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Viral suppression and mortality among HIV infected adults initiated Anti-Retroviral Therapy at Temeke Regional hospital: Programmatic achievements and Opportunities for improvement

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Abstract

Background
Despite the fact that HIV disease has greater impact in the Sub-Saharan Africa (SSA) region, treatment outcomes are scarcely reported at implementation level. Programmatic data present real life implementation challenges of public health importance which should inform policies. This study was conducted to describe mortality, viral suppression and document challenges at secondary facility HIV clinic in Temeke, Dar es Salaam Tanzania.

Methods
Hospital-based retrospective cohort study was conducted among HIV patients initiated on ART between May and November 2016 at Temeke Hospital, Dar es Salaam, Tanzania. Data was collected from HIV database between May and November 2017. Mortality was reported as proportion while viral suppression was defined as HIV-RNA below 50 copies per ml.

Results
A total of 747 PLHIV were eligible and were included in the study. Out of these, forty (5.4) patients died. Good adherence to Antiretroviral therapy was seen in 70% of PLHV only. Of the 419 participants with HIV viral load measurements, viral suppression was achieved in 318 (75.9%) patients. Viral suppression is more likely for patients with CD4+ T lymphocyte count greater than 200 cells/µL. There was high attrition rate from the clinic, more than one-third 35.2% of those initiated ART were still attending the clinic at one year.

Conclusion
HIV viral suppression and adherence to ART at Temeke HIV CTC are still sub-optimal. Good tracking, enhanced adherence as well as early diagnosis and treatment might improve viral suppression at one year. High attrition from the clinic may need careful examination.

Keywords: Viral suppression, HIV, SSA, treatment failure, AIDS, Tanzania

Background

HIV disease is a global epidemic with greater impact in the Sub-Saharan Africa (SSA) region (1). By 2018 there were 800,000 new HIV infections in HIV SSA (2), which is unacceptably high number given advancements in the field. At present, initiating combination Antiretroviral Therapy (cART) to all people living with HIV (PLHIV) regardless of CD4+ T Lymphocyte count is the main strategic intervention to eliminate new HIV infections, reduce morbidity and mortality in Tanzania and worldwide (3). The World Health Organization (WHO) recommends six monthly viral load measurements for HIV patients in first year of cART to monitor effectiveness of the intervention at programmatic level (4).

Reports on HIV viral suppression in SSA are scarce and whenever available have wide variations (5, 6). At programmatic level, viral suppression is reported to range between 50% to 78% in SSA within the first year of cART (5, 6). Scarcity of published reports at implementation level may impede sharing of success stories and challenges and consequently retard the gains in HIV fight.

In Tanzania few studies report program level data (7). In the year 2017, viral suppression in Tanzania was reported as low as 49% (7). On the other hand, between the year 2009 and 2017, in observational or clinical trial research settings, viral suppression was documented to range between 84 - 91% within the first year of ART use (8-10).

Several factors affect viral suppression among PLHIV on cART. Adherence to ART medication is among the biggest challenge facing HIV care and treatment programs in low and middle-income countries (LMIC's) (11, 12). It is reported that 14 – 28% of PLHIV in Tanzania are non-adherent to ART through various methods (13-15). Other contributing factors include; delayed treatment initiation, ART adverse effects, complex drug regimens as well as lack of social support including stigma (5, 11, 16).

The HIV treatment landscape is constantly changing owing to scientific evidence for improved outcomes. Phasing out of Stavudine, introduction of Tenofovir and later

intergrase strand inhibitors are all associated with better treatment outcomes (4, 5, 17). It is important therefore to document real life treatment outcomes and challenges facing PLHIV on cART at programmatic level from LMIC's, so lessons learnt can inform policies and strategic interventions towards elimination of new HIV infections.

Methods

Study design, Setting and Patients

A hospital-based retrospective cohort study was conducted between May and November 2017. We included all adults (18 years and above) PLHIV attending Temeke Regional Hospital HIV Care and Treatment clinic (CTC), Dar es Salaam – Tanzania and were on cART for one year at the time of data collection.

Study procedures

List of eligible participants was obtained from the electronic CTC2 data based. Data was extracted from both electronic CTC as well as patients' files using structured case record form (CRF). Telephone calls were made to check vital status (death, defaults) or/and whereabouts of those who missed clinics. Information documented included (demographics, anthropometric, clinical and laboratory data. A sub set of study patients were interviewed to assess, adherence and factors associated with adherence.

