

## Survival probability and predictors of mortality and retention in care among patients enrolled for first-line antiretroviral therapy, Andhra Pradesh, India, 2008–2011

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**Background:** The national antiretroviral therapy (ART) initiative in India began in 2004. In order to better inform the national program, we estimated the mean cumulative survival probability and loss to follow-up (LFU) rate among patients initiated on ART.

**Methods:** We identified a cohort of people living with HIV (PLHIV) aged  $\geq 15$  years initiated on ART in two ART centres in Hyderabad city, Andhra Pradesh state, India between January 2008 and December 2008. The cohort was followed-up until 31 December 2011 and death and/or LFU were the primary endpoints. Death from any cause during the study period was considered to be the result of HIV infection. We used the Kaplan-Meier estimation method for survival probability and Cox proportional hazard model to identify the predictors.

**Results:** Of the 1690 patients initiated on ART, 259 (15.3%) were transferred out during the study period. Mortality rate was 7.6/100 person-years. Male gender, low CD4 count, history of tuberculosis before initiation of ART, and weight  $< 48$  kg were the predictors of mortality. Patients who were LFU were more likely to be males, unemployed, widowed, and had weight below 48 kg.

**Conclusion:** Survival rates on ART were higher compared to other resource-limited settings. Delayed diagnosis and initiation of ART and co-infection with TB were important predictors for both mortality and retention in care.

**Keywords:** ART, HIV, India, Loss to follow-up, Survival analysis

### Introduction

The primary goal of antiretroviral therapy (ART) is to reduce HIV associated morbidity, mortality and transmission of HIV at the population level.<sup>1</sup> Since the inception of national ART programs in low and middle income countries, by 2011 a total of 2.5 million AIDS related deaths have been averted.<sup>2</sup> These countries contributed to 86.5% (5.2 million) of the total number of people living with HIV (PLHIV) accessing ART world-wide.<sup>3</sup> However, early mortality and retention of PLHIV in care after initiation of ART remain significant challenges for the national ART programs in developing countries.<sup>4,5</sup> Loss to follow-up (LFU) to ART is an independent risk factor for the development of drug resistance resulting in treatment failure and mortality.<sup>6,7</sup> Early initiation of ART and retention in care are critical to maximize survival and preventive benefits of ART.<sup>7–9</sup>

The HIV epidemic in India is concentrated among high-risk groups and in certain regions of the country. The national ART

program was launched on 1 April 2004 and by 2011, over 450 000 PLHIV were initiated on first-line treatment across 345 national ART centres. In 2009, the adult HIV prevalence was 0.31% with an estimated 2.4 million (range: 1.9–3 million) PLHIV and nearly 0.17 million AIDS related deaths.<sup>10</sup> The state of Andhra Pradesh had the second highest HIV prevalence (0.90%) and accounted for 21% of all HIV cases in the country.<sup>10</sup> The ART initiative in Andhra Pradesh is in its eighth year of implementation and has been scaled up from three centres in 2004 to 45 centres by 2011. From inception until March 2011, nearly 88 696 enrolled patients were alive and on ART.

Information on patient demographics, clinical and treatment details, at the initiation of ART as well as during subsequent follow-up visits, is maintained as part of the medical record at ART centres, and analysis of this information is the mandate of the national program.<sup>11</sup> In 2004, the first-line ART was introduced at three ART centres in Andhra Pradesh, which was scaled up to 45 centres by 2012. There is limited data about the outcomes of

PLHIV initiated on first-line ART in Andhra Pradesh, especially after the introduction of standard guidelines issued by the National AIDS Control Program (NACP) in 2008. We analyzed three year follow-up data of PLHIV initiated on ART in 2008 from two ART centres in Andhra Pradesh to estimate the mean cumulative survival probability, and to determine the factors associated with mortality and LFU.

