7)	371 (7.3)	1	<.0001
	Other ART	1412 (21.6)	1186 (84.0)	226 (16.0)	0.41 (0.34–0.49)	
Age categories						
Children	TDF + 3TC + DTG	82 (36.9)	60 (73.2)	22 (26.8)	1	.043
	Other ART	140 (63.1)	83 (59.7)	56 (40.3)	0.54 (0.29–0.98)	
Adolescents	TDF + 3TC + DTG	138 (60.8)	111 (80.4)	27 (19.6)	1	.010
	Other ART	89 (39.2)	58 (65.2)	31 (34.8)	0.45 (0.24–0.83)	
Adults	TDF + 3TC + DTG	6897 (80.3)	6364 (92.3)	533 (7.7)	1	<.0001
	Other ART	1688 (19.7)	1437 (85.1)	251 (14.9)	0.47 (0.40–0.56)	

Other ART: ARV [ABC + 3TC + EFV (n = 13), ABC + 3TC + NVP (n = 2), AZT + 3TC + EFV (n = 36), AZT + 3TC + NVP (n = 14), TDF + 3TC + NVP (n = 51), TDF + 3TC + EFV (1511)], Lopinavir based (n = 173) and atazanavir based (n = 117).

3TC = lamivudine, ART = antiretroviral therapy, ARV = antiretroviral, ATVr = ritonavir boosted atazanavir, CI = confidence interval, DTG = dolutegravir, EFV = efavirenz, IQR = interquartile range, LPVr = ritonavir boosted lopinavir, OR = odds ratioTDF = tenofovir disoproxil fumarate, TLD = Tenofovir + Lamivudine + Dolutegravir.

* *P value for virological success at < 1000 copies/M.*

† Percentages in this column represent column percentage.

‡ Percentages in this column represents row percentage.

as the median duration), the adult age group (≥20 years old) was independently associated with a higher proportion of VS than other age groups (adjusted odd-ratio (aOR: 3.72). Men were less likely to be virally suppressed compared to women (aOR:0.65). Patients on other ART regimens were less likely to be virally suppressed compared to patients on TLD (aOR:0.47) Also, patients on ART duration ≥ 25 months were less likely to be virally suppressed compared to patients who have been on ART for 6 to 24 (aOR: 0.76) (Table 4).

4. Discussion

The overall proportion of VS (< 1000 copies/mL) was 89.8%, with females registering a higher VS (90.9%). Children showed a higher and quite worrisome virological failure (VF) proportion of 35.1%, and those on TLD based regimens showed more sustained VS of 91.8% compared to those on non-TLD regimens (86.4% for other first-line regimens and 59.7% for ATVr or LPVr Based ART).

The 89.8% VS obtained here is about 5% away from the 3rd 95% target set by UNAIDS for 2025[5] but close to the current 90% performance achievement reported globally.[8] The proportion of patients with undetectable viraemia, (<50 copies/mL) was 75.8%, indicating the effectiveness of viral undetectability in ensuring viral untransmissibility in RLS like Cameroon is still a challenge, thus highlighting the need to continue reinforcing an integrated approach where condom uses, access to ART, and awareness of HIV prevention methods play a role in reducing transmission.

Even though the findings here are far below the achievements reported from many western countries,[13] our findings, however, provide great hope in the control of HIV transmission even in difficult-to-reach settings with highly potent ART regimens like TLD.[13] With the integration of DTG in the first-line of treatment, the degree of viral failure has dropped from 20.6% prior to TLD era to about 10%, which falls within the current range in other RLS where a 3.7% to 26.0% prevalence have been reported.[14] In 2016, the UNAIDS welcomed new goals, targets, and commitments of the 2016 United Nations General Assembly Political Declaration on Ending the AIDS epidemic by 2030. Following these new commitments and the transition to TLD in 2020, the availability and scalability of TLD based ART coverage in Cameroon improved, thus underscoring the positive impact TLD based regimes has had in polling down VF among PLHIV. To this end, health systems in RLS are encouraged to make multiple efforts to provide a wider access to TLD in the near future.

