

Original Article

## Evaluation of HIV viral load turnaround time in Moshi, Tanzania

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### Abstract

**Introduction:** Viral load measurement is an important gold standard for monitoring anti-retroviral treatment among people living with human immunodeficiency virus. The optimal use of the viral load results for guiding antiretroviral therapy depends on timely availability of the results at the clinic. The objective of the current study was to evaluate the turnaround time and utilization of viral load results in the clinical decision process.

**Methodology:** This was a retrospective cohort study which involved patients receiving cART from 1 August 2018 to 31 January 2017 at three clinics in Tanzania. Data was extracted from patient files at the clinics and relevant records were kept at the viral load determining laboratory. The data were analysed with the Statistical Package for Social Sciences version 20.

**Results:** 445 subjects had a viral load in test results and 88% had a viral load of > 1,000 copies/mL. The median duration on the current regimen was five years. Median time between the clinics receiving the results and communicating them to the patients was 40 days. Shorter turnaround time was observed for patients with virological failure ( $p = 0.003$ ). A higher prevalence of virological failure was found in patients monitored at the Kilimanjaro Christian Medical Centre (KCMC) compared to the two primary health clinics ( $p = 0.04$ ).

**Conclusions:** The median viral load turnaround time was longer than stipulated by the national Tanzanian guidelines. Interventions that may reduce viral load turn-around-time, including point of care viral load testing, are needed to optimise monitoring of anti-retroviral therapy.

**Key words:** Viral load; HIV; turnaround time; Tanzania; PLHIV; ARV.

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### Introduction

Antiretroviral therapy has been proven to reduce viral transmission through suppressing viral replication, thereby reducing HIV related morbidity and mortality [1]. The current gold standard of monitoring the effectiveness of antiretroviral therapy in a patient is by measuring the concentration of HIV RNA in blood using real time polymerase chain reaction (PCR) [2]. Viral load (VL) testing is the most precise test to define the effectiveness of cART including the detection of early virological suppression. Virological suppression and hence treatment success is defined as the presence of < 1000 copies/mL. In the case of viral failure (VF) three Enhanced Adherence Counselling (EAC) sessions should be undertaken followed by a new viral load (VL) test after three months [3,4].

Early detection of VF is important to ensure that appropriate actions are taken by healthcare personnel to ensure optimal treatment outcome and prevent the

development of resistance [5]. However, the guidelines lack recommendations about the maximum interval that is allowed between receiving the result by the clinic and the time that the result is communicated to the patient [4-6].

The main aim of this study was to investigate viral load turn-around time (TAT). TAT has previously been used to define the number of days from phlebotomy to the time that the results were communicated back to the patients. In this study, TAT was further divided into TAT-1 and TAT-2. TAT-1 was the time from phlebotomy to the results being received at the clinics. While TAT-2 was the time from when the clinics received the results to the time when the results were communicated to the clients (Figure 1). We also investigated the percentage of patients with viral suppression and whether the actions recommended in the case of viral failure were undertaken.

**Methodology**

*Study design and study setting*

This was a hospital-based retrospective study conducted at three sites in the northern part of Tanzania; Kilimanjaro Christian Medical Centre (KCMC), a tertiary referral hospital, and Majengo and Pasua Health Centres. Samples from Majengo and Pasua were transported to a hub, a central mini-laboratory, where the samples were centrifuged and stored in a -20 °C freezer until shipment to the laboratory at KCMC.

*Viral load monitoring*

The doctors used a standardized form to request the VL tests at the clinical level [8]. The samples were collected by laboratory personnel and sent either directly to the laboratory or the hub for plasma separation and storage while awaiting transportation to the testing laboratory (Figure 1). The CobasAmpliPrep/CobasTaqMan 48 from Roche Mannheim, German was used for VL analysis at KCMC.

*Turnaround time (TAT)*

Three intervals were calculated: The total TAT, i.e., the total interval from phlebotomy until the people living with HIV (PLHIV) received their VL results, TAT-1, i.e., the interval from phlebotomy until the

clinics received the results, and TAT- 2, i.e., the interval from when the clinics received results until the time when the results were communicated to the clients (Figure 1).

