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Long-term virologic response in a cohort of HIV-infected patients in South Africa

Health Economics and Epidemiology Research Office
Helen Joseph Hospital
Perth Road, Westdene, Johannesburg
kshearer@heroza.org
www.heroza.org

Kate Shearer[1], Alana T Brennan[1,2], Mhairi Maskew[1], Rebecca Berhanu[3], Lawrence Long[1], Matthew P. Fox[1,2,4]

[1]Health Economics and Epidemiology Research Office, Department of Internal Medicine, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa; [2]Center for Global Health & Development, Boston University, Boston, MA, USA; [3]Right to Care, Johannesburg, South Africa; [4]Department of Epidemiology, School of Public Health, Boston University, Boston, MA, USA

ABSTRACT

Background: While much is known about virologic response to antiretroviral therapy (ART) in resource-rich settings, much less is known about long-term rates of virologic suppression in resource-limited settings. We aimed to describe virologic response on ART over 8 years among a cohort of patients initiating ART the first year of public sector roll out in South Africa.

Methods: We included all ART-naïve patients, ≥18 years, who initiated first-line ART from April 2004-March 2005 at 4 public sector HIV treatment clinics in Gauteng and Mpumalanga Provinces. Patients were followed from ART initiation until death, transfer, loss to follow-up (LTF) or dataset closure (May 2013). LTF was defined as being ≥3 months late for a scheduled visit with no subsequent visit. Virologic suppression was defined as a viral load (VL) <400 copies/ml while a failing VL was defined as >1000 copies/ml. A transient elevated viral load (TEV) was defined as a suppressed VL followed by a failing VL followed by a suppressed VL.

Results: 2220 patients were included. 67.4% were female with a median (IQR) age of 35.8 (30.9-42.3) years and a median (IQR) baseline CD4 count of 78 (32-138.5) cells/mm^3. Patients were followed for a median (IQR) of 6.2 (2.1-8.3) years. At the end of follow-up, 18.4% of patients had died, 23.3% of patients were LTF, and 30.4% of patients had transferred.

1858 (83.7%) patients had ≥1 VL recorded with a median (IQR) of 11 (5-13) VLs over the duration of follow-up. Of those, 95.5% (n=1774) achieved virologic suppression and 84.1% (n=1491) of those patients suppressed on their first VL. Among those 1491 patients, 52.6% remained suppressed at every subsequent VL (median: 10; 1QR: 5.5-12). For the 599 patients who did not remain suppressed, patients experienced a median (IQR) of 2 (1-4) detectable VLs and the first detectable VL occurred in a median (IQR) of 2.8 (1.1-6.1) years after the first suppressed VL (Figures).

279 (17.5%) patients experienced ≥1 TEV and were less likely to die (4.3%) or become LTF (15.4%) compared to patients who never experienced a TEV (death: 10.2%; LTF: 19.8%), potentially due to increased monitoring of patients experiencing adverse virologic response.

Conclusions: Long-term suppression is common in this cohort of HIV-infected individuals. However, among patients who did not transfer out, approximately 60% of patients left the cohort (died or LTF) by the end of follow-up. Further research is needed to determine successful interventions for retaining patients in care in order to ensure continued success of the ART program in South Africa.

BACKGROUND

- Viral load is used to measure a patient's response to antiretroviral therapy (ART)
- Patients who experience virologic failure may do so as a result of adherence issues or drug resistance
- While much is known about virologic response to ART in resource-rich settings, much less is known about long-term rates of virologic suppression in resource-limited settings
- We aimed to describe virologic response on ART over 8 years among a cohort of patients initiating ART during the first year of public sector roll out in South Africa.

METHODS

- This study was conducted at 4 public-sector HIV treatment clinics in Gauteng and Mpumalanga Provinces in South Africa
- Under the 2004 National Antiretroviral Treatment guidelines, viral load monitoring was conducted at ART initiation and then every 6 months
- Monitoring guidelines updated to 6 months, 12 months, and yearly thereafter under 2010 guidelines

Study Population

- Included ART-naïve, adult (≥18) patients who initiated standard first-line ART between April 2004 and March 2005
- Patients were followed from the date of ART initiation until death, transfer, loss to follow-up or dataset closure (May 2013)

Analytic Variables

- **Loss to follow-up (LTF)**: ≥3 months late for a scheduled visit with no subsequent visit
- **Virologic suppression**: viral load <400 copies/ml
- **Detectable viral load**: viral load >400 copies/ml
- **Virologic failure**: two consecutive viral loads >1000 copies/ml between 2 weeks and 6 months apart
- **Transient elevated viral load**: One viral load <400 copies/ml followed by one viral load >1000 copies/ml followed by one viral load<400 copies/ml

Statistical Methods

- Results are examined using proportions for categorical variables and medians for continuous variables
- A cumulative incidence curve depicts time to first detectable viral load and first virologic failure after initial suppression, controlling for death, LTF, and transfer as competing events
- An adjusted log-binomial regression model was used to estimate the effect of suppression at the first viral load on death

RESULTS

- 2220 patients were included
- 67.4% were female; median (IQR) age was 35.8 (30.9-42.3) years; median (IQR) baseline CD4 count was 78 (32-138.5) cells/mm^3
- 1858 (83.7%) patients had ≥1 viral load recorded with a median (IQR) of 11 (5-13) viral loads over the course of follow-up

Figures

Figure 1 – Proportion of patients with a suppressed viral load in 6 monthly intervals

