The Effect of appointment spacing model of care on virological suppression and associated factors among HIV positive individuals on antiretroviral therapy at public health facilities of Debre Markos town, northwest Ethiopia: Interrupted time series design.

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Research Article

Keywords: Appointment spacing model, HIV, virological suppression, Ethiopia

Posted Date: February 14th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1328734/v1

Abstract

Background

Appointment spacing model (ASM) of care is crucial for HIV patients receiving antiretroviral therapy in order to improve service quality, and patient's clinical outcomes including viral suppression. However, there is a paucity of information about the effectiveness of ASM on viral suppression. Therefore, this study aimed to assess the level and trends of virological suppression and associated factors among clients on antiretroviral therapy enrolled into ASM in northwest Ethiopia.

Methods

An interrupted time-series study design was conducted among 272 adults HIV clients who were stable and enrolled in ASM. They were selected by using a systematic random sampling technique. Data were collected from the patient's charts, registration books, and computer databases using abstraction sheets. Regression coefficients with a 95% confidence interval (CI) computed and variables having less than 0.05 P-value in the segmented regression model were considered significant predictors of virological suppression.

Result

This study revealed that virological suppression was decreased from the baseline of 99.22–96% after the implementation of ASM. The trends of virological suppression were significantly decreased by 1.38(95%CI: -2.2, -0.5, P-value=0.0007) after the implementation of ASM. Poor adherence was the most influential variable that caused level and trend decrements over time (P-value=0.04).

Conclusion

The level of virological suppression was significantly reduced after the implementation of ASM. The most significant factor associated with decreased levels and trends over time was poor adherence. It would be beneficial to assess and maintain good adherence of clients on antiretroviral therapy throughout the clinical visit during the implementation of ASM.

Background

Globally, Human Immunodeficiency Virus (HIV) remains a major public health concern[1]. Approximately 37.9 million people were living with HIV and about 23.3 million people were accessing antiretroviral therapy (ART)[1, 2]. Sub-Saharan Africa accounts for two-thirds of all new HIV infections worldwide[3]. According to the United Nation Programme on HIV/AIDS(UNAIDS) 2019 report, Ethiopia is one of the 30 countries that account for most of the world's people newly infected with HIV[4]. In 2018, the national HIV prevalence rate in adults aged 15-49 was 0.9%, 1.2% for women, and 0.6% for male[5]. According to the UNAIDS spectrum estimate, there were a total of 665,723 people living with HIV (PLHIV) in Ethiopia, of which 97.1% of adults were receiving ART and 87.6% had suppressed viral loads[6].A fixed-dose combination of Tenofovir(TDF)+Lamivudine (3TC)+Efavirenz(EFV) orTDF+3TC+Doultegravir(DTG)as a once-daily dose is the preferred first-line ART regimen for adult HIV patients in Ethiopia[5].Globally, UNAIDS plan to have 95% of people on HIV treatment have a suppressed viral load by 2030 in order to assure global HIV epidemic control[4]. Despite this ambitious goal, a systematic review of HIV treatment cascades in 69 countries found that viral suppression ranged from 7% in China to 68% in Switzerland[7]. From the UNAIDS fact sheet report, of all people accessing ART, only 53% were virally suppressed[8],which was below the target set by UNAIDS [9–14].

Approximately 95% of HIV service delivery worldwide was facility-based and undifferentiated to individual needs[15].This increases the challenges for HIV programs in managing the diverse needs of patients and makes meeting the target difficult, even if different strategies were implemented to improve virological suppression for those on ART[15, 16]. Patient- centered HIV care aims to deliver all services closer to the individual. This reduces the difficulty, cost of travel, and shortens waiting times[16]. In many settings, lack of transportation and money, as well as long waiting times in health facilities were the major barriers to access to services and retention in care, particularly in rural areas[17]. Therefore, to address the growing number of stable individuals on ART and to improve the outcome, World Health Organization (WHO) endorsed and recommends the appointment spacing model of care (ASM) by the end of 2014 [18]. In the appointment spacing model of care, clients are expected to have a clinical visit to health facilities twice a year only. In the standard of care, a client is required to have a frequent clinical visit, which is usually every three-month appointment period[19]. ASM provides safer, discreet, and more accessible healthcare options and implemented for stable patients on ART. This model of care provides clinical check-ups, laboratory monitoring, and antiretroviral drug refills every six months, which is very important to treat all and in order to improve the quality of life with better treatment outcomes, including viral suppression[15, 20]. ASM is vital for relieving unnecessary burden on health care facilities and clinicians, as well as meeting the needs of care recipients[16].Ethiopia adopted ASM of service delivery by the end of 2017 as a continuum of care, and enrolled 69,074 patients [21, 22].