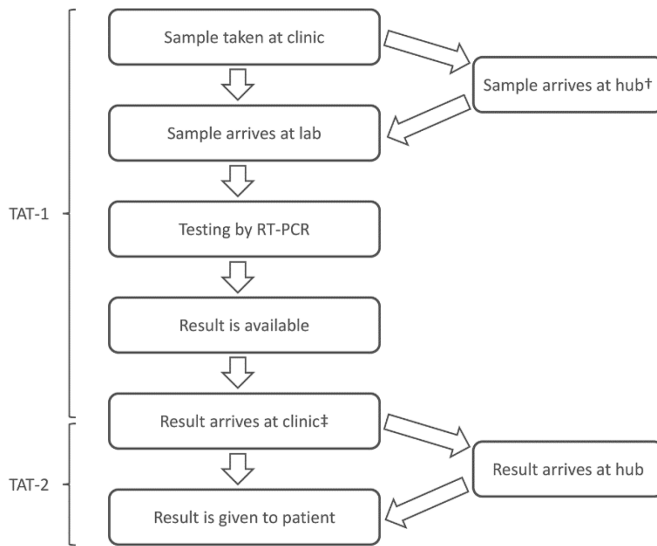
*Sample size and sampling*

The study included all HIV infected adults and adolescents (> 15 yrs) at the three clinics, who had received combined antiretroviral therapy cART for a minimum of six months and had a VL test done from 1 August 2016 to 31 January.2017.

*Data collection*

Data on the VL tests that were done during the specified period were obtained from the phlebotomy registers. The following data were extracted from the patient records: date of sample collection, date when the VL results were received at the clinic, date of communicating the results to the patient, whether EAC sessions were carried out and any supplementary VL tests. We extracted the dates of sample arrival, analysis, authorization of results and dates when the viral load results were dispatched to the clinics from the zonal laboratory database at KCMC. Demographic information, treatment regimen, duration on regimen, CD4 (if available) and the number of previous VL measurements were obtained from the Care and Treatment Clinic 2 Card (CTC-2).

**Figure 1.** VL Samples testing pathway used in calculating TAT.



TAT-1: Time from sample collection to receipt of results at the clinic, TAT-2: time from the receipt of the results at the clinic until the results were communicated to the patients. †Samples from Majengo and Pasua are sent to/from laboratory at KCMC via the hub. Also, the results to these sites are dispatched via the hub. ‡The viral load results for the samples from KCMC are sent (in paper format) directly from the laboratory to the clinic.

*Statistical analysis*

The data was analyzed using the Statistical Package for Social Sciences (SPSS) version 20. The mean, standard deviation (SD) or median and interquartile ranges (IQR) were calculated for the descriptive analysis of patients’ characteristics. Mean and SD were used to summarize the continuous data with a normal distribution (age) while non-normally distributed data were summarized using median and range (i.e., duration on cART and TAT). Frequencies and percentages were used to summarize categorical variables. The median TAT-1 and TAT-2 were compared between clinics.

*Ethical clearance*

The study protocol was ethically approved by the Kilimanjaro Christian Medical College Research Ethics and Review Committee (CRERC) (No. 2221), in Moshi, Tanzania and by the National Health Research Ethics Review Committee (NatREC) at the National Institute for Medical Research (NIMR) in Dar-es-Salaam, Tanzania (NIMR/HQ/R.8a/Vol.IX/2757). A permit to access the laboratory forms and medical files were obtained from the Executive Director of KCMC

and the Medical Officer of Health, Moshi Municipal Council. In addition to these procedures, the management of each facility was requested to access patients' records. All information which could be used to trace back to the patients were removed and replaced by unique identifiers.

## Results

445 patients had a viral load sample taken during the six-month period between 1 August 2016 and 31 January 2017. The majority of patients were monitored at KCMC (n = 346, 78%), while 70 (16%) and 29 (6 %) were monitored at Majengo and Pasua Health Centres, respectively. The mean age was 43 years and the median duration on the current cART regimen was five years.

### Turnaround times.

The median combined TAT (TAT-1 and 2) for all clinics was 56 (IQR: 56-68) days. The median total TAT for the patients with VF was 19 days (IQR: 7-46) days.