Previous studies in Cameroon reported VS proportions between 72.1 and 90.2%,[4,15–18] with disparities attributed to differences in the study periods, population characteristics, and duration on ART. For instance, the 89.8% reported in our current findings is higher than the countrywide population-based HIV impact assessment study, which reported an 80% VS in a study conducted prior to transitioning to DTG-based ART.[18] As aforementioned, the lower VS proportions in previous studies in Cameroon were linked to the use of efavirenz- or NVP-based regimens that were in use then, thus calling for a wider phase-out or use of NNRTI-sparing ART combinations for the benefit of wider TLD coverage following transition from NNRTI-containing regimens.[19,20] Of note, a high proportion of adults switching to TLD achieved VS despite substantial baseline NRTI resistance, and the majority had low-level viraemia (≤100 copies/mL),[19,20] with caution mainly for those with previous exposure to first-generation integrase inhibitors (Raltegravir).[21–28]

The poor proportion of VS in children and adolescents could be attributed to suboptimal adherence and inadequate psychological support, which increases the risks of virological failure in this group.[29,30] The very poor VS performance in children, in particular, is a cause for concern, especially in a context as this where the availability and coverage of pediatric DTG-based therapy recorded the lowest coverage of merely about 37% compared to older populations. The need to improve the availability and access to pediatric DTG formulation in Cameroon and similar RLS cannot be overemphasized,[31,32] as this is going to aid redress the problem of pediatrics Virological failure.

It has been reported that men are more likely to experience VF than females,[33–35] supported mainly by their limited attendance of health care services, which leads to poor adherence,[27–30] with an increased risk of VF and mortality.[36–39] While TLD showed a higher virological response, protease inhibitors boosted with ritonavir-based regimens need to be monitored closely as they are often used with recycled NRTIs in several RLS.[36] Also, duration on ART was associated with VS and this is likely due to tolerability overtime despite possible risks of HIV drug resistance emergence.[14,15,28,41] In a nutshell, the switch to DTG in 2020 in Cameroon shows encouraging performance with reducing resistance profiling, thereby supporting its fast track strides for achieving the 95% VS target.[38–40]

Table 4

Factors associated with viral suppression.

Variables	OR (95% CI)	*P* value*	aOR (95% CI)	*P* value*
Gender				
Female	1		1	
Male	0.65 (0.56–0.75)	<.0001	0.69 (0.60–0.81)	<.0001
Age categories, N (%)				
0–10	1		1	
11–19.	1.57 (1.05–2.36)	.028	1.28 (0.84–1.94)	.242
≥20	5.39 (4.05–7.16)	<.0001	3.72 (2.76–5.02)	<.0001
ART combination				
TDF + 3TC + DTG	1	<.0001	1	<.0001
Other ART	0.42 (0.36–0.48)		0.47 (0.40–0.55)	
ART Duration (mo)				
≤24	1	.46	1	.024
≥25	0.78 (0.62–0.99)		0.76 (0.59–0.96)	

Other ART: ARV [ABC + 3TC + EFV (n = 13), ABC + 3TC + NVP (n = 2), AZT + 3TC + EFV (n = 36), AZT + 3TC + NVP (n = 14), TDF + 3TC + NVP (n = 51), TDF + 3TC + EFV (1511)], Lopinavir based (n = 173) and atazanavir based (n = 117).

3TC = lamivudine, ART = antiretroviral therapy, aOR = adjusted odds ratio, CI = confidence interval, DTG = dolutegravir, OR = odds ratio, TDF = tenofovir disoproxil fumarate.

* *P* value for virological success at < 1000 copies/M.

The lower representation of children and adolescents seemingly represents a bias to assess VS achievement in this key group. Notwithstanding, the representation here reflects the real-life population distribution of HIV epidemics at country level.[41] To mitigate this potential bias, statistical adjustments were implemented. The cross-sectional design could not allow assessing long-term outcomes, which supports conducting studies on the long-term benefits of TLD which is currently unknow.

5. Conclusion

In this study participants receiving ART in Cameroon, about 9 out of 10 patients on combination antiretroviral therapy have achieved VS, with poorer outcomes among children and adolescents. Of note, 3-quarter (3/4) have achieved an undetectable VL, might indicate the prevention of HIV transmission at community-level. High rate of viral suppression is independently associated to TLD based regimens, adults (especially females). The current limited access to pediatric DTG-containing therapies calls for urgent actions to improve on VS in these vulnerable populations living mainly in SSA settings.

Acknowledgements

We would like to thank the CIRCB for giving us the opportunity to initiate this peace of work and all the care unit for people living with HIV that refer their patients to the CIRCB for HIV viral load monitoring.