## Methods

### Site selection and study setting

Of the 45 ART centres in Andhra Pradesh, 14 centres with >8000 PLHIV registered under HIV care were considered as high case load centres. We purposively selected two of them: Gandhi General Hospital and Andhra Pradesh General and Chest Hospital in Hyderabad, that had low transfers out and had at least two new registrations for ART every day indicating that the centres were active. The national ART program was introduced at these two centres in 2007. PLHIV with CD4+ lymphocyte count (CD count) <200 cells/mm<sup>3</sup> and/or WHO clinical stage 3 or stage 4 were eligible for ART in compliance with 2007 National AIDS Control Organization (NACO) guidelines.<sup>12</sup> At the ART centres patients were clinically assessed monthly in addition to multiple counselling sessions pertaining to drug adherence and follow-up visits. CD4 counts were estimated at baseline and at 6-month intervals during follow-up. In addition to ART, co-trimoxazole prophylaxis was provided to all PLHIV with CD4 count <200 cells/mm along with drugs for treatment of opportunistic infections as indicated.<sup>13</sup> Anti-TB treatment was provided to PLHIV with HIV-TB co-infection through linkage with the Revised National Tuberculosis Control Programme (RNTCP).<sup>12,14</sup> As per the RNTCP guidelines, fully intermittent thrice-weekly regimen Category I (2EHRZ3/4HR3) was recommended for newly diagnosed HIV-TB co-infected cases and ART regimen was initiated as soon as the patient tolerated TB treatment with the regimen containing efavirenz.

### Study design, population and inclusion criteria

PLHIV aged ≥15 years and who were initiated on ART between 1 January 2008 and 31 December 2008 at the two selected ART centres were included in the analysis. The cohort was followed-up until 31 December 2011 and death and/or LFU were the primary endpoints. Transferred out patients were excluded from analysis as it was not possible to collect the end-point data from such patients. Following the national guidelines, all the transferred out patients are given new registration numbers in the new centres and there is no link between the earlier and new registration numbers.

### Operational definitions

ART was defined as a combination of two nucleoside reverse transcriptase inhibitors (NRTIs) and one non-nucleoside reverse transcriptase inhibitor (NNRTI) group of drugs prescribed as per the national guidelines.<sup>12</sup> First line ART regimens consisted of two NRTIs and one NNRTI. The available drugs included zidovudine, stavudine, lamivudine, nevirapine and efavirenz.<sup>13</sup> Mortality from any cause during the follow-up period after initiation of ART was considered HIV/AIDS related. Patients missing more than three out of 60 doses of ART (<95% adherence) in a

month at any time during the follow-up period were considered to be non-adherent.<sup>13</sup> Patients missing ART refills/appointments for more than three consecutive months at an ART centre are considered as LFU.

### Data collection

From the patient treatment cards available at the ART centres, we abstracted the data on demographic details, baseline and follow-up CD4 counts, weight, personal history, WHO clinical stage, antiretroviral regimen, date of HIV diagnosis, death, adherence, substitution of ART, past history of TB and LFU. We compared the baseline characters of the transferred out patients with those who remained at the original ART centres.

### Data analysis

We calculated the median, inter-quartile range (IQR) for continuous variables, and proportions for categorical variables. Mortality and LFU rates were calculated using number of deaths or LFU as numerator and duration of treatment (in person years) as denominator. Data was censored at 31 December 2011. We used Kaplan-Meier product limit estimation method to assess cumulative probabilities of survival and retention in care. The log rank test was used to examine the statistical difference of survival and retention in care by gender and CD4 cell count at initiation of treatment. Cox proportional hazard regression model was used to calculate the hazard ratios for death and LFU as primary outcomes at any time during the follow-up period. Variables with p value of 0.2 or below and having biological relevance on the outcome were included in the final model. We used SPSS v. 16 (SPSS Inc., Chicago, IL, USA) for data analysis.

### Human subject protection

Approval for the study was obtained from the Institutional Ethics Committee of the National Institute of Epidemiology, Chennai. Permission to access the data was obtained from NACO. No personal identifying information was collected from patient records during data abstraction. Data quality assurance included validation of 10% of the data with the patient treatment card.

## Results

From 1 January 2008 to 31 December 2008, 1690 adolescent and adult PLHIV were initiated on ART at Andhra Pradesh Chest and General Hospital and Gandhi General Hospital, Hyderabad. Of these, 259 (15.3%) patients were transferred to other government ART clinics in the State during the follow up period and the remaining 1431 (84.7%) were included in our analysis. PLHIV who were followed-up and those who were transferred out were not different with respect to their median age (34 vs 33 years respectively,  $p=0.57$ ), gender (39 vs 42% females,  $p=0.82$ ), median baseline CD4 count (136/mm<sup>3</sup> vs 140/mm<sup>3</sup>,  $p=0.18$ ), median baseline weight (47 kgs vs 49 kgs,  $p=0.34$ ), WHO stage 3 or 4 (62 vs 58%,  $p=0.28$ ).