Laboratory test

Laboratory tests were performed at Temeke regional reference laboratory. HIV viral amplification was done through polymerase chain reaction (PCR) using COBAS®AmpliPrep/COBAS®TaqMan 48 analyzer (Roche Diagnostics, USA) with a detection limit of 20 – 10,000,000 copies/ml. This machine provides accurate quantification with automated dual target assay of HIV RNA copies and has a

specificity of 100%. CD4 + T lymphocyte (cells/µl) were measured by BD FACS Count™ Flow Cytometer from BD Biosciences (USA).

Data management and analysis

Completed and unidentified CRF were entered into created data capture tool by using Epi-info software version 7. statistical Package for Social Sciences (SPSS) version 23 was used for data analysis. The main outcome variable of interest in this study was mortality and viral load both as binary variables. Viral suppression was defined as HIV RNA measurement below 50 copies/ml as per national HIV treatment guideline (1), done at 6 and 12 months ± 2 – 3 months depending on clinic appointment.

Explanatory variables included: self-reported adherence, as a binary variable, defined as good when patient reported taking more than 95% of the prescribed doses in the previous 30 days.

Other explanatory variables were: CD4 + T lymphocyte (cells/µl), weight (kg), height (m), monthly income in TZS and WHO HIV clinical stage (I – IV).

Data analysis

Categorical variables were expressed as proportions while continuous variables were summarized as means and standard deviation (SD); or median and interquartile range – (IQR). WHO clinical stage was categorized as I (asymptomatic) vs II-IV (symptomatic - milder bacterial infections to advanced HIV disease).

Viral suppression was summarized as proportions and compared with other explanatory variables by using the chi-square test (categorical) or students' T test (continuous variables). Multivariate logistic regression analysis was used to examine factors associated with Viral suppression provided it was associated at $p \leq 0.2$ in univariate model. Since, WHO HIV clinical stage correlated with CD4+, only CD4+ T

Lymphocyte was put in the final model. Association was considered statistically significant when P value < 0.05.

Ethics statement

Study was approval by the Muhimbili University of Health and Allied Sciences Institutional Review Board in a letter referenced MU/PGS/SAEC/Vol.IX. Permission to conduct the study was obtained from Temeke Municipal council as well as Temeke Regional Referral Hospital. All patients who were interviewed signed informed written consent form.

Results

Baseline demographic, clinical and laboratory characteristics of participants

A total of seven hundred and forty-seven (747) PLHIV were recruited. Participants were young adults with a median age of 39 years; majority were females 479 (64%); almost half (n =319; 48.2%) had WHO HIV clinical stage III or IV while median baseline CD4+ T lymphocyte count (IQR) was 249 (104 – 421) cells/µl at the time of ART initiation. Almost all PLHIV (98%) at the clinic were initiated Tenofovir Disoproxil Fumarate (TDF) in combination with other nucleoside (NRTI) and non-nucleoside (NNRTI) reverse transcriptase inhibitors. **Table 1**

Among the 747 PLHIV eligible for our study, 40 (5%) are known to have died within the first year of initiating cART, the median time to death was 4.9 months. About 263 (35.2%) stopped attending the clinic at Temeke CTC for various reasons including transfer to another clinic immediately after cART initiation (104), loss to follow up 119 (figure 1). Finally, our analysis included 419 participants who had 6 or 12 months' viral load measurements. **Figure 1**

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Table 1: Baseline social demographic, clinical and laboratory characteristics of patients who started ART between May and November 2016 at Temeke Regional Referral Hospital (n =747)

Characteristics	Missing Data (%)	N (%)
Age groups (years)	0	
18 – 29		145 (19.4)
30 – 39		281 (37.6)
40 – 49		208 (27.8)
50+		113 (15.1)
Sex	0	
Male		268 (35.9)
Female		479 (64.1)
Weight (Kg)	70 (9.4)	677 (90.6)
Height (Centimeters)	331 (44.3)	416 (55.7
Baseline CD4 (cells/µl)	512 (68.5)	
≤ 350		160 (68.1)
> 350		75 (31.9)
WHO-HIV stage	85 (11.4)	
I		149 (22.5)
II		194 (29.3)
III		259 (39.1)
IV		60 (9.1)
Adherence to ART	469	
Good		144 (70.1)
Poor		34 (29.9)
Type of ART	263 (35.2)	
TDF/3TC/EFV		476 (98.3)
TDF/FTC/EFV		3 (0.6)
TDF/FTC/NVP		3 (0.6)
ATV/r/TDF/FTC		1 (0.2)
AZT/3TC/NVP		1 (0.2)