Author contributions

Conceptualization: Joseph Fokam, Alex Durand NKA, Flore Yollande Mamgue Dzukam, Jeremiah Efakika Gabisa, Yagai Bouba, Michel Carlos Tommo Tchouaket, Ezechiel Ngoufack Jagni Semengue, Desire Takou, Sylvie Moudourou, Nadine Fainguem, Willy Pabo, Rachel Audrey Nayang Mundo, Aurelie Minelle Kengni Ngueko, Collins Ambe Chenwi, Junie Flore Yimga, Marie Krystel Nnomo Zam, Nelly Kamgaing, Paul Ndombo Koki, Etienne Kembou, Lifanda Ebiama Lifanda, Bouba Pamen, Alice Ketchaji, Edith Saounde Temgoua, Hamsatou Hadja, Edie Gregory Halle Halle, Vittorio Colizzi, Carlo-Federico Perno, Samuel Martin Sosso, Alexis Ndjolo.

Data curation: Joseph Fokam, Alex Durand NKA, Flore Yollande Mamgue Dzukam, Jeremiah Efakika Gabisa, Yagai Bouba, Michel Carlos Tommo Tchouaket, Aude Christelle Ka'e, Collins Ambe Chenwi, Sylvie Moudourou, Edie Gregory Halle Halle, Vittorio Colizzi, Carlo-Federico Perno, Samuel Martin Sosso, Alexis Ndjolo.

Formal analysis: Joseph Fokam, Alex Durand NKA, Jeremiah Efakika Gabisa, Yagai Bouba, Michel Carlos Tommo Tchouaket, Anne-Esther Njom-Nlend, Edie Gregory Halle Halle, Vittorio Colizzi, Carlo-Federico Perno, Alexis Ndjolo.

Funding acquisition: Vittorio Colizzi, Carlo-Federico Perno, Alexis Ndjolo.

Investigation: Aude Christelle Ka'e, Junie Flore Yimga, Vittorio Colizzi, Carlo-Federico Perno, Alexis Ndjolo.

Methodology: Yagai Bouba, Michel Carlos Tommo Tchouaket, Aude Christelle Ka'e, Rachel Simo Kamgaing, Alexis Ndjolo.

Project administration: Aude Christelle Ka'e, Carlo-Federico Perno.

Resources: Ezechiel Ngoufack Jagni Semengue.

Supervision: Collins Ambe Chenwi, Daniel Kesseng, Suzie Ndiang Tetang, Hamsatou Hadja, Edie Gregory Halle Halle, Samuel Martin Sosso.

Validation: Ezechiel Ngoufack Jagni Semengue, Charlotte Tangimpundu, Edie Gregory Halle Halle, Samuel Martin Sosso.

Visualization: Serge Clotaire Billong, Anne-Cecile Zoung-Kanyi Bissek, Edie Gregory Halle Halle, Vittorio Colizzi, Samuel Martin Sosso.

Writing – original draft: Ezechiel Ngoufack Jagni Semengue, Etienne Kembou, Edie Gregory Halle Halle, Vittorio Colizzi, Samuel Martin Sosso.

Writing – review & editing: Edie Gregory Halle Halle.

References

[1] Organisation Mondiale de la Santé. Lignes directrices de l'OMS: recommandations sur les interventions numériques pour le renforce ameroo systèmes de santé. Genève: Organisation mondiale de la Santé; 2022. Available at: https://apps.who.int/iris/handle/10665/354400. [access date November 29, 2022].

[2] Egpafadmin. UNAIDS issues new fast-track strategy to end AIDS–by 2030 - EGPAF. Elizabeth Glaser Pediatric AIDS Foundation; 2014. Available at: https://www.pedaids.org/2014/11/20/unaids-issues-new-fast-track-strategy-to-end-aids-by-2030/. [access date January 7, 2023].

[3] World Health Organisation. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach, 2nd ed. Available at: https://www.who.int/publications/i/item/9789241549684. [Access date January 8, 2023].

[4] Fokam J, Sosso SM, Yagai B, et al. Viral suppression in adults, adolescents and children receiving antiretroviral therapy in Cameroon: adolescents at high risk of virological failure in the era of "test and treat". AIDS Res Ther. 2019;16:36. Available at: https://doi.org/10.1186/s12981-019-0252-0. [access date January 6, 2023].

[5] UNAIDS. 2025-AIDS-Targets_en.pdf. Available at: https://www.unaids.org/sites/default/files/2025-AIDS-Targets_en.pdf. [Access date January 8, 2023].

[6] Aghokeng AF, Mpoudi-Ngole E, Dimodi H, et al. Inaccurate diagnosis of HIV-1 group M and O is a key challenge for ongoing universal access to antiretroviral treatment and HIV Preve Ameroon Cameroon. PLoS One. 2009;4:e7702. Available at: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0007702. [access date January 7, 2023].