### Baseline characteristics

The majority (60.6%, 867/1431) of the cohort members were male and aged between 31 and 45 years (52.1%, 746/1431). More than 50% of them had completed primary education, were married and unemployed. At the initiation of ART, their

**Table 1.** Demographic, clinical and immunological characters of 1431 patients initiated on antiretroviral therapy (ART) as part of the National ART Program, Hyderabad, Andhra Pradesh, India, 2008–2011 (n=1431)

Characteristics		n	%
Age in years	15–30	538	37.6
	31–45	746	52.1
	>45	147	10.3
Employment	Employed	625	43.7
Gender	Male	867	60.6
Literacy	Illiterate	577	40.3
Marital status	Married	986	68.9
	Widowed	239	16.7
	Single	150	10.5
	Divorced/Separated	56	3.9
Baseline WHO stage	Stage 1	120	8.4
	Stage 2	426	29.8
	Stage 3	795	55.6
	Stage 4	90	6.3
Baseline CD4 count	0–99/mm <sup>3</sup>	514	35.9
	100–199/mm <sup>3</sup>	542	37.9
	>200 cells/mm <sup>3</sup>	375	26.2
Baseline regimen	D4T+3TC+NVP	1189	83.1
	D4T+3TC+EFV	46	3.2
	AZT+3TC+NVP	162	11.3
	AZT+3TC+EFV	34	3.2
Ever missed doses of ART	Not missed	1064	74.4
Outcomes	Death	275	19.2
	Lost to follow up	263	18.4
	Alive on ART	893	62.4
History of TB (n=310)	Present	310	21.7
	Pre ART	188	60.6
	During ART	122	39.4

3TC: lamivudine; AZT: zidovudine; D4T: stavudine; EFV: efavirenz; NVP: nevirapine.

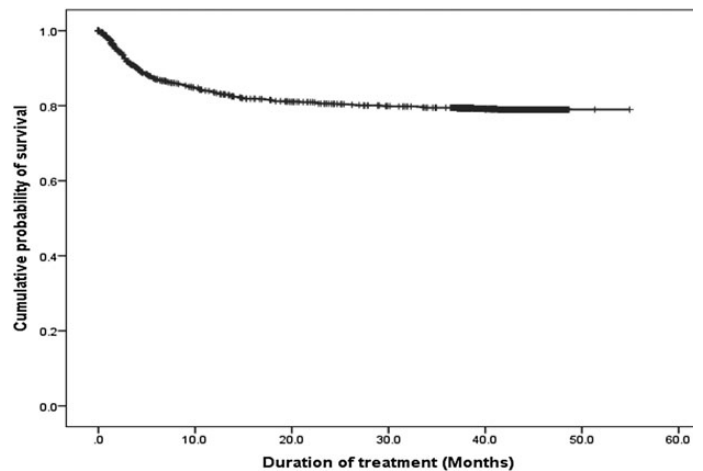
median age, weight and CD4 count were 34 years (IQR 29–40), 47 kg (IQR 41–55) and 136 cells/mm<sup>3</sup> (IQR 76–203), respectively. Over one-third of the patients had baseline CD4 count below 100 cells/mm<sup>3</sup> and 61.8% (885/1431) had WHO stage 3 or 4 disease. About 85% of patients received stavudine-based ART regimen. More than 20% of the PLHIV had history of TB (Table 1).

**Follow-up duration and outcome**

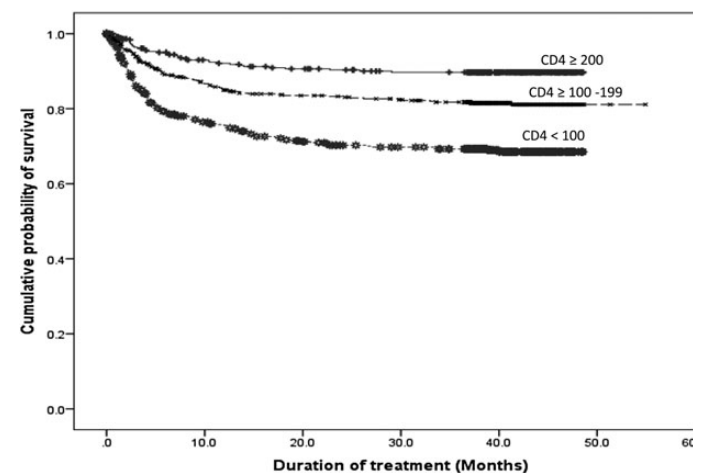
The 1431 PLHIV accounted for 3609.4 person years of follow-up between 2008 and 2011. By the end of the follow-up period, 275 (19.2%) had died, 263 (18.4%) were LFU and 893 (62.4%) were on continued follow-up.

