HIV and Schistosoma spp. interactions: epidemiology and consequences for detection and prevention in the lake region of Tanzania

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CHAPTER 2 - CASCADE OF CARE FOR HIV-SEROCONVERTERS IN RURAL TANZANIA: A LONGITUDINAL STUDY.

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Adapted from AIDS Care. 2019 Jul 10:1-6. doi: 10.1080/09540121.2019.1640842

ABSTRACT

We examined the HIV care cascade in a community-based cohort study in Kisesa, Magu, Tanzania. We analyzed the proportion achieving each stage of the cascade - Seroconversion, Awareness of HIV status, Enrollment in Care and Antiretroviral therapy (ART) initiation- and estimated the median and interquartile range for the time for progression to the next stage. Modified Poisson regression was used to estimate prevalence risk ratios for enrollment in care and initiation of ART.

From 2006 to 2017, 175 HIV-seroconverters were identified. 140(80%) knew their HIV status, of whom 97(69.3%) were enrolled in HIV care, and 87(49.7%) had initiated ART. Time from seroconversion to awareness of HIV status was 731.3[475.5-1345.8] days. Time from awareness to enrollment was 7[0-64] days, and from enrollment to ART initiation was 19[3-248] days. There were no demographic differences in enrollment in care or ART initiation. Interventions that increase enrollment are likely to have the most impact in achieving the Joint United Nations Programme on HIV and AIDS targets.

Keywords: HIV Care Continuum, Linkage to care, Testing, ARV, Tanzania

INTRODUCTION

Widespread availability of antiretroviral therapy (ART) has led to tremendous declines in HIV/AIDS related mortality, especially in Africa. By 2015, 10.3 million people (54% of those with HIV infection) were accessing ART in sub-Saharan Africa[1], with a reported 50% decrease in crude death rates among people living with HIV (PLHIV) following the introduction of ART in eastern and southern Africa[2]. In North-west Tanzania, mortality in HIV-infected people declined by a third between the mid 1990s and 2004[3].

Despite these important declines, mortality among HIV-infected adults remains unacceptably high, with a crude death rate among HIV-infected adults three times higher than non-infected adults in 2009–11 in eastern and southern Africa[2]. Most of deaths in HIV-infected individuals are still due to tuberculosis and HIV/AIDS, suggesting sub-optimal use of HIV services[2]. In Northwest Tanzania, although overall incidence and prevalence had reduced slightly, both are consistently higher in the age group 35-44 years, likely due to poor linkage to care allowing on-going transmission (unpublished results).

This indicates substantial room for improvement in current services in order to promote the benefits of earlier HIV testing and to encourage access to care for those diagnosed positive. Even among HIV-infected individuals who know their status, a large proportion do not enroll into care and treatment[1-3].

The target for ART programs worldwide has been defined by the Joint United Nations Programme on HIV and AIDS (UNAIDS) using the slogan 90-90-90 targets[4]. This aims to achieve 90% of PLHIV diagnosed (knowing their status), 90% of those diagnosed initiated on ART, and 90% of individuals on ART being virologically suppressed. Reaching the UNAIDS targets requires early diagnosis and effective linkage to and retention in care[5, 6]. Not only is it important to be aware of the presence and nature of obstacles to care, but identification of key factors associated with linkage to care are also needed to improve benefits of ART through the continuum of care[7].

We used data from a community-based cohort in Tanzania to assess the spectrum of engagement in care of PLHIV in Northwest Tanzania and estimate the achievement of the 90-90-90 targets in this population.

METHODS

Study population

The data for this paper is derived from a community-based cohort study in Kisesa, Tanzania, covering an area of about 115 km2 with 35000 inhabitants residing in the study area[3,8,9]. Approximately every 3 years all residents aged 15 years or more are invited to a sero-survey to determine the health needs in the population, with the first in 1994, and the 8th sero-survey finished in February 2016. All sero-survey participants were offered Voluntary Counseling and Testing (VCT), and if found to be HIV-infected were referred to the main clinic in Kisesa for treatment. Dried blood spot samples (DBS) from all consenting participants, whether or not they had VCT, were tested for HIV-1 at the National Institute for Medical Research (NIMR) reference laboratory in Mwanza. We identified seroconverters from HIV testing of DBS between September 2006 (sero-survey 5) and February 2016 (sero-survey 8). Seroconverters were defined as those with at least one HIV negative test, and a subsequent HIV positive test, with the date of seroconversion defined as the mid-point between dates of the last negative test and the first positive test.