The median combined TAT-1 from phlebotomy to the receipt of results was 19 days (IQR: 11-28). The median TAT-1s at the three clinics were: KCMC 19 days (IQR: 9-28), Majengo Health Centre 23 days (IQR: 14-36) and Pasua Health Centre 20 days (IQR: 16-31). There was no significant difference in TAT-1

between the three clinics. Among the samples for which the duration of all steps could be traced, 36 /320 (11.3%) samples were tested within the three days recommended by the guidelines. The median combined TAT-2 from the date the clinics recorded the results to the date the clinic communicated the results to the patients for the three clinics was 40 days (IQR: 25-50) days. The median TAT-2 was 40 (IQR: 25-50), 36 (IQR: 22-55) and 41 (IQR: 36-48) days for KCMC, Majengo and Pasua Health centres, respectively. Virologically failing patients had significantly shorter median TAT-2 than those without failure: 29 (IQR 10-43) and 40 days (IQR) respectively ( $p = 0.003$ ).

### Proportion of VL results with viral suppression of <1,000 copies /mL

Viral suppression was found in 88% of the samples. The rates of VL suppression were not associated with treatment regimens or sex, but were significantly associated with site (Table1).

### Clinical decision making

Among the 55 patients who had virologic failure, only 34 (62%) received the stipulated EAC sessions and only 9/55 (16%) were switched to another regimen. Furthermore, only 21/34 (62%) of the patients, who received EAC sessions had a VL repeat test as per the national guidelines.

**Table 1.** Demographic characteristics by virological outcomes.

Characteristics	Viral load suppression, N = 390		Viral failure, N = 55		p*
	N (%)		N (%)		
<b>Clinic site</b>					
KCMC	296	(85.5)	50	(14.5)	0.04
Majengo	66	(94.3)	4	(5.7)	
Pasua	28	(96.6)	1	(3.4)	
<b>Age (years)</b>					
Mean ( $\pm$ SD)	43	(13)	43	(13)	
<b>Gender</b>					
Female	289	(88.9)	36	(11.1)	0.18
Male	101	(84.2)	19	(15.8)	
<b>CD4 cell counts cells/mm<sup>3</sup></b>					
CD4 $\geq$ 350cells/mm <sup>3</sup>	132	(88.6)	17	(11.4)	0.78
CD4 < 350cells/mm <sup>3</sup>	234	(87.6)	33	(12.4)	
<b>Treatment regimen</b>					
First line regimen (NNRTI- based)	344	(88.7)	(11.3)		0.09
Second line regimen	46	(80.7)	11	(19.3)	
<b>Duration on ART (years)</b>					
Median (IQR)	5	(4-7)	5	(4-7)	
<b>Marital status</b>					
Married	166	(90.2)	18	(9.8)	0.21
Cohabiting	9	(69.2)	4	(30.8)	
Single	53	(85.5)	9	(14.5)	
Divorced/Widowed	39	(92.9)	3	(7.1)	
Unknown	123	(85)	21	(15)	

Viral failure: HIV-1 RNA more than 1000 copies/mL; p\*: Pearson Chi Square; KCMC: Kilimanjaro Christian Medical Centre; NNRT: non-nucleoside reverse transcriptase inhibitors; SD: Standard deviation; IQR: Interquartile range; ART: Antiretroviral therapy.

## Discussion

The median TAT-1 was 19 days, longer than the ≤ 14 days stipulated by the guidelines [13-15]. The TAT-1 was shorter than the mean TAT-1 of 30 and 34 days in 2015 and 2016 previously reported from Tanzania and longer than the median TAT of 6 days (IQR: 3-7) reported from Cameroon [7]. Among the samples for which the duration of all steps could be traced, 36/320 samples were tested within the three days recommended by the guidelines and the duration was longer for the rest.

The TAT-1s from the three clinics were not significantly different even though samples from Pasua and Majengo HC had to be taken to a hub first where they were processed and later transported to KCMC, while this was not the case for the samples collected at clinics at KCMC. The results support centralisation of viral load measurements. However, longer than recommended median TAT-1 calls for optimization to comply with the national guidelines. Some initiatives to minimise the TAT have already been implemented (from October 2017). These initiatives include electronic dispatch of results to the hub. During the study period, samples from Majengo and Pasua health centres were transported to a hub, once per week; this has been increased to twice weekly (personal communication Laboratory Technologist James Kimaro, KCMC).