**Duration of survival and survival probability**

Mean duration of survival of the cohort was 40 months (95% CI=39.01–40.85). Cumulative survival probability at the end of



**Figure 1.** Cumulative survival probability of people living with HIV (PLHIV) in the National Antiretroviral Therapy (ART) Program 2008–2011, Andhra Pradesh, India.



**Figure 2.** Cumulative survival probability of people living with HIV (PLHIV) in the National Antiretroviral Therapy (ART) Program stratified by CD4 count, Andhra Pradesh, India, 2008–2011.

12, 24, 36 and 48 months were 82, 80, 79 and 79% respectively (Figure 1). The overall mortality rate of the cohort was 7.6 per 100 person years. The mortality rate at 90 and 180 days after treatment initiation was 3.1 and 4.9 per 100 person years, respectively. Hazard rate of mortality was 0.02% in the first six months and 0.01% at 12 months. Of 275 total deaths 176 (64.0%) had occurred during the first 6 months of therapy. The mean survival time for PLHIV with CD4 counts <100 cells, 100–200 cells and >200 cells/mm<sup>3</sup> was 35.5 (95% CI=33.7–37.2), 40.97 (95% CI=39.5–42.3) and 44.2 (95% CI=42.97–45.58) months, respectively (p<0.001) (Figure 2). Females had significantly higher survival compared to males (p<0.001).

**Predictors of mortality**

Male patients (adjusted hazard ratio (AHR)=1.98, 95% CI=1.49–2.63), patients with baseline CD4 count <200 cells/mm<sup>3</sup>

**Table 2.** Hazard of death among adults initiated on antiretroviral therapy (ART) as part of National ART Program, Hyderabad, Andhra Pradesh, India, 2008–2011

Variable		PLHIV	Deaths	Duration Treatment (years)	Rate (100 person years)	HR	95% CI	p	Adjusted HR	95% CI	p
Age group	15–30	538	86	1421	6.1	0.54	0.37–0.78	0.001	0.57	0.38–0.84	0.001
	31–45	746	149	1861	8	0.69	0.49–0.98	0.04	0.67	0.47–0.96	0.03
	>45	147	40	328	12.2	1			1		
Gender	Male	867	198	2044	9.7	1.85	1.42–2.4	0.001	1.98	1.49–2.63	0.001
	Female	564	77	1567	4.9	1					
Literacy	Illiterate	577	86	1480	5.8	0.67	0.52–0.87	0.002	0.83	0.64–1.09	NS (0.17)
	Literate	854	189	2131	8.9	1					
Baseline regimen	D4T/3TC/NVP	1189	214	3014	7.1	0.6	0.32–1.14	NS (0.18)	0.79	0.41–1.55	NS (0.49)
	D4T/3TC/EFV	46	15	94	15.9	1.18	0.53–2.62	NS (0.69)	1.00	0.45–2.26	NS (0.99)
	AZT/3TC/NVP	162	36	420	8.6	0.72	0.35–1.43	NS (0.34)	1.00	0.48–2.09	NS (1.00)
	AZT/3TC/EFV	34	10	83	12	1					
Baseline CD4 count	0–100	514	146	1118	13.1	3.51	2.44–5.06	0.001	2.37	1.62–3.47	0.001
	101–200	542	96	1409	6.8	1.9	1.29–2.79	0.001	1.54	1.04–2.27	0.03
	>200	375	36	1084	3.3	1					
WHO stage	Stage 1	120	4	378	1.1	0.07	0.02–0.20	0.001	0.21	0.07–0.60	0.001
	Stage 2	426	71	1136	6.3	0.4	0.26–0.60	0.001	0.73	0.46–1.62	NS (0.19)
	Stage 3	795	170	1918	8.9	0.56	0.38–0.82	0.001	0.92	0.61–1.39	NS (0.68)
	Stage 4	90	30	179	16.8	1					
History of ART	Previous history of ART	178	36	470	7.7	1.1	0.71–1.44	NS (0.94)			
	No previous history of ART	1253	239	3140	7.6	1					
Mean weight, kg	<48	793	193	1825	10.6	2.13	1.648–2.763	0.001	2.28	1.87–3.26	0.001
	>48	638	82	1786	4.6	1					
TB status	Present	309	66	812	8.1	1.082	0.82–1.42	NS (0.58)			
	Absent	1121	209	2795	7.5	1					
History of TB	Pre ART	188	55	438	12.6	1.57	1.17–2.12	0.003	1.10	0.78–1.54	NS (0.58)
	Post ART	121	11	378	2.9	0.41	0.23–0.77	0.001	0.34	0.19–0.63	0.001
	No TB	1122	209	2795	7.5	1					
Adherence	Adherence	1064	211	2685	7.9	1.14	0.86–1.53	NS (0.37)			
	Non adherence	367	64	925	6.9	1					