Three stages of the HIV care cascade were included in our framework:

1) Awareness of HIV status: defined as the awareness of positive HIV status either through VCT at the sero-survey, or through self-reported HIV Counseling and Testing (HCT) attendance or other proof of HCT (available in public health facilities unrelated to the sero-surveys). The date of awareness of HIV status was defined as the date the person first knew of his or her own HIV status.

2) Enrollment in HIV care: defined as completing and/or self-reporting at least 1 visit to a Care and Treatment Clinic (CTC). Those diagnosed with HIV through a positive HIV test at any of the HCT clinics, or through VCT in the sero-surveys, are referred to a CTC. The date of CTC enrolment was defined as the date of the first reported attendance at CTC.

3) ART initiation: defined as having a clinically confirmed ART initiation report and/or self-reported use of ART. Until 2010, the criteria for ART initiation were a CD4 count ≤200 cells/mm3 or a WHO clinical stage of 4 for all adults. The criteria changed to ≤350 cells/mm3 from 2010-2012, ≤500 from 2013-2015, and all HIV-infected in 2016[10-13]. The date of ART initiation was defined as the first reported date that ART was given to participants.

Follow-up

The follow-up period spanned from date of seroconversion to March 15th 2017, the date at which everyone who had not progressed to the next stage was censored. We searched for each seroconverter manually and via a record linkage computer algorithm using name, sex, date of birth, and place of residence in all the health clinics providing HIV care within a 10

km radius around the sero-survey catchment area. We additionally visited the two oldest and largest HIV clinics in the region (in Mwanza City, 20 km from the DSS) to search for seroconverters.

Statistical analysis

The proportion of HIV-positive persons achieving each stage in the cascade was calculated. Statistical inference for differences between levels of explanatory variables was based on a $\chi 2$ test for categorical variables. We also used modified Poisson regression to estimate prevalence risk ratios (PRRs) and 95% confidence intervals (95%CIs) for enrollment in care and initiation of ART. All plausible variables were individually included into the model and model goodness-of-fit assessed. Data were entered into Microsoft Excel and all analyses were performed in STATA 14.1 (College Station, TX, USA).

Ethical considerations

Ethical approval for retrospective analysis of these data was obtained from Bugando Medical Centre in Mwanza (BREC/001/04/2011), the National Institute for Medical Research in Dar es Salaam (NIMR/HQ/R.8a/Vol.IX/1489), and Weill Cornell Medicine in New York (1108011883). Study participants provided consent at the time of enrollment into the cohort study in accordance with the approved procedures of the TAZAMA project[8, 9].

RESULTS

From September 2006 to February 2017, a total of 207 HIV-seroconverters were identified in the cohort. Among those, 175 HIV-seroconverters were available for follow-up. A total of 20 health facilities (HCTs and CTCs) contributed to the analysis. All facilities are government-run. All provide HIV testing and 10/20 (50%) provide CTC services, including monthly disease monitoring, provision of ART and TB screenings.

The demographics of the HIV-seroconverters are presented by stage of the cascade in **Table 1**. There was no difference in the proportions of HIV-seroconverters by area of residence.

As of March 2017, end of follow-up, 140/175 (80.0%) knew their HIV status, 97/175 (55.4%) were enrolled in HIV care, and 87/140 (62.1%) had initiated ART. The cascade of care is presented in **Figure 1**.

Table 1 - Proportion of the 175 HIV-seroconverters engaged in each of the HIV care cascade stages by selected characteristics.