Despite WHO's recommendation for innovative approaches like ASM to address HIV/AIDS-related problems[23–26], different pieces of literature revealed that virological non-suppression is still high and remains a public health problem that leads to high number of AIDS-related morbidity, mortality and increased new HIV infection, Monitoring and evaluating the model was an important part of the implementation of the service. However, there is a paucity of information about the effectiveness of ASM on virological suppression in many resource-limited settings, including Ethiopia. Therefore, the purpose of this study was to assess the level and trends of viral suppression before and after ASM, which is vital to show the effect of ASM on virological suppression and identify its associated factors among patients enrolled in ASM in the public health facilities of Debre Markos Town. Thus, this information will be helpful for healthcare professionals, policymakers, governmental and non-governmental organizations in enhancing the implementation of the ASM and the development of an evidence-based intervention to improve the survival of individuals on ART.

Methods

Study design and setting

An institution-based interrupted time series design was conducted at public health facilities in Debre Markos town from October to November 30/2020. Debre Markos is the capital town of the East Gojjam zone, located 300 kilometers from Addis Ababa, the capital city of Ethiopia, and 265 kilometers from Bahir-Dar, the capital of the Amhara regional state. The town has four public health facilities sites, which provide ART services for the town and the catchment area population. Debre Markos health center and Debre Markos referral hospital started to implement ASM and viral load tests, whereas Wuseta and Hidase health centers do not provide ASM. According to health management information system (HMIS) reports, there were a total of 5060 clients taking ART in Debre Markos town. From these, 3,168 clients were enrolled in ASM until June 2020.

Population and sample

All adult HIV patients who were enrolled into ASM for HIV care and treatment were the source population. Whereas, the study population were those patients who had at least two viral load measurements before and after ASM in the selected public health facilities were included. Patients who were lost to follow-up, discontinued from ASM, died, and transferred out from the catchment area were excluded. The target sample size was calculated by considering the previous study report as 68% of patients had virological suppression in the standard of care (three months follow-up) and 79% had viral suppression after being enrolled in ASM[27]. Using G-power version 3.1.9.4 software by assuming 5% margin of error, 95% level of confidence, and 80% power, then the sample size to determine viral suppression was calculated by the following formula:

$$n = (p1q1 + p2q2)\,(f(\alpha, \beta)) \,/\, ((p1 - p2)^2$$

The final sample size was 276 people after a 10% attrition rate. A simple random sampling technique with proportional allocations was used to determine the participants from each facility.

We took 62 samples from Debre Markos health center $Ni(\frac{n}{N})$=703 (276/3168) and 214 from Debre Markos referral hospital ($Ni(\frac{n}{N})$=2465 (276/3168) because Wuseta and Hidase health centers do not provide ASM. Finally, 272 clients who met the inclusion criteria were included in the final analysis.

Study Variables and Operational Definition

The dependent variable was virological suppression, whereas socio-demographic and clinical characteristics like age, sex, religion, marital status, educational level, occupation, residence disclosure status, treatment supporter, nutritional status, regimen type, adherence, Isoniazid, and cotrimoxazole preventive therapy (CPT), WHO clinical stages, TB-co infection, functional status, and opportunistic infections other than TB were collected.

Virological suppression: Viral load below the detected threshold using viral assay (<1000copies of viral RNA/ml of blood)after taking plasma and separated from whole blood[1, 28].