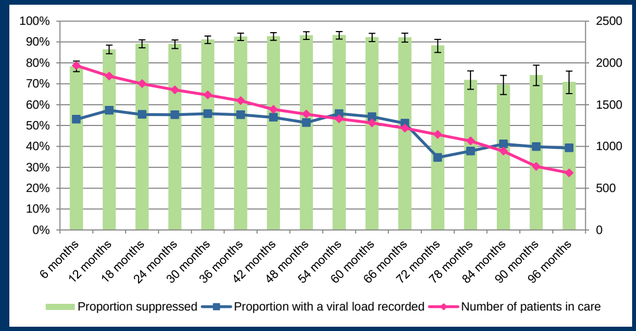

Figure 2 – Time to first detectable viral load and first virologic failure after initial suppression

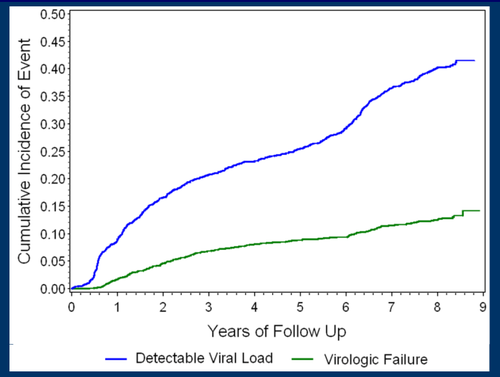

Table 1 – Characteristics of patients who initiated ART between April 2004-March 2005 stratified by virologic outcomes

Characteristic	Category	TOTAL	Never had a viral load recorded	Suppressed on the first viral load	Not suppressed on the first viral load
TOTAL	N (%)	2220 (100%)	362 (100%)	1491 (100%)	367 (100%)
Follow-up time (years)	Median (IQR)	6.2 (2.1-8.3)	0.4 (0.2-0.7)	7.2 (4.2-8.5)	6.1 (3.1-8.3)
Sex	Male	723 (32.6%)	147 (40.6%)	469 (31.5%)	107 (29.2%)
Age at initiation	Median (IQR)	35.8 (30.9-42.3)	36.1 (30.9-42.2)	35.9 (31.1-42.4)	35.2 (30.3-42.6)
CD4 Count	Median (IQR)	78 (32-138.5)	48 (15-105)	82 (37-142)	89 (42-140)
(cells/mm3)	Missing	132 (6.0%)	21 (5.8%)	86 (5.8%)	25 (6.8%)
	<50	721 (32.5%)	172 (47.5%)	451 (30.3%)	98 (26.7%)
	50-99	532 (24.0%)	78 (21.6%)	367 (24.6%)	87 (23.7%)
	100-199	709 (31.9%)	78 (21.6%)	495 (33.2%)	136 (37.1%)
	≥200	126 (5.7%)	13 (3.6%)	92 (6.2%)	21 (5.7%)
BMI	Median (IQR)	21.5 (19.1-24.6)	20.3 (17.7-22.8)	21.7 (19.4-25.0)	21.6 (19.2-24.1)
WHO Stage	I/II	1235 (55.6%)	184 (50.8%)	844 (56.6%)	207 (56.4%)
	III/IV	985 (44.4%)	178 (49.2%)	647 (43.4%)	160 (43.6%)
Hemoglobin (g/dL)	Median (IQR)	11.0 (9.4-12.4)	10.0 (8.6-11.7)	11.1 (9.6-12.4)	10.9 (9.4-12.4)
TB at ART Initiation	Yes	267 (12.0%)	50 (13.8%)	170 (11.4%)	47 (12.8%)
First ART Regimen	d4T-3TC-EFV	1972 (88.8%)	325 (89.8%)	1321 (88.6%)	326 (88.8%)
	d4T-3TC-NVP	194 (8.7%)	23 (6.4%)	138 (9.3%)	33 (9.0%)
	AZT-3TC-EFV/NVP	54 (2.4%)	14 (3.9%)	32 (2.1%)	8 (2.2%)
Outcome	Alive and in care	619 (27.9%)	2 (0.6%)	513 (34.4%)	104 (28.3%)
	Dead	409 (18.4%)	187 (51.7%)	152 (10.2%)	70 (19.1%)
	Loss to follow-up	518 (23.3%)	141 (39.0%)	295 (19.8%)	82 (22.3%)
	Transferred out	674 (30.4%)	32 (8.8%)	531 (35.6%)	111 (30.3%)

- 95.5% (n=1774) of patients reached virologic suppression over the course of follow-up
- 1491 patients suppressed on their first viral load; 784 (52.6%) remained suppressed on all following viral loads while 40.2% (n=599) did not
- Patients who did not suppress on their first viral load (n=367) were almost twice as likely to die as patients who did suppress (aRR: 1.94; 95% CI: 1.44, 2.60)
- 17.5% (279/1597) of patients experienced at least 1 transient elevated viral load (TEV) and were less likely to die (4.3%) or become LTF (15.4%) compared to patients who never experienced a TEV (death: 10.8%; loss: 19.6%)

CONCLUSIONS

Long-term suppression is common in this cohort. However, at the end of follow-up, among patients who did not transfer out, approximately 60% left the cohort (died or LTF). In order for the success of the South African national treatment program to continue, further research on effective interventions to retain patients in care is needed to prevent the ongoing spread of HIV and deaths.

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