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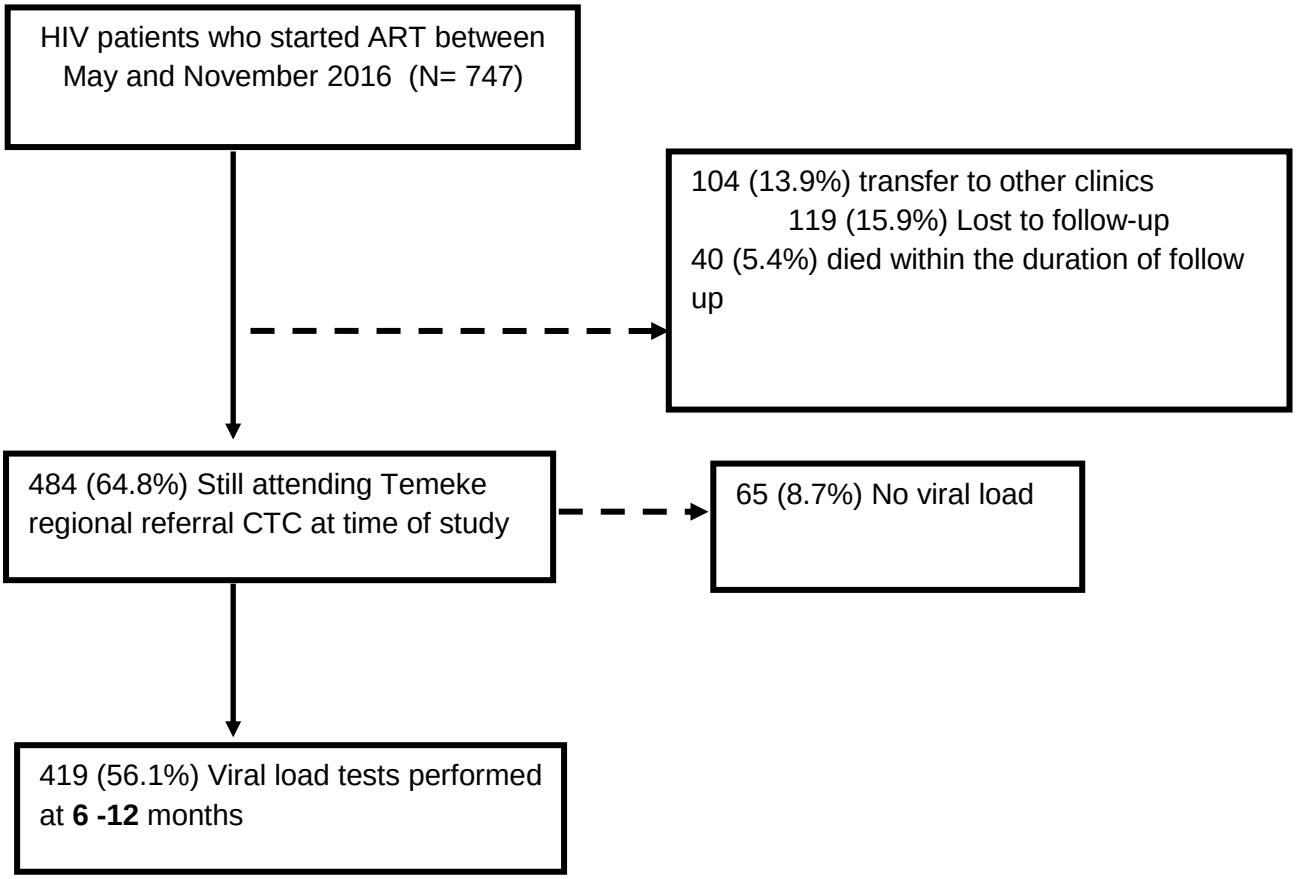

Figure 1: Consort diagram (n=747)

Participants included in the analysis did not differ significantly from those excluded from this analysis in: proportion of females (66% vs 62%; p = 0.27), Tenofovir base regimen (98% vs 97%; p = 0.26), median age (38 years vs 39 years; p =0.29), median CD4+ T lymphocyte count (280cell/µl vs 286cells/µl; p=0.96); as well as BMI (21.1 kg/m^2 vs 21.8 kg/m^2 p=0.34).