[7] UNAIDS. 90-90-90 treatment target. Available at: https://www.unaids.org/en/90-90-90. [Access date January 8, 2023].

[8] UNAIDS DATA 2021. JC3032_AIDS_Data_book_2021_En.pdf. Available at: https://www.unaids.org/sites/default/files/media_asset/JC3032_AIDS_Data_book_2021_En.pdf. [Access date January 7, 2023].

[9] Tenofovir, Lamivudine, and Dolutegravir (TLD) Transition. linkages-tld-transition-information.pdf. Available at: https://www.fhi360.org/sites/default/files/media/documents/linkages-tld-transition-information.pdf. [Access date January 7, 2023].

[10] World Health Organisation. Update on the transition to dolutegravir-based antiretroviral therapy. Available at: https://www.who.int/publications-detail-redirect/9789240053335. [Access date January 7, 2023].

[11] World Health Organisation. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach, 2nd ed. Available at: https://www.who.int/publications-detail-redirect/9789241549684. [Access date April 2, 2023].

[12] BHIVA guidelines for the treatment of HIV-1 positive adults with antiretroviral therapy 2015 (2016-interim-update).pdf. Available at: https://www.bhiva.org/file/RVYKzFwyxpgiI/treatment-guidelines-2016-interim-update.pdf. [Access date April 2, 2023].

[13] Journal of the International AIDS society published by John Wiley & Sons Ltd on behalf of the International AIDS society. HIV Glasgow 2018, 28–31 October 2018, Glasgow, UK. J Int AIDS Soc [Internet]. 2018;21(Suppl Suppl 8):e25187. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6202722/. [Access date January 7, 2023].

[14] Aghokeng AF, Monleau M, Eymard-Duvernay S, et al. Extraordinary heterogeneity of virological outcomes in patients receiving highly antiretroviral therapy and monitored with the World Health Organization public health approach in Sub-Saharan Africa and southeast Asia. Clin Infect Dis Off Publ Infect Dis Soc Am. 2014;58:99–109.

[15] Boullé C, Guichet E, Kouanfack C, et al. Virologic failure and human immunodeficiency virus drug resistance Ameroon Cameroon with regard to the UNAIDS 90-90-90 treatment targets. Open Forum Infect Dis. 2016;3:ofw233. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5170495/. [access date January 7, 2023].