The care and treatment guidelines for HIV and AIDS from 2015 to 2017 included VL testing as the standard of care for monitoring and recommended expansion of testing platforms [4]. In 2015 Tanzania tested < 25% PLHIV on cART after six months and could not test all persons at least once per year [8]. Like many other countries adopting the viral load monitoring recommendations, Tanzania has been facing challenges such as lack of personnel to run the machines, poor sample transportation and longer turnaround times than what has been deemed acceptable [8-9]. Reported reasons for long TAT's include: inefficient systems for specimen transport, reagent stock depletion, personnel shortages and equipment breakdown [10].

The median TAT-2 was 40 days for all study patients and 29 days for patients with virological failure, i.e., the patients with virological failure had significantly shorter TAT-2 than those without ( $p < 0.003$ ). This indicates that the clinic staff made an extra effort to contact patients with VL > 1,000 copies/mL. VL is expected to guide clinical management; whenever the VL is > 1,000 copies/mL, interventions must be initiated immediately upon availability of result. The current guidelines do not include advice on

how to proceed in the case of virologic failure concerning notifying patients prior to their next planned visit.

Initiatives to shorten TAT, i.e., by introducing viral load point of care (VL-POC) assays, as recommended in the guidelines, are needed. A key achievement of the VL-POC assay is the reduction in TAT as same-day results communication helps to link patients to EAC and plan for intensified follow-ups aiming at reducing time on a failing cART regimen [11].

Even though the overall rate of suppression was high (88%), there were significant differences between the three sites with suppression rate being lower at KCMC compared to the rates at the two health clinics. This may be due to patients having suspected or confirmed signs of failure and in need of second-line treatment being referred to centres with higher expertise i.e. KCMC, leading to a higher proportion of patients, with virological failure at KCMC. The overall viral suppression rate was close to reaching the third 90 of the 90-90-90 UNAIDS targets. The rate is comparable to the suppression rate reported from Malawi 266 (86%) but lower than the suppression rate found in a study from Cameroon (95%) [12-13]

Previous studies from Sub-Saharan African settings have consistently shown low and delayed switching from first- to second-line cART, which has been linked to poorer treatment outcomes, increased mortality and risk of development and transmission of resistance [14-15]. In the current study, the rates of both EACs and switching among the patients with viral failure was low at 62% and 16%, respectively, similar to the rates previously reported from the Sub-Saharan region [16-17]. The current practice, according to the nurses at the clinics, is to contact the patient with virological failure by phone as soon as possible for scheduled follow-up to be conducted at an earlier date (personal communication Zawadiel Hillu, KCMC). Even so, the rates of both initiation of EAC and subsequent VL re-testing were low (both at 62%). This study adds to the knowledge demonstrating the uptake and utilization of viral load test results for HIV patient management.

## Conclusions

The median viral load turnaround time, from phlebotomy to when the clinics received the viral load results, at both a referral hospital with direct access to a laboratory performing viral load testing and two sites without, was longer than the 14 days stipulated by the national guidelines. Furthermore, for all three the clinics, the median time from when the clinics received the results to when the patients received the results

varied extensively. Shortening this period is essential especially for patients who have VF. There is a need for more specific guidelines concerning communicating VF to the patients and initiating appropriate actions. Thus, it is recommended that the guidelines should include advice on both TAT-1 and TAT-2. Additionally, a better understanding of the deterrents of conducting enhanced adherence counselling and/or treatment switch in case of VF is needed. Introducing the use of VL-POC testing might substantially reduce the TAT leading to faster initiation of enhanced adherence counselling.

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### Authors' Contributions

ELM, EPM, IK, RM, ZT and TLK conceived and designed the study. ELM and JK retrieved data from the patients' records and the laboratory records. ELM and EPM analyzed the data. ELM and EPM drafted the manuscript with contributions from ZT and TLK. All the authors read and approved the final version of the manuscript.

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