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Brief communication: The extent and determinants of viral suppression among patients on protease inhibitor-based Anti-retro-viral therapy undergoing intensive adherence counselling in a public HIV care center in Uganda

Zubair Lukyamuzi[1,2*], Hood Ibanda[1], Joseph Ggita[2], Denis Mawanda[2], Brenda M Gati[2], Rita Nakalega[2] and Ronald Kiguba[1]

Abstract

Background Protease inhibitor (PI)-based Antiretroviral Therapy (ART) regimens are key drugs in HIV management, especially when used as second line drugs. However, some PI-based ART have high adherence demands or tolerable adverse effects which may affect adherence and subsequently viral suppression. We assessed the extent of viral suppression, its determinants, and the experiences of clients on PI-based ART undergoing intensive adherence counselling (IAC) in a public HIV clinic.

Methods Mixed methods sequential explanatory study involving a quantitative retrospective chart review for clients on PI-based ART who had received IAC from Dec 2016 to May 2023 and qualitative interviews for clients on PI-based ART who had received IAC in the past six months at an urban public HIV clinic in Uganda.

Results In this study, a total of 189 client charts were included. The median number of IAC sessions received was three (interquartile range, IQR, of 3 to 4) with median time of receiving IAC of three (IQR, of 2 to 4). One half (51%, 95/186) of the clients had achieved viral suppression and the odds of suppression increased by 30% for every additional month on IAC. Respondents perceived the effectiveness of PI-based ART and IAC in achieving and supporting viral suppression, respectively.

Conclusion Despite the perceived effectiveness of PI-based ART and IAC, suboptimal levels of viral suppression were observed among clients on PI-based ART who had received IAC. Therefore, it is important to provide IAC for optimal duration as it increases the chances of viral suppression. Further investigation of the barriers of viral suppression for clients on PI-based ART undergoing IAC is needed.

*Correspondence:
Zubair Lukyamuzi
zlukyamuzi@mujhu.org

Full list of author information is available at the end of the article

Keywords Viral suppression, Intensive adherence counselling, Protease inhibitors, Mixed methods study

Introduction

Protease inhibitor (PI)-based ART regimens have had a profound impact on HIV treatment paradigm since their introduction. These regimens effectively reduce HIV viral load (VL) levels and increase CD4+lymphocyte [1, 2]. They are mostly used as 2nd line regimens when are given to people living with HIV (PLHIV) who have failed on the initial regimens. They may also be used as 1st line regimens in children and adults who cannot tolerate the recommended 1st line regimens [3]. Despite the critical role of PI-based ART in HIV management, some of PI-based ART require high levels of adherence and others have tolerable side effects which may affect ART adherence and subsequently VL suppression [2, 4–6].

To improve ART adherence, the world health organization (WHO) recommends intensive adherence counseling (IAC) for all PLHIV with unsuppressed VL after six months on ART including those on PI-based ART [7, 8]. IAC improves ART adherence and viral suppression in about 71% of the recipients [9–11]. Uganda adopted IAC in 2016 [9] to improve ART adherence and subsequently viral suppression [12]. However, non-adherence remains a significant challenge and the major cause of unsuppressed VL in Uganda and beyond [13–19]. In 2022, more than 6% of PLHIV on ART in Uganda were not suppressed [20]; and a recent study in Uganda showed that PLHIV on PI-based ART undergoing IAC were less likely to suppress compared to their counterparts on other regimens [21]. Thus, assessing the outcomes of IAC among PLHIV on PI-based ART would guide and optimize strategies for management of HIV in this population. In this study, we set out to determine the extent of viral suppression, associated factors, and experiences of PLHIV on PI-based ART who underwent IAC at a large urban public HIV care facility in Uganda.