Appointment spacing model: Stable adult patients are offered the opportunity to provide six months' worth of ART and have a clinical follow-up at each visit to an appointment[29].

Stable patient: Defined as an individual's>15 years old and on ART for at least one year, no adverse drug reactions requiring regular monitoring, good understanding of lifelong adherence, two consecutive viral load measurements <1000copies/ml, no acute illness, not pregnant or breastfeeding[29].

Adherence: Drug adherence was defined as the percentage of doses taken as prescribed; using a number of doses missed in the last one month.; good if equal to or greater than 95% adherence i.e., missing only 1 out of 30 doses or missing 2 from 60 doses. Fair if the clients taking 85-94% of the prescribed medications and poor less than 85% adherence[30]. However, drug non-adherence was defined if there was history of at least one poor or fair drug adherence throughout the study period.

Data collection and quality control

Data were collected using an extraction checklist prepared in English and extracted from HMIS reports, patient medical charts, and computer databases. Four data collectors (two data clerks and two monitoring and evaluation officers), and two supervisors who were working at ART treatment initiation centers were recruited. Two days' intensive training regarding the objective of the study, and how to review the documents, as well as about confidentiality of information was given to data collectors and supervisors. Before data collection, records (both baseline and follow-up) were reviewed and identified by their medical registration.

Data management and analysis

Data were checked for completeness, edited, coded, and entered using Epi-data version 3.1 and exported to STATA version 14 software for analysis. Descriptive statistics, including frequencies, proportions, and scatter plots to show the patterns and trends, were computed to summarize the variables. For the goodness of fit of the model, R and adjusted R square were used. The presence of 1st order-autocorrelation was tested by using Durbin-Watson (DW) statistics and co-linearity as well as multi co-linearity between independent variables were assessed by a variance inflation factor (VIF) and tolerance test. A logistic segmented regression model was used to estimate trend and level changes from pre-intervention to post intervention.

We estimated the level and trend changes before and after ASM at public health facilities in Debre Markos town using a segmented regression model. The following multivariable regression model was specified to estimate the level and trend of virological suppression among clients enrolled in the ASM. $Yt=\beta o+\beta_1 time\boldsymbol{t}+\beta_2\ intervention\boldsymbol{t}+\beta_3 time\ after\ intervention\boldsymbol{t}+\ et.$ Here, Yt is the mean virological suppression per patient in month t; time is a continuous variable indicated in months at time t from the start of the observation period; intervention is an indicator for time t occurring before (intervention=0) or after (intervention=1) ASM, which was implemented at month 30 in the series; and time after the intervention is a continuous variable containing the number of months after the intervention at time t coded as 0 before ASM and (time-24) after the ASM. In this model, βo estimates the baseline levels of the outcome; mean virological suppression per patient per month, at time zero; β1 estimates the change in the trend of virological suppression per patient for each observation; β2 estimates the level change just after the intervention, and β_3 estimates the change in the trend of virological suppression per patient after the implementation of ASM, which compares the trend before ASM and after ASM. The sum of β1 and β_3 is the post-intervention slope. To estimate the level and trend change associated with the intervention, controlling the baseline level and trends. The error term (et) at time t represents random variability not explained by the model. Parameter estimates from the segmented regression model effects of ASM on virological suppression; adherence was included in the model since it was the most influential variable in this study.

Regression coefficients with a 95% confidence interval (CI) were used to determine the strength of the association between the dependent and independent variables. Variables with a p-value < 0.05 in the segmented regression model were considered as statistically significant predictors of virological suppression.

Results

Socio-demographic and clinical characteristics

A total of two hundred seventy-two adults on ART and enrolled in ASM were included in the analysis, which gives a response rate of 98.60%. More than half (56.25%) of the clients were female, and the majority (95.59%) of the participants were Orthodox Christian followers. Nearly half (47%) of the clients were never married, and the majority (93.68%) were urban dwellers. Most of the respondents (90.44%) had good adherence, and 71.58% of the clients were within the catchment areas. More than three-fourth (79.65%) of the clients completed CPT and the majority (93.75%) of the clients disclosed their HIV status and had treatment supporter **(Table 1)**.