3TC: lamivudine; AZT: zidovudine; D4T: stavudine; EFV: efavirenz; NVP: nevirapine. NS: not significant; PLHIV: people living with HIV.

(AHR=1.54, 95% CI=1.04–2.27), and mean baseline weight <48 kg (AHR=2.28, 95% CI=1.87–3.26) were at significantly higher risk of dying. (Table 2).

### Loss to follow-up

Mean duration of retention in care was 40 months (95% CI=40.1–41.02). Cumulative probability of retention in care at the end of 12, 24, 36 and 42 months was 86, 82, 79 and 76%, respectively (Figure 3). Overall rate of LFU was 7.2 per 100 person years. During the first 6 months of therapy, 176 (67.0%) of 263 patients were LFU. Probability of retention in care was significantly higher in females ( $p<0.001$ ; Figure 4), employed ( $p<0.003$ ) and widowed ( $p<0.001$ ) patients.

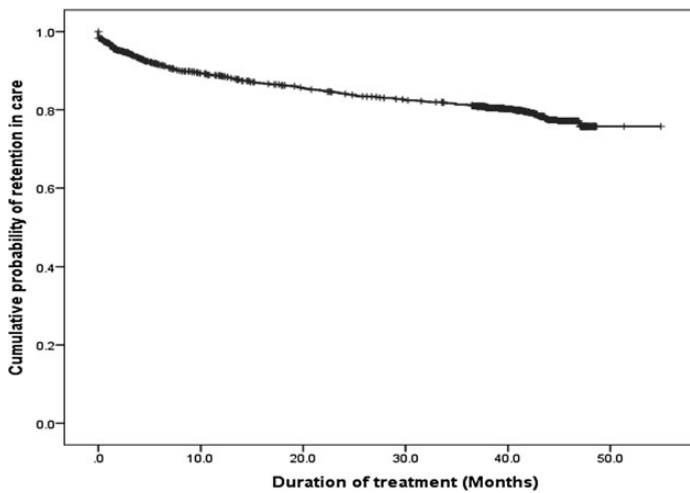
### Predictors of loss to follow-up

Patients who were LFU were more likely to be male, unemployed, widowed and weighing below 48 kg. Patients who had TB either before or after ART were also more likely to be LFU (Table 3).