HIV viral suppression

Out of 419 patients who had HIV viral load test, 318 (75.9%, 95% CI (71.6 – 79.7%) attained viral suppression within the first year of cART. Although fewer PLHIV had viral load test at six months, viral suppression was higher (78.8%) at six months compared to twelve months (74.4%) (table 2). Furthermore, a significantly higher

proportion of females had viral suppression as compared to males (79.4% vs. 69.4%); RR = 1.7; 95%CI 1.1 – 2.7; p =0.02) Table 3. Gender disparity was more conspicuous among patients aged more than 50 years where 87.2% of females were virally suppressed as compared to only 57.1% of males. **Table 2**

Table 2: Proportion of participants with viral suppression at different time interval from commencement of ART

Duration from the commencement of ART	Number of patients with viral suppression (%)	Number of patients tested	Median viral load (IQR)
6 Months	108 (78.8)	137	20 (0 – 40)
12 Months	232 (74.4)	312	0 (0 – 52)
Both 6 and 12 Months	20 (66.7)	30	20 (0 – 57)
6 – 12 Months	318 (75.4)	419	0 (0 – 44)

Figure 2: Proportion of patients with HIV viral suppression within 12 months of using ART at Temeke Regional referral hospital by age and sex (n = 419)

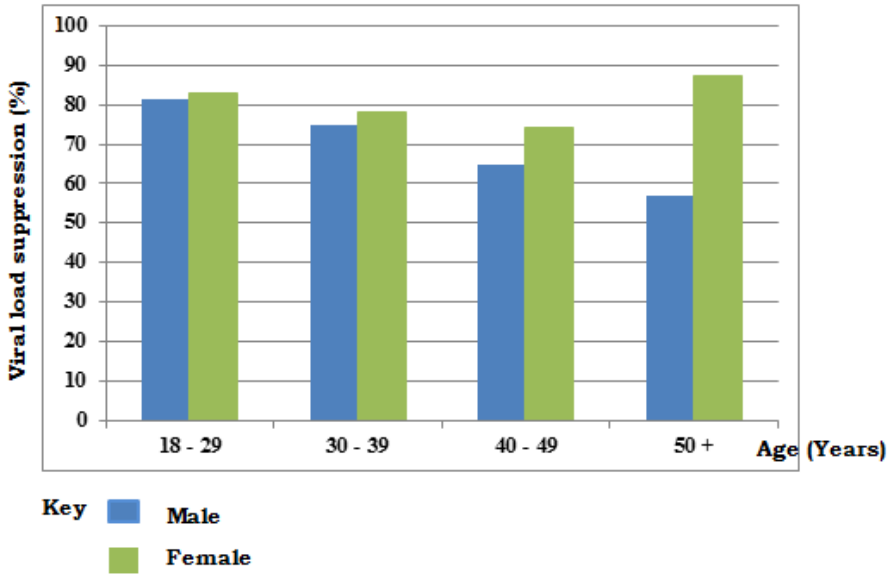

Table 3 provides univariate and multivariate factors associated with HIV viral suppression within 12 months of follow up. At univariate analysis, Female gender,

WHO class I and CD4+ T lymphocyte count greater than 200 cell/ml were associated with increased likelihood to attain vial suppression within the first year of cART. However, at multivariate analysis CD4+ > 200 cell/ µL was associated with four-fold increase chance to attain viral suppression within the first year of cART (RR: 4.1; 95% (1.0 – 16.7; P = 0.04) independent of age, sex and adherence as below. **Table 3**

Table 3: Univariate and multivariate analysis of factors associated with HIV viral suppression (N=419)

Variable	Univariate analysis		Multivariate Analysis	
	RR (95% CI)	P value	RR (95% CI)	P value
Gender		0.02		0.30
Male	Ref		Ref	
Female	1.7 (1.1 – 2.7)		0.4 (0.1 – 2.1)	
Age (years)	0.98 (0.9 – 1.0)	0.18	0.9 (0.9 – 1.0)	0.75
Adherence		0.40		
Good	1.3 (0.7 – 2.6)		2.7 (0.49 – 16.7)	0.25
Poor	Ref		Ref	
WHO HIV clinical stage		<0.01		
I	5.5 (2.1 – 14.7)			
II – IV	2.7 (1.1 – 6.6)			
BaselineCD4 (cells/µL)				
≤200	Ref	0.003	Ref	0.04
>200	3.5 (1.5 – 8.2)		4.1 (1.0 – 16.7)	
Marital status		0.33		
Single	Ref			
Married/Cohabiting	1.6 (0.9 – 2.9)			
Divorced/Widowed	1.4 (0.7 – 2.9)			
Mean BMI (Kg/m^2)	1.1 (1.0 – 1.1)	0.44		
ART type		1.0		
Single-tablet regimen	0.0 (0.0)			
Others	Ref			
Level of education		0.53		
Primary and below	1.4 (0.5 – 3.6)			
Above Primary	Ref			

Discussion

This study unveils the following ART outcomes within the first year of ART at programmatic setting in Temeke CTC: first, at least 5 out of 100 PLHIV initiating cART died. Secondly, among the surviving PLHIV, 7 in 10 attained HIV viral suppression within the first year of cART. Third, CD4+ T lymphocyte count >200 cells per µL at the initiation of cART was significantly associated with HIV viral suppression. Finally, we noted low (64.8%) patient retention at 12 months in Temeke CTC.