Characteristic	HIV seroconverters	Aware of HIV status		Enrolled in care		Initiated ART	
	n (%)	n (%)	p-value[a]	n (%)	p- value[a]	n (%)	p-value[a]
Total	175	140 (80.0%)	-	97 (55.4%)	-	87(49.7%)	-
Sex							
Female	118 (67.4%)	93 (78.8%)	0.57	69 (58.5%)	0.24	63 (53.4%)	0.16
Male	57 (32.6%)	47 (82.5%)		28 (49.1%)		24 (42.1%)	
Occupation							
Farmer	142 (81.1%)	111 (78.2%)	0.42	74 (52.1%)	0.17	69/142 (48.6%)	0.77
Businessman	12 (6.9%)	11 (91.7%)		9 (75.0%)		6/12 (50.0%)	
Mix of farming and business	21 (12.0%)	18 (85.7%)		14 (66.7%)		12/21 (57.1%)	
		Median (IQR)	**p-value[a]**	**Median (IQR)**	**p-value[a]**	**Median (IQR)**	**p-value[a]**
Age							
Aware/enrolled/initiated	36 (27-46)	36.5 (28-46)	0.46	35(27-43)	0.15	36.5 (27.5-48)	0.42
Not aware/enrolled/initiated		34 (26-43)		37(28-52)		36 (27-45)	
Years of education							
Aware/enrolled/initiated	7(2-7)	7(2-7)	0.75	7(0-7)	0.16	7 (3.5-7)	0.062
Not aware/enrolled/initiated		7(0-7)		7(3-7)		7 (0-7)	

[a]*Use of Chi-square test for categorical variables and rank-sum test for continuous variables.*

Figure 1 - Cascade of care in the study population, Tanzania. The first two 90-90-90 targets are in bold.

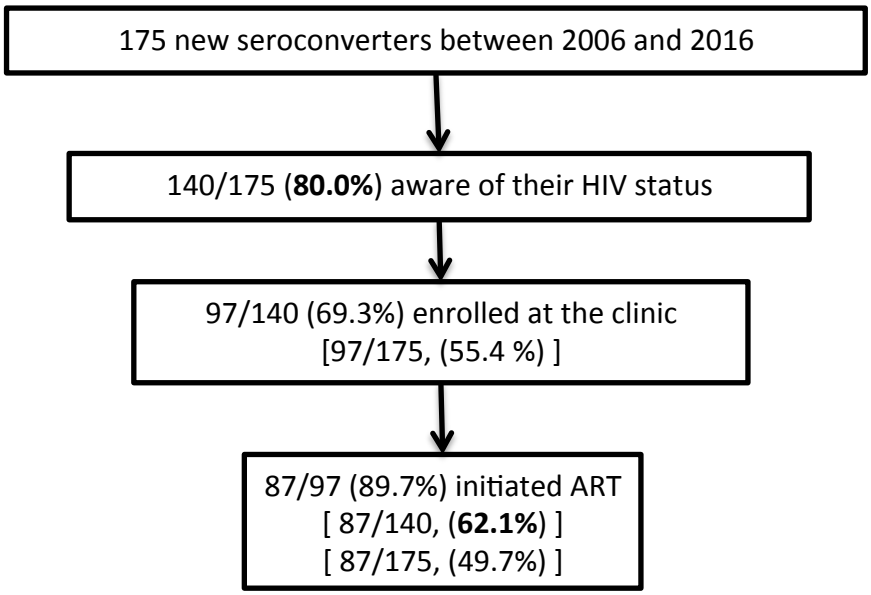

Figure 1 depicts the cascade of care in our study population. 80% of HIV-infected people knew their HIV status and 62% of these were on ART.

The majority of the seroconverters learned about their positive status for the first time at the sero-survey (67/140, 47.8%), or at a HCT clinic (47/140, 33.6%). 20/140 (14.3%) of the seroconverters discovered their status via provider-initiated testing and 6/140 (4.3%) at Ante-Natal Care (ANC).

Out of the 97 individuals who had reached a CTC, 19 of them migrated or had transferred. 12/97 (12.4%) transferred from one clinic to another within the 20 clinics searched, mostly after 2008 when new CTCs opened. 1 out of 97 deliberately opted out of CTC, 4 out the 97 were reported as transferred out of the clinic and moved outside the catchment area and 2 temporarily transferred care to a larger CTC clinic during their pregnancies.

The median time from seroconversion to being aware of one's HIV status was 731.3[475.5-1345.8] days while time from awareness of HIV status to enrollment was 7[0-64] days. The overall median time from enrollment to ART initiation was 19[3-248] days. The key time variables are presented in **Table 2**.

Table 2 - Key time variables (in days) for the 175 seroconverters.