[16] Tchouwa GF, Eymard-Duvernay S, Cournil A, et al. EHRICA Study Group. Nationwide estimates of viral load suppression and acquired HIV drug resistance in Cameroon. EClinicalMedicine. 2018;1:21–7.
[17] Cameroon population-based HIV impact assessment CAMPHIA 2017: summary sheet: preliminary findings. Available at: https://stacks.cdc.gov/view/cdc/120050. [access date January 7, 2023].
[18] Billong SC, Fokam J, Aghokeng AF, et al. Population-based monitoring of emerging HIV-1 drug resistance on antiretroviral therapy and associated factors in a Sentinel Ameroon Cameroon: low levels of resistance but poor programmatic performance. PloS One. 2013;8:e72680. Available at: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0072680. [access date January 7, 2023].
[19] Cao P, Su B, Wu J, et al. Treatment outcomes and HIV drug resistance of patients switching to second-line regimens after long-term first-line antiretroviral therapy. Medicine (Baltimore). 2018;97:e11463. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6076136/. [access date January 7, 2023].
[20] Keene CM, Griesel R, Zhao Y, et al. Virologic efficacy of tenofovir, lamivudine and dolutegravir as second-line antiretroviral therapy in adults failing a tenofovir-based first-line regimen. AIDS Lond Engl. 2021;35:1423–32.
[21] Seminari E, Silvestri AD, Meini G, et al. Response to antiretroviral treatment after failure of NNRTI Plus NRTIs-based therapy. Data from the ARCA collaborative group. Curr HIV Res. 2012;10:334–40. Available at: https://www.eurekaselect.com/article/43380. [access date January 7, 2023].
[22] Geretti AM, Smith C, Haberl A, et al. Determinants of virological failure after successful viral load suppression in first-line highly active antiretroviral therapy. Antivir Ther. 2008;13:927–36. Available at: https://doi.org/10.1177/135965350801300707. [access date January 7, 2023].
[23] Cheng C-Y, Tsai M-S, Yang C-J, et al. Patterns of emergent resistance-associated mutations after initiation of non-nucleoside reverse-transcriptase inhibitor-containing antiretroviral regimens in Taiwan: a multicenter cohort study. Infect Drug Resist. 2018;11:849–59. Available at: https://www.dovepress.com/patterns-of-emergent-resistance-associated-mutations-after-initiation--peer-reviewed-fulltext-article-IDR. [access date January 7, 2023].
[24] Charpentier C, Karmochkine M, Laureillard D, et al. Drug resistance profiles for the HIV integrase gene in patients failing raltegravir salvage therapy. HIV Med. 2008;9:765–70. Available at: https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1468-1293.2008.00628.x. [access date January 7, 2023].
[25] Mbisa JL, Martin SA, Cane PA. Patterns of resistance development with integrase inhibitors in HIV. Infect Drug Resist. 2011;4:65–76. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3108751/. [access date January 7, 2023].
[26] Blanco J-L, Varghese V, Rhee S-Y, et al. HIV-1 integrase inhibitor resistance and its clinical implications. J Infect Dis. 2011;203:1204–14. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3069732/. [access date January 7, 2023].
[27] Thierry E, Deprez E, Delelis O. Different pathways leading to integrase inhibitors resistance. Front Microbiol. 2017;7:2165. Available at: https://www.frontiersin.org/articles/10.3389/fmicb.2016.02165. [access date January 7, 2023].
[28] Marcelin A-G, Grude M, Charpentier C, et al. Resistance to integrase inhibitors: a national study in HIV-1-infected tIent-naive and -experienced patients. J Antimicrob Chemother. 2019;74:1368–75. Available at: https://academic.oup.com/jac/article/74/5/1368/5353171. [access date January 7, 2023].
[29] Bulage L, Ssewanyana I, Nankabirwa V, et al. Factors associated with virological non-suppression among HIV-positive patients on antiretroviral therapy in Uganda, August 2014-July 2015. BMC Infect Dis. 2017;17:326.
[30] World Health Organisation. A global research agenda for adolescents living with HIV - research for an AIDS free generation. Available at: https://www.who.int/publications/i/item/WHO-HIV-2017.33. [Access date May 3, 2023].
[31] Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) accelerating access to optimal child-friendly antiretroviral formulations. Available at: https://www.pedaids.org/wp-content/uploads/2019/12/SPAAN_FS-2019.pdf.
[32] Paediatric HIV & TB: Rome action plan. Available at: https://www.paediatrichivactionplan.org/viiv. [Access date January 7, 2023].
[33] Reliefweb. Ending AIDS: progress towards the 90–90–90 targets - World | ReliefWeb [Internet]. Available at: https://reliefweb.int/report/world/ending-aids-progress-towards-90-90-90-targets. [Access date January 7, 2023].
[34] Novitsky V, Gaolathe T, Mmalane M, et al. Lack of virological suppression among young HIV-positive adults in Botswana. J Acquir Immune Defic Syndr 1999. 2018;78(5):557–65. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6069598/. [access date January 7, 2023].
[35] Agolory S, de Klerk M, Baughman AL, et al. Low case finding among men and poor viral load suppression among adolescents are impeding Namibia's ability to achieve UNAIDS 90-90-90 targets. Open Forum Infect Dis. 2018;5:ofy200.
[36] Mujugira A, Celum C, Tappero JW, et al. Younger age predicts failure to achieve viral suppression and virologic rebound among HIV-1-infected persons in serodiscordant partnerships. AIDS Res Hum Retroviruses. 2016;32:148–54.
[37] Mekuria LA, Nieuwkerk PT, Yalew AW, et al. High level of virological suppression among HIV-infected adults receiving combination antiretroviral therapy in Addis Ababa, Ethiopia. Antivir Ther. 2016;21(5):385–96. Available at: https://doi.org/10.3851/IMP3020. [access date January 7, 2023].
[38] Cihlar T, Fordyce M. Current status and prospects of HIV treatment. Curr Opin Virol. 2016;18:50–6.
[39] Peñafiel J, De Lazzari E, Padilla M, et al. Tolerability of integrase inhibitors in a real-life setting. J Antimicrob Chemother. 2017;72:1752–9.
[40] Office of AIDS Research Advisory Council (OARAC). Guidelines for the use of antiretroviral agents in adults and adolescents with HIV. Available at: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/archive/AdultandAdolescentGL_2021_08_16.pdf.
[41] World Bank. Cameroon - Enquête Démographique et de Santé 2018. Available at: https://microdata.worldbank.org/index.php/catalog/3717. [access date April 3, 2023].