Methods

Study design and population

We conducted a mixed-methods sequential explanatory study involving both quantitative and qualitative methods. For the quantitative study, we used the electronic medical records (EMR) system and VL register to conduct a retrospective cross-sectional chart review for PLHIV on PI-based ART who had unsuppressed VL between Dec 2016 and May 2023. All PLHIV who had received IAC were consecutively included in the study. For the qualitative study, we sequentially conducted explanatory interviews among PLHIV on PI-based ART who had completed IAC in the prior six months. The study was conducted at Kisenyi Health center IV (KHCIV), the largest urban public HIV clinic in Kampala, Uganda, and was approved by Makerere University School of Biomedical Sciences Research Ethics Committee (SBS-2023-309).

Data collection procedures and study outcomes

We generated a list of PLHIV on PI-based ART that had received IAC between Dec 2016 and May 2023. IAC was a systematic counselling program offered by health workers to PLHIV with unsuppressed VL (≥1000 copies per ml) after at least six months on ART. The program consisted of three counselling sessions each provided one month apart. After completion of the sessions, VL testing was repeated. If the repeat VL was suppressed (<1000 copies per ml), the client continued with their current ART regimen but If the repeat VL was unsuppressed (≥1000 copies per ml), the client was considered for a switch to a second or third-line ART regimen after ensuring that all adherence issues had been addressed [7]. We retrospectively followed up all study enrolled charts from the date of initiation of IAC to the date of repeat VL test or up to 31st May 2023, whichever came first. We used a data abstraction form to collect data on various variables including the number of IAC received, time (in months) taken while receiving IAC, and viral suppression status after completion of IAC. We also used the VL register to purposively [22] select eight clients on PI-based ART who had completed IAC in the prior six months. The selected clients were invited to the clinic, consented, and interviewed using an in-depth interview (IDI) guide. The interviews were guided by the principles of Medication Adherence Model (MAM) [23] and were conducted in the participant's preferred language by the principal investigator in a calm place where conversations could not be overhead.

Statistical analysis

We analyzed quantitative data using Stata version 17 (StataCorp, College Station, TX, USA) [24]. We used proportions to determine the extent of viral suppression and logistic regression to determine the independent factors associated with viral suppression. The IDIs were recorded and collected data on perceived behavior for uptake of PI-based ART, perceived purpose of PI-based ART, and the perceived role of IAC in achieving viral suppression. All the information was audiotaped, transcribed by a professional and analyzed using a deductive approach [25] in Atlas.ti 8 (ATLAS.ti Scientific Software Development GmbH, Berlin- Germany) [26]. We methodologically triangulated [27] the categorized qualitative data with quantitative results at thematic analysis stage to obtain final themes.

Table 1 Characteristics of clients on protease inhibitor-based ART regimens who underwent intensive adherence counseling at an urban public HIV care center in Uganda

Characteristic	Frequency	Proportion (%)
Age (median, IQR), *n* = 189	35, (17–43)	
Sex,*n* = 189		
Male	71	38
Female	118	62
Marital status,*n* = 189		
Married	65	34
Not married	124	66
Residence,*n* = 189		
Urban	135	71
Rural	54	29
Initial ART regimen,*n* = 189		
Efavirenz-based	80	42
Nevirapine-based	75	40
Protease Inhibitor-based	34	18
Years on ART (median, IQR),*n* = 189	9 (6–11)	
Current ART regimen		
Atazanavir/Ritonavir-based	114	60
Lopinavir/Ritonavir-based	75	40
Years on PI-based ART (median, IQR),*n* = 189	5 (5–6)	
Number of IAC sessions (median, IQR),*n* = 189	3 (3–4)	
Duration on IAC in months (median, IQR), *n* = 189	3 (2–4)	
Days to viral load test after IAC (median, IQR),*n* = 189	35 (4-121)	
Suppression status after IAC (95% CI),*n* = 186		
Yes (Suppressed)	95 (44–58)	51

Table 2 Factors associated with viral suppression among clients on protease inhibitor-based ART who underwent Intensive Adherence Counseling at an urban public HIV care center in Uganda