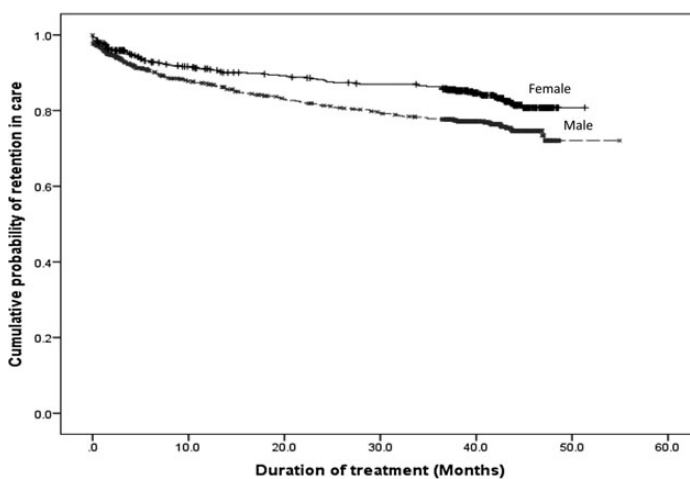
### Discussion

In the cohort of PLHIV initiated on ART in 2008 at the two ART centres in Hyderabad, more than 60% of patients were alive at 48 months of follow-up evaluation. The cumulative survival probability of PLHIV on ART was higher than the survival rates reported from other parts of India<sup>11,15</sup> and other developing countries.<sup>16,17</sup> Consequently, mortality rate in our analysis was lower than that





**Figure 3.** Cumulative probability of retention of people living with HIV (PLHIV) in the National Antiretroviral Therapy (ART) Program 2008–2011, Andhra Pradesh, India.



**Figure 4.** Cumulative probability of retention of people living with HIV (PLHIV) in National antiretroviral therapy (ART) Program stratified by gender, Andhra Pradesh, India, 2008–2011.

reported by other studies in India, including other ART program estimates (range 8.2–13.13 per 100 person years)<sup>15–18</sup> and also in other developing countries.<sup>19–21</sup> The observed lower mortality in Andhra Pradesh could possibly be due to access to special travel schemes, presence of dedicated staff to assess the patients both clinically and psychologically and focus on home visits by the program staff in addition to free supply of ART. Further, the studies from other program settings were from 2004–2005 cohorts when the ART program had not matured compared to our study cohort of 2008 in terms of streamlining of operational protocols related to ART management.

Consistent with the published literature, mortality was significantly higher among those with advanced disease, and among men. Nearly 60% of deaths occurred within the first 6 months of initiation of therapy.<sup>11,15,18–20</sup> Some of the early mortality

could possibly be due to undiagnosed opportunistic infections as was observed in other studies.<sup>18</sup> However, we were unable to confirm this due to non-availability of relevant information in patient records. In the two ART centres in Hyderabad, more than one-third of the patients had baseline CD4 count of  $<100$  cells/ $\text{mm}^3$  and 62% of patients were in WHO stage 3 or 4 at initiation of ART, indicating that they presented late for HIV care. The potential factors for such delays could be delay in HIV diagnosis as well as lack of access and availability of HIV care and treatment after HIV testing.<sup>22–24</sup> PLHIV weighing less than 48 kg at the initiation of ART were more likely to die. In most resource-poor countries of Africa and Asia, where most of the world's HIV-infected people live and where food insecurity is widespread, diagnosis of HIV infection is often made only at the advanced stage. Delayed diagnosis coupled with malnutrition leads to increased HIV disease progression and mortality due to suboptimal response to ART.<sup>25–27</sup> There is uncertainty surrounding the issue of supplementation of nutritional supplements in HIV Patients.<sup>28</sup> PLHIV with history of TB before initiating ART had a higher risk of all-cause mortality. However, we cannot attribute all these deaths to TB alone as the patients could be suffering from other opportunistic infections as well, about which data were not available in the records.

Similar to other studies from India,<sup>11,14,29</sup> probability of retention in care in our cohort was low among unemployed and married patients. Probable reasons for LFU in the Indian setting include longer distance to travel to reach HIV care facilities, loss of income, difficulty in travelling when sick, stigma and stopping therapy when symptomatically better.<sup>30</sup> This information however is not collected from the patients in the routine program settings and hence not available in patient records. To address the issue of access to ART, NACO established Link ART centres in 2009 with an aim to provide ART services closer to the patient's residence to reduce the travel cost of the patients.

Our study had certain limitations. First, the patient records were incomplete, particularly for follow up measurements of clinical details (23%) and behavioural parameters adverse side effects (37%), history of opportunistic infections (28%), alcoholism (44%) and sexual behaviours (31%). We therefore were not able to comment if these patient characteristics influenced mortality and LFU rates in our cohort. Second, 15% of patients who were transferred out during the follow-up period were not included in our analysis. It is unlikely that mortality among these transferred patients was higher than the rest of the cohort as all of them were transferred after one year of ART initiation when the mortality rate was likely to be lower, whereas  $>60\%$  of the total deaths in the cohort that was followed up occurred during the first 6 months of follow-up. Third, some treatment outcomes recorded as LFU may actually be deaths, thereby underestimating mortality in this study.<sup>31</sup> Lastly, we did not select the ART centres randomly and hence the findings of the study might not be generalized to all the ART centres in Andhra Pradesh. The two centres which were selected, however, are likely to represent high case load centres in Andhra Pradesh.