Level and trends of virological suppressions

All were suppressed when enrolled in the ASM, while 90% remained virologically suppressed by the end of the study.   program . With the baselines, there was also an abrupt drop in changes from segment to segment in the series **(figure1).**

We took two years of virological measurements in the standard treatment (every three months) and two years of virological measurements after the implementation of ASM. Since virological measurements were done every six months, four virological measurements before the implementation of ASM and four measurements after the start of ASM were taken. From this observation, the proportion of the viral load was decreased from 97% to 85.33% (Table 2).

Table 2 Virological suppression of HIV clients on ART before and after enrolled to ASM in public health facilities of Debre Markos town

ble	Number of observations	Proportion	STD.DEV	Min	Max	95%CI
gical suppression ASM	4	97	3.829	92	100	81.6-110.3
gical suppression ASM	4	85.33	10.172	70	100	67.3-96.7

Min: -Minimum, Max: -Maximum, STD. DEV: - standard deviation

Estimating change in level and trend through segmented regression

Results from this study indicate that the change (slope) in VS was positive, estimated as a 0.6 percentage point increase per time segment (p-value for baseline trend=0.06). Right after ASM, the VS dropped abruptly by 3.2; there was a significant change in the VS after ASM (p-value for trend change =0.001). After step-wise elimination of none of the significant terms, the most parsimonious model contains trend and level changes **(Table 3).**

Virological suppression related to associated factors

The regression coefficient for VL suppression related to adherence problem β2 was -1.5, which was statistically significant (p-value<0.004). This showed that there was a decreased level of VL associated with the adherence problems of clients after enrolling in ASM. The trend of VL was decreasing, β[illegible] (-0.36) was statistically significant (p-value=0.003) which revealed there was a decrease in the trends of the VL suppression rate after the implementation of ASM. Patients enrolled in ASM who have history of poor/fair adherence , had a decrease in the level and trend of the VL suppression rate. The trend after the implementation was decreased by 1.38, which was significant (p-value=0.007, 95% CI= -2.2, -0.5); there was a gradual decline in virological suppression. We found that the trend and level change were significantly associated with adherence (p-value=0.004, 95%CI=57.69-72.98) **(Table 4)**.

Table 3 Parameter estimates, standard errors, and p-values from the full and most parsimonious segmented regression models predicting the mean virological suppression per patient per month in public health facilities of Debre Markos town over time

	Coefficient	Standard error	t-statistics	p-value	95%(CI)
The full segmented regression model					
Intercept βo	99.22	2.258	43.94	<0.001	86.7, 105.3
Baseline trend β1	0.605	0.264	2.29	0.06	-0.04 , 1.2
Level change after ASM β2	-3.2	3.821	25.12	<0.001	93.7, 104.8
Trend change after ASM β	-0.771	0.124	-6.21	0.001	-1.08, -0.5
The most parsimonious segmented regression model					
level β2	-3.238	4.439	0.73	0.04	-7.6, -4.09
Trend change after ASM β	-1.376	0.340	4.04	0.007	-2.2, -0.5

Discussion

The Interrupted time series (ITS) study is a valuable and strong quasi-experimental approach for evaluating the longitudinal effects of a population-level health intervention that has been implemented [31]. In this study, the baseline trend of viral load suppression was not significant, which showed that, there were no significant changes in trends as compared to before enrolled in ASM. But there were noticeable changes in the baseline level, which indicated that, there was a significant level change from segment to segment in the series both before and after enrolled into ASM. The study also found that, there was significant changes in virological suppression trends after enrolling in ASM HIV care, as shown by the overall segmented regression model, compared to before they enrolled in ASM care and to baseline trends. The trend after the implementation was decreased by 1.38, and there was a gradual decline in virological suppression. The study also revealed that the mean virological suppression was 97% before the implementation of ASM and was 85% after ASM, as well as the overall mean virological suppression was 90%. We found that changes in trend and level of VS were significantly associated with adherence, but no other variables were found to be significantly related to changes in trend and level of VS.