Characteristic	Not suppressed (*n* = 91)	Suppressed (*n* = 95)	Crude Odds Ratio	*P*-value	Adjusted Odds Ratio (95% CI)	*P*-value
Age (median, IQR)	35(25–43)	35(11–44)	1	0.077	1 (0.97–1.01)	0.283
Sex						
Male (37.8%)	32(35.2)	37 (39.0)	1		1	
Female (62.2%)	59 (64.8)	58 (61.1)	0.9	0.594	0.8 (0.45–1.54)	0.552
Current ART regimen						
Atazanavir/Ritonavir- based (61.6%)	61 (67.0)	51 (57.3)	1		1	
Lopinavir/Ritonavir- based (38.4%)	30 (33.0)	44 (46.3)	1.8	0.064	1.4 (0.70–2.92)	0.321
Years on PI-based ART (median, IQR)	5 (5–6)	6 (4–6)	1	0.858	1.1 (0.83–1.40)	0.583
Number of IAC sessions received (median, IQR)	3 (3–4)	3 (3–4)	0.8	0.325	0.7 (0.45–1.01)	0.054
Duration on IAC in months	3 (2–4)	3 (2–4)	1.2	0.053	1.3 (1.04–1.55)	**0.018**

Results

Quantitative assessments

A total of 189 client charts were enrolled, and 186 participants (98%, *n* = 189) had VL results available after completion of IAC. The extent of viral suppression following IAC was 51% (95/186; 95%CI: 44–58) as shown in Table 1.

Factors associated with viral suppression among PLHIV on PI-based ART who underwent IAC at KHCIV

In the multivariable logistic regression, the odds of viral suppression increased by 30% for every additional month on IAC (OR = 1.3, 95% CI: 1.04–1.55) and this was statistically significant, p-value = 0.018 as shown in Table 2.

Qualitative exploration of IAC experiences for PLHIV on PI-based ART

A total of eight participants were interviewed. The average age was 34 years and the majority, 5/8 were females.

All had completed IAC and their average years on PI-based ART was three years. Three themes evolved from the IDIs: perceived behavior for ART adherence, purposeful actions required for ART adherence, and positive feedback on PI-based ART and IAC.

Perceived behaviour for adherence to PI-based ART

The main category was *good adherence to ART following regimen switch*: Respondents mentioned good ART adherence especially after switching to PI-based ART.

> *"They have changed my drugs, and I have swallowed the current one well for about three years." 46-year-old man mentioned.*

Purposeful actions required for ART adherence

The main category was *persistent uptake of PI-based ART despite minor side effects*: Participants reported occurrences of some side effects like nausea, vomiting, and feeling weak or sleepy especially on initiating this type of regimen but later disappeared on persistent uptake:

> *"I used to get nausea/vomiting initially, but I no longer get it." 20-year-old-female.*

Positive feedback on PI-based ART and IAC

This consisted of two categories: *PI-based ART was perceived effective in achieving viral suppression and IAC was perceived effective in supporting adherence and hence viral suppression*.

PI-based ART is effective in achieving viral suppression

Respondents highlighted the benefits of PI-based ART, they expressed their belief in the efficacy of the medication:

> *"Ever since I started taking this new drug, they test and find the virus suppressed. But they still tell me that I should not stop taking the medicine because the virus may be hiding in the bones and when you stop taking the drugs, it appears again." 27-year-old male.*

IAC effectively support ART adherence and hence viral suppression

Respondents consistently highlighted the significant role of IAC in supporting ART adherence leading to viral suppression:

> *"The counseling (IAC) helped me so much because during that counseling, there are certain things they tell you to forego when you are using these drugs. So, when you forego those things and swallow your drugs well, eat well, you achieve suppression. So, that counselling helps a lot". 47-year-old male.*

> *"Like I explained, I got that counseling (IAC) after finding out that my virus was very active, they would call me on phone to come to the hospital every month and this helped because these days, the virus is suppressed and these days I take long to come back to the health facility." 46-year-old female.*

Discussion

PI-based ART regimens are key drugs in HIV management, especially as second line drugs. Evidence shows that the number of patients requiring second-line ART in sub-Saharan Africa will exceed 4 million by 2030 [28]. Therefore, evaluating viral suppression attributed to these regimens among clients undergoing adherence enhancing interventions is imperative to addressing potential barriers to viral suppression. In this study, we found the extent of viral suppression at 51% among clients on PI-based ART undergoing IAC, and this suppression was influenced by the duration of receiving IAC. We also found that clients on PI-based ART regimen perceived both PI-based ART and IAC to be effective in achieving viral suppression and supporting viral suppression, respectively.