Variable	Median	IQR	Min	Max	N
Time from seroconversion to awareness	731.3	475.5 - 1345.8	135.5	2889	140
Time from seroconversion to enrollment	965.5	511.5 - 1652.5	135.5	2889	93[a]
Time from seroconversion to ART initiation	1247.5	803.5 - 1867.5	206.5	3324.5	83[a]
Time from awareness to enrollment	7.0	0 - 64	0	2170	93[a]
Time from awareness to ART initiation	146.0	19 - 535	0	2989	83[a]
Time from enrollment to ART initiation	19.0	3 - 248	0	2988	83[a]
Time being followed-up at the clinic (up to March 15th 2017)	803.0	378 - 1646	64	3009	93[a]

IQR= Interquartile range; Min=minimum; Max=maximum

[a] *4 people self-reported attending a clinic and initiation ART but did not provide us with exact dates.*

Time to ART initiation decreased sharply with the successive implementation of new guidelines. Time from awareness of HIV status to enrollment transiently increased with the creation of new clinics where old seroconverters who had not previously been enrolled in care could now enroll in care more easily. Throughout the study period, the time from awareness of HIV status to enrollment was longer for those receiving their results at sero-surveys than for those receiving their results at a clinic ($p<0.001$). These results are presented in **Figure 2**.

Figure 2 - Variations in reaching each stage of the cascade by year of enrollment.
A) Timeline of the different guidelines and sero-surveys
B) Boxplot of time from seroconversion to awareness of HIV status by year of enrollment
C) Boxplot of time from awareness of HIV status to enrollment in a CTC by year of enrollment
D) Boxplot of time from enrollment in a CTC to initiation of ART by year of enrollment