After ASM implementation, the proportion of patients with less than 1000 copies of viral load per millilitre of blood was 96%, which was higher than previous studies conducted in other parts of Ethiopia, Amhara regional referral hospitals(91.3%)[32],Tigray region(91%)[33], Addis Ababa(70.1%)[11] and Uganda(89%)[34],Botswana(70.2%)[35], South Carolina(82%)[36], and Latin America (92.20%)[37]. Our study's higher proportion of viral suppression could be attributed to differences in study participants and ART regimens. Accordingly, the majority of our study participants had good adherence, and they were from urban residences, which might have access to health care facilities that might not require walking long distances to get HIV care services; this could make them to take their medication on time, which would have an impact on the control of viral replication and the improvement of immunological status[38, 39].Previous studies have demonstrated that those clients who live far from healthcare facilities where services are offered had delayed healthcare-seeking behavior; this in turn leads to virologic-non suppression[40, 41]. The other possible explanation could be that most of our study participants were disclosed their HIV status and had treatment supporters. This could help them to take their medication effectively, since a study showed that the role of a treatment supporter goesbeyond monitoring the daily intake of drugs[42]. Poor ART adherence was associated with a lack of family support and those who did not disclose their HIV status, which resulted in poor immunological and virological treatment outcomes[43, 44].It could also be due to the recent implementation of ASM in the study area. A previous study revealed that, disparities in engagement in care had an impact on viral suppression[45].Another difference could be that clients enrolled in ASM who take their medication at six-month intervals might place their medications in inappropriate places at home, which could have an impact on drug safety due to the inconvenient location of the drug store in their home for a long time, which could reduce the effectiveness of the drugs[46].

In this study, there was a significant decrement in the level and trend of virological suppression for those individuals enrolled in ASM HIV care, and it was significantly affected by poor adherence. Adherence is identified as a potential associated factor for virological suppression in the current study, both before and after enrolling in ASM. This study finding was supported by previous studies conducted in northern Ethiopia[23, 47], United States[48],South Carolina[49],Uganda[34], Mozambique[50],France[51], China[52], and Sub-Saharan Africa[53].Poor adherence results in the loss of the opportunity to suppress viral replication and leads to virological failure[54].This is because, as the drug concentration decreases in the blood, the viral load might not be suppressed, which in turn leads to an increase in the viral load. Findings from the systematic review and meta-analysis showed that improved adherence results in an increased likelihood of achieving viral suppression[55].This suggests that an effort should be made to strengthen adherence counseling at the facility and community level[56] and careful assessment of adherence for the day preceding the visit may provide an efficient and reliable adherence measure for clients on ART[57].This study has implications for clinicians, public health experts, and patients at large. To successfully implement the new ASM; efforts should be made to improve the adherence of the clients. Global recommendations, like SMS or telephone call reminders, and client-managed community adherence and support groups, should be practiced in the study setting. That could play an active role in supporting adherence to treatment.

Limitation

There were several limitations to this study. First, this study was based on secondary data obtained from patients' medical records and registers. As a result, potentially important variables, such as a lack of laboratory results, including CD4, haemoglobin tests, and organ function tests, to determine their relationship with the level and trend changes of virological suppression, were not assessed. It was also difficult to quantify the reasons for the VL documentation problems. Second, the implementation of ASM is continuous and semi-annually, which restricts us to collect the data per month, and showing the month-to-month trend and level changes. Moreover, interrupted time series design cannot exclude confounding due to co-interventions or other events occurring around the time of the intervention. Finally, with the adoption of the new model of care in the study settings, the sample size and the number of years of data were small, and a longer follow-up period as well as a large sample size will be required to assess the long-term trends of ASM.