## Conclusions and recommendations

Mortality rates observed in this cohort of PLHIV on ART were lower than other studies conducted in both program and non-program settings.<sup>15,18,19,21</sup> Mortality and LFU were higher during the first

**Table 3.** Risk of loss to follow-up among adults initiated on antiretroviral therapy (ART) as part of the National ART Program, Hyderabad, Andhra Pradesh, India, 2008–2011

Variable		PLHIV	LFU	Duration of treatment (years)	Rate (100 person years)	HR	95% CI	p	Adjusted HR	95% CI	p
Gender	Male	867	176	2044	8.6	1.49	1.152–1.93	0.001	1.60	1.19–2.17	0.001
	Female	564	87	1567	5.6	1.00					
Age group	15–30	538	95	1421	6.7	0.67	0.45–0.98	NS (0.13)	0.70	0.46–1.05	0.09
	31–45	746	135	1861	7.3	0.72	0.49–1.05	0.04	0.79	0.54–1.16	NS (0.23)
	>45	147	34	328	10.4	1.00					
Literacy	Illiterate	577	138	1480	9.3	1.60	1.26–2.04	0.00	1.11	0.82–1.45	NS (0.50)
	Literate	854	125	2131	5.9	1.00					
Employment	Employed	625	96	1670	5.7	0.69	0.53–0.88	0.00	0.61	0.46–0.79	0.001
	Unemployed	806	167	1941	8.6	1.00					
Marriage	Married	986	185	2460	7.5	0.8	0.45–1.40	NS (0.43)	0.74	0.42–1.32	NS (0.30)
	Widow	239	25	676	3.7	0.4	0.20–0.79	0.01	0.40	0.20–0.79	0.001
	Single	150	40	335	11.9	1.2	0.66–2.30	NS (0.51)	1.22	0.64–2.33	NS (0.54)
	Divorce/ Separate	56	13	137	9.5	1.00					
Occurrence of TB	Pre HAART	188	33	438	7.5	0.95	0.66–1.38	NS (0.80)	0.68	0.45–1.014	0.05
	Post HAART	121	16	378	4.2	0.58	0.35–0.97	0.04	0.49	0.25–0.86	0.001
	No TB	1122	214	2795	7.7	1.00					
Baseline regimen	D4T/3TC/NVP	1189	221	3014	7.3	2.04	0.65–6.38	NS (0.22)	1.63	0.05–5.27	NS (0.41)
	D4T/3TC/EFV	46	14	94	14.8	3.82	1.09–13.27	0.04	2.70	0.77–9.45	NS (0.12)
	AZT/3TC/NVP	162	25	420	6.0	1.66	0.50–5.50	NS (0.41)	1.42	0.42–4.84	NS (0.58)
	AZT/3TC/EFV	34	3	83	3.6	1.00					
Baseline CD4 count	0–100	514	105	1118	9.4	1.52	1.12–2.09	0.01	1.19	0.85–1.67	NS (0.30)
	101–200	542	96	1409	6.8	1.16	0.84–1.59	NS (0.41)	0.99	0.72–1.38	NS (0.97)
	>200	375	62	1084	5.7	1.00					
Base line WHO stage	Stage 1	120	13	378	3.4	0.36	0.18–0.74	0.01	0.53	0.25–1.14	NS (0.10)
	Stage 2	426	64	1136	5.6	0.57	0.34–0.96	0.03	0.71	0.41–1.24	NS (0.22)
	Stage 3	795	167	1918	8.7	0.86	0.53–1.38	NS (0.36)	1.01	0.61–1.68	NS (0.97)
	Stage 4	90	19	179	10.6	1.00					
Mean weight	<48	793	161	1825	8.8	1.47	1.145–1.88	0.00	1.59	1.21–2.08	0.001
	>48	638	102	1786	5.7	1.00					
History of ART	Previous history of ART	178	27	470	5.7	0.78	0.52–1.15	NS (0.53)			
	No previous history of ART	1253	236	3140	7.5	1.00					
Adherence	Adherence	1064	188	2685	7.0	0.86	0.66–1.13	NS (0.28)			
	Non adherence	367	75	925	8.1	1.00					

3TC: lamivudine; AZT: zidovudine; D4T: stavudine; EFV: efavirenz; LFU: loss to follow-up; NS: not significant; NVP: nevirapine; PLHIV: people living with HIV.