The 51% extent of viral suppression in this study was moderately high and similar to 42.2% that was reported in military health facilities of Uganda [29]. However, the current proportions of suppression were higher than those reported by Nassuna et al. (23%) and Lukyamuzi et al. (15.3%) [21, 30]; and these variations might have been due to the differences in the study periods. This is because the current study was conducted when IAC program was fully integrated in HIV care and embraced by health workers as opposed to the two previous studies which were conducted when the program was still new or piloted. Conversely, the current proportions of suppression were lower than 81.6% and 70.5% that were reported by Izudi et al. [31] and HIV care policy makers, respectively [9–11, 32]. These variances could be due to the differences in the study populations whereby the current study specifically targeted clients on the PI-based ART as opposed to all PLHIV targeted by Izudi et al. and policy makers. Therefore, the observed suboptimal viral suppression in the current study calls for a need to examine and evaluate the implementation of IAC among clients on PI-based ART.

In this study, viral suppression was directly proportion to the duration of receiving IAC. This was consistent with the fact that IAC is intended to provide the recipient with

adequate time to realize and understand the importance of ART adherence [32]. These findings, therefore, implies that the longer the duration a client takes receiving IAC, the higher the chances of understanding the purpose and the importance of ART adherence, and hence viral suppression.

Respondents on PI-based ART perceived IAC to be helpful in supporting ART adherence and consequently viral suppression. This was consistent with Ugandan ministry of health and WHO reports [8, 32]. Additionally, Lukyamuzi et al. [21] and Najjuma et al. [33] interviewed IAC recipients who also perceived IAC to be informative and important in supporting ART adherence. The current respondents also perceived PI-based ART to effectively suppress VL. This was consistent with previous literature which asserts the effectiveness of PI-based ART in suppressing VL and increasing CD4+lymphocyte counts [2]. Pharmacologically, PIs selectively block HIV protease, an enzyme involved in a critical step in HIV replication hence preventing the virus from replication, and thus viral suppression [34]. Conversely, 49% of clients on PI-based ART undergoing IAC didn't achieve suppression in the current study which can be attributed to various factors including drug resistance. Future studies would look at comprehensive evaluation of non-suppression among clients PI-based ART undergoing IAC.

In conclusion, IAC program was embraced in this setting for clients on PI-based ART. However, suboptimal viral suppression was realized despite the recipients of the program demonstrating an understanding of the purpose and the benefits of both ART and IAC. Therefore, there is a need to provide IAC for adequate duration as it increases the chances of suppression. Future studies would examine fidelity of IAC procedures and barriers to viral suppression among PLHIV on PI-based ART.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12981-024-00661-0.

Supplementary Material 1

Supplementary Material 2

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Author contributions

All authors contributed to the study conception and design. Material preparation was performed by ZL, HI. Data collection was performed by DM and ZL. Analysis was performed by ZL, JG, and RK. The first draft of the manuscript was written by ZL, BGM, and RN. RK and HI provided overall guidance in the conceptualization, study implementation, and manuscript writing. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Consent for publication

N/A.

Competing interests

The authors declare no competing interests.

Author details

[1]School of biomedical sciences, department of pharmacology and therapeutics, Makerere University College of Health Sciences, Kampala, Uganda

[2]Makerere University, Johns Hopkins University Collaboration (MU-JHU), Upper Mulago Hill Road, Kampala, Uganda

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