Conclusion

This study showed that, individuals on ART and enrolled in ASM had decreased trends and levels of virological suppression, especially those clients who had adherence problems were at the greatest risk of a decreased levels and trends in virological suppression. Overall, the findings showed that the new ASM, implemented in August 2018, could not be a successful public health intervention unless and otherwise maintained the adherence of clients on ART throughout the clinical visit. This suggests that efforts should be made to improve the adherence of clients and to maintain the trend and level of changes in a positive way. Healthcare providers, case managers, and treatment supporters provide continuous counseling on the importance of life-long adherence to treatment outcomes, including virological suppression. In addition, supportive supervision with capacity building for care providers by providing special training on adherence and ASM should be given due emphasis. Further study is also recommended to actually measure the effectiveness of ASM on the overall VL suppression at the population level using large number of health facilities.

Abbreviations

ART

Anti-Retroviral Therapy

ASM

Appointment Spacing Model

HIV

Human Immunodeficiency Virus

VS

Virological Suppression

WHO

World Health Organization.

Declarations

Ethical consideration

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki. Ethical clearance was obtained from the Ethical Review Committee of Debre Markos University College of Health Science. A permission letter was obtained from the zonal health office of Debre Markos town, and oral permission was also obtained from the respective health facility focal person to use the data for the purpose of this study. Since we used retrospective data, the need of informed consent was waived by Ethical Review Committee of Debre Markos University College of health science. Moreover, the name or any other identifying information was not recorded on the questionnaire, and all information taken from the chart was kept securely in locked cabinets.

Acknowledgement

The authors would like to thank the data collectors, supervisors, and respective health facility administrators of Debre Markos town.

Authors’ Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

No funding was obtained

Competing interests

The authors have declared that they have no competing interests.

Availability of data and materials

Data is available from the corresponding author upon request.

Consent for publication

Not applicable.

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Tables

Tables 1 and 4 are not available with this version.

Figures

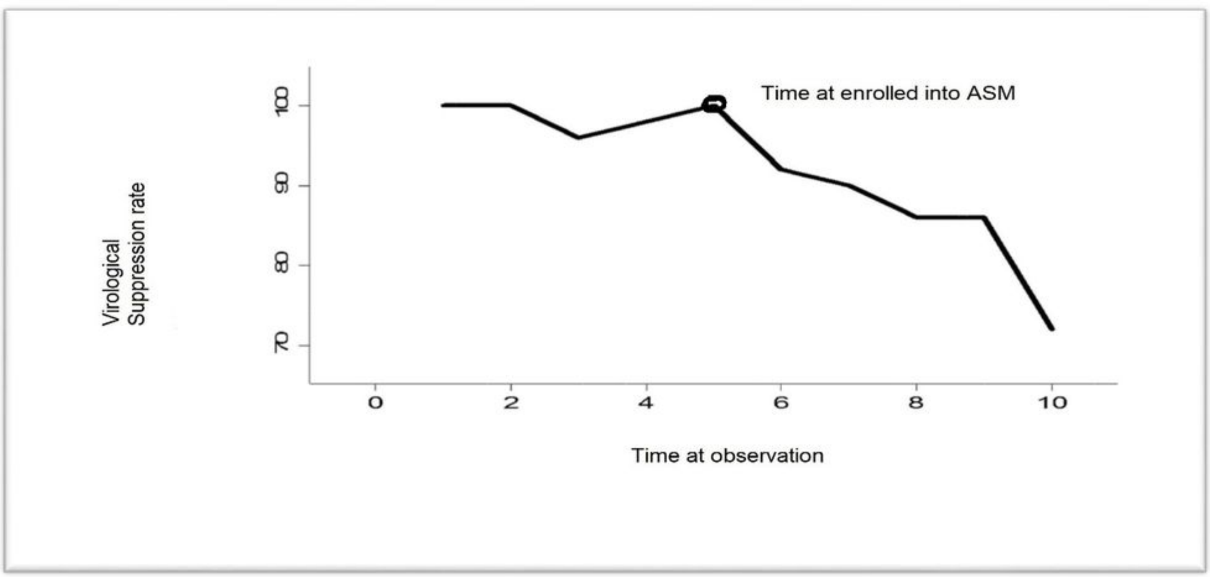

Figure 1

Trends, and levels of virological suppression among HIV patients on ART before and after enrolled into ASM at public health facilities of Debre Markos town, Northwest Ethiopia from 2016-2020.