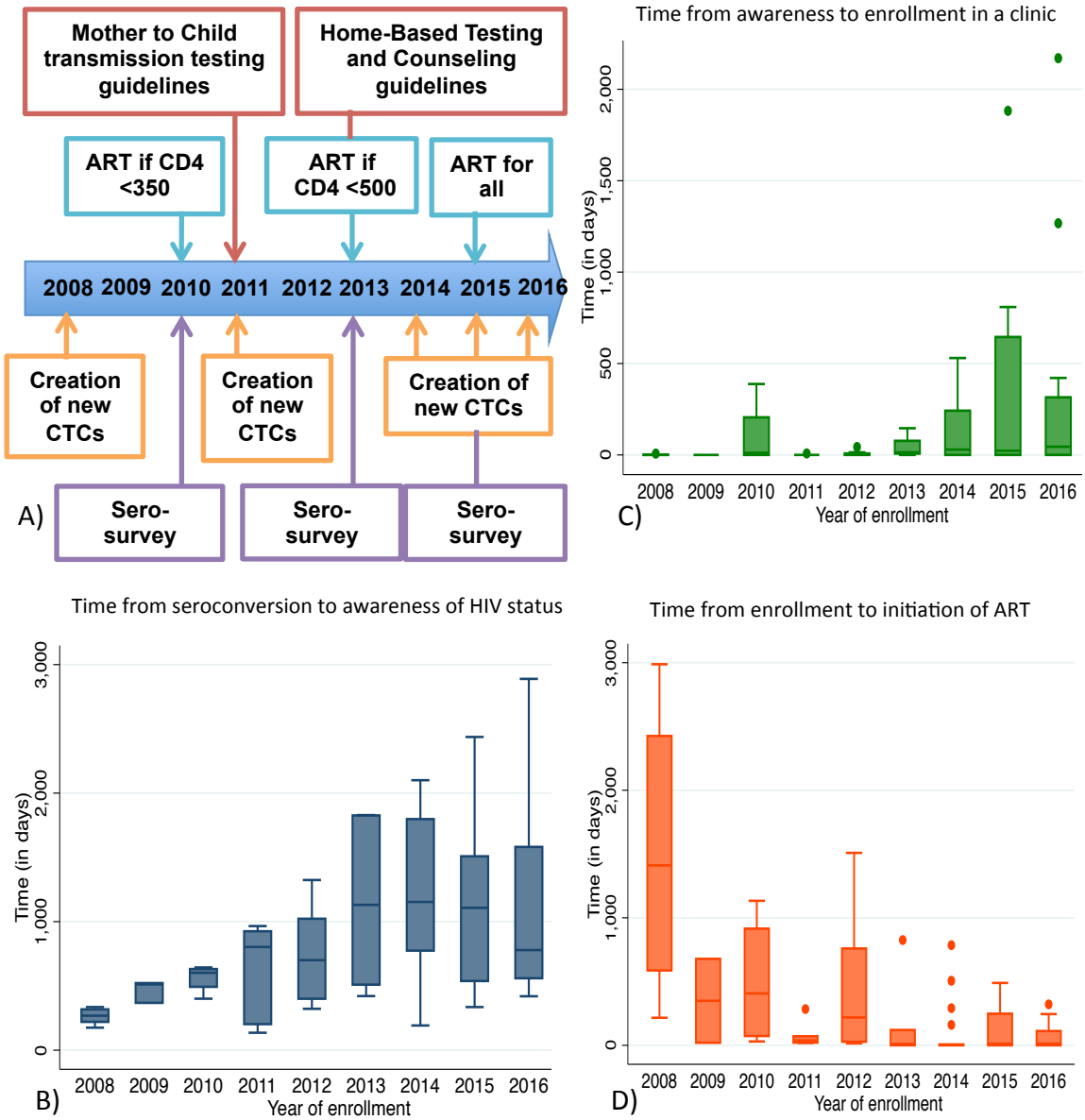

Figure 2 shows the variation in key time variables over the years, following major HIV/AIDS testing and care interventions. Time to ART initiation decreased dramatically with the successive implementation of new guidelines while time from diagnosis to enrollment transiently increased with the creation of new clinics. The first sero-survey was conducted in 2006-2007 and is not represented on this figure.

There was no difference by sex in enrollment in care (adjPRR=0.85, 95%CI 0.61-1.17), and no other significant differences. There was also no difference by sex in ART initiation (adjPRR=0.75, 95%CI 0.51-1.08), and no other significant differences.

DISCUSSION

This is the first report, to our knowledge, on Tanzania's achievements regarding the 90-90-90 targets. This longitudinal study in Tanzania occurred at a unique time during which new HIV clinics were opening and ART eligibility was increasing. Our Tanzanian study population demonstrates some moderate successes, with 80% of HIV-infected people knowing their HIV status and 62% of these on ART. Routine viral load monitoring was not yet fully implemented at the time of our study and future studies will evaluate the 3rd target of the UNAIDS 90-90-90 goal.

The success in our rural study population is that the percentage of HIV-positive individuals knowing their status is high. This effect was largely driven by the recent strategy change of the final sero-survey in 2016, which provided opt-out HIV testing for all participants rather than requiring the person providing blood to take initiative to obtain their results. This highlights the need for more regular access to opt-out testing and a greater encouragement for uptake of HIV testing[1]. Due to the logistical challenges and the expense of large-scale sero-surveys, provider-initiated testing might be more able to fit those criteria[14].

Very few women in our study population received their HIV results through antenatal testing. No other demographic factor predicted enrollment into care or initiation of ART, which strongly suggests that failure in linkage to care is inherent to the system, and not due to patient factors[1,15]. There is also a possibility that our team was not able to find everyone in the clinics, either because they moved out of the region, or because they changed names at the clinic to avoid stigma.

Still too few people are initiating ART. The low percentage of diagnosed individuals beginning care and treatment can be explained partially by the fact that not many easily accessible CTCs were opened until 2014. Thus the increasing time from seroconversion to enrollment in care over the years is indeed the result of more old seroconverters enrolling in CTCs as they open. This suggests that as access to care is expanded, linkage to care in our population will continue to increase. Importantly, more CTCs continue to open in the region and the country and home-based testing is also currently being investigated in Tanzania[16]. Both of these will likely serve as powerful resources to strengthen linkage of HIV-infected individuals to testing and care.

ACKNOWLEDGMENTS
The authors thank the participants of the Kisesa cohort study and the study and HTC staff, without whom this analysis would not have been possible.

FUNDING
The Kisesa cohort study is funded by the Global Fund to Fight AIDS, Tuberculosis and Malaria. Kisesa CTC receives support from IeDEA (East Africa International Epidemiological Database to Evaluate AIDS) Grant (NIH) No. 5U01A1069911-12(CFDA No. 93.855). Data management activities have been supported by a grant from the Wellcome Trust.

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