The mortality rate in this cohort of PLHIV attended at Temeke regional hospital is at least 5% in the first year of cART. This is certainly lower mortality than 13% recorded by Chalamilla et al. before scale up of ART in Tanzania and when ART with more side effects were used in HIV treatment (17, 18). Several changes have been made since then, more efficacious and less side effect ART regimens are currently used (4) use of simple regimens and earlier initiation of ART may have contributed to the lower mortality as documented previously (4)**.** On the other hand, 16% (119) of the participants were lost to follow up. In Kenya tracking PLHIV revealed that 21% of loss to follow up patients were dead and 29 had other reasons including silently transferred to another clinic due to access or family challenges (19). The worst case scenario, mortality would be 21% considering all loss to follow up as dead, suggesting true mortality would be between 5% - 21%.

The level of HIV viral suppression in our study (75.9 %) is low compared to previous studies conducted in the northwest, rural and urban Tanzania, which reported HIV viral suppression ranging from 84 to 91% (8-10), but certainly higher than the Tanzania national average of 49% in 2017 (7). The differences observed may be attributed to several factors; studies in clinical trials have stringent recruitment of PLHIV population with relatively well-preserved immunity (8). Secondly, our definition of viral suppression (<50 copies/ml) was more stringent compared to HIV RNA 400 – 1000 copies/mL as employed in the other studies (8-10). It has been documented

that persistent low HIV viremia (<1000 copies/mL) predicts subsequent viral failure and poor treatment outcomes, in such scenario, we found it prudent to keep stringent definition (20).

In our study CD4+ lower than 200cells/µL was associated with reduced likelihood to attain viral suppression in the first year of ART. Advanced HIV at ART initiation has been shown to affect HIV viral suppression in previously published studies (10, 21). Likewise, female gender was associated with higher likelihood to attain HIV viral suppression as compared to males across all age groups at univariate analysis. Gender disparity in HIV care and treatment outcomes is of great interest. Our findings are similar to gender differences in HIV disease progression reported in Tanzania by Mosha et al (22). This could be a result of many interventions targeting women such as prevention of mother to child transmission of HIV (PMTCT) and family planning clinics which might foster earlier diagnosis and treatment (23). Females are also known to be better at seeking health services as soon as they feel unwell (24), our data seem to agree with this finding, where 41.6% males vs 57.2% females were staged HIV WHO stage I or II at first presentation to the clinic.

Early loss to follow-up observed in our study is different from reports from sentinel treatment sites in limited resource countries where loss to follow-up is noted mainly after the initial 6 months of using cART (5). Temeke being a regional hospital, is possibly an entry point to HIV care through provider initiated HIV testing and counseling (PITC) strategy for all patients consulting facility (3). These patients upon discharge might relocate to health facilities in close proximity to their domicile (52).

This study has some strengths; it was conducted in routine clinical environment, representing actual bottlenecks in HIV care and treatment including quality of data as well as clinical care. This is among the first few studies to report HIV suppression since the adoption of more efficacious Tenofovir-based regimens and roll out of HIV viral load as a monitoring tool for HIV patients in a programmatic setting in Tanzania. Participants of this study mimic in many ways the PLHIV in Tanzania HIV clinics (7,

13, 25), therefore, these findings may shade light for possible generalization in similar settings.

Equally, our study has some limitations. The inherent retrospective design was limited to availability of data. As seen, there were missing data which may have impacted our findings. Mortality and virological suppression reported in this study was limited to patients who maintained contact with the clinic and had tests done resulting in selection bias. Attempts were made to compare excluded and included PLHIV which revealed no significant differences.

Conclusion

The mortality and viral suppression in the first year of cART in Temeke regional hospital CTC is 5% and 75%, respectively. Viral suppression is more likely for patients with CD4+ T lymphocyte count greater than 200 cells/µL. Opportunities for improved treatment outcomes at this clinic include aggressive tracking as well as enhance adherence counseling. There is high attrition rate which warrants thorough examination.

Declarations

None to make.

Acknowledgment

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Availability of data and materials

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

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Authors' contribution

TN conceptualized the research, EB and TN developed the proposal. Data collection and analysis was done by EB under the supervision of TN. Both authors contributed to the writing original the manuscript and agreed on the final manuscript.

Competing interest

Authors have no competing interest.

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