6 months after initiation of treatment. During the study period, PLHIV with CD4 counts below 200 cells/mm<sup>3</sup> were eligible for ART. Initiation of ART at an early stage of the disease could further reduce these rates. The national guidelines have recently been revised to initiate ART at CD4 count below 350 cells/cmm and HIV-TB co-infected patients would be placed on ART irrespective of their CD4 count to prevent early deaths.<sup>32</sup> From the program perspective, there is an urgent need to standardize definitions of LFU to effectively monitor and establish mechanisms for tracking

deaths in LFU patients.<sup>30</sup> Patients with HIV with low body weight, male gender, illiterate and unemployed should be counselled and followed up by counsellors and outreach staff of the national care and support program. Our estimates of mortality and LFU rates based on data from the two ART centres established at the beginning of ART program are not representative of the entire country. Nevertheless, it would be prudent for the program managers to take appropriate programmatic and operational decisions aimed at reducing morbidity and mortality, and

increasing retention rates of PLHIV in the program. As recommended by India's national program for the control of HIV/AIDS, similar cohort analysis needs to be done at the program level in various sub-populations and in different geographic areas in order to generate vital information in timely manner on a routine basis.<sup>11</sup>

**Authors' contributions:** RRA and MVM conceived the study and designed the study protocol; RRA, NC, MVM and TB analysed and interpreted the data. RRA, MVM, TB, NC drafted the manuscript; CKU, BBR, SV and SMM critically revised the manuscript for intellectual content. All authors read and approved the final manuscript. RRA and MVM are guarantors of the paper.

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## References

- Cohen MS, Chen YQ, McCauley M et al. Prevention of HIV-1 Infection with early antiretroviral therapy. *N Engl J Med* 2011;365:493–505.
- UNAIDS. AIDS scorecards: overview: UNAIDS report on the global AIDS scorecards. Geneva: UNAIDS; 2010. Report No. UNAIDS/10.12E | JC2035E.
- WHO. Towards Universal Access: Scaling Up Priority HIV/AIDS Interventions in the Health Sector: Progress Report 2010. Geneva: World Health Organization; 2010.
- Braitstein P, Brinkhof MW, Dabis F et al. Mortality of HIV-1-infected patients in the first year of antiretroviral therapy: comparison between low-income and high-income countries. *Lancet* 2006;367:817–24.
- Rosen S, Fox MP, Gill CJ. Patient retention in antiretroviral therapy programs in sub-Saharan Africa: a systematic review. *PLoS Med* 2007;4:e298.
- Wang X, Yang L, Li H et al. Factors associated with HIV virologic failure among patients on HAART for one year at three sentinel surveillance sites in China. *Curr HIV Res* 2011;92:103–11.
- El-Khatib Z, Katzenstein D, Marrone G et al. Adherence to drug-refill is a useful early warning indicator of virologic and immunologic failure among HIV patients on first-line ART in South Africa. *PLoS One* 2011;6:e17518.
- Attia S, Egger M, Müller M et al. Sexual transmission of HIV according to viral load and antiretroviral therapy: systematic review and meta-analysis. *AIDS* 2009;23:1397–404.
- Kitahata MM, Gange SJ, Abraham AG et al. Effect of early versus deferred antiretroviral therapy for HIV on survival. *N Engl J Med* 2009;360:1815–26.
- National AIDS Control Organization. Technical Report India HIV Estimates. New Delhi: Ministry of Health and Family Welfare (Govt of India); 2011.
- Bachani D, Garg R, Rewari BB et al. Two-year treatment outcomes of patients enrolled in India's national first-line antiretroviral therapy programme. *Natl Med J India* 2010;23:7–12.
- National AIDS Control Organization. Antiretroviral Therapy Guidelines for HIV-Infected Adults and Adolescents Including Post Exposure Prophylaxis. New Delhi: Ministry of Health and Family Welfare (Govt of India). 2007; p. 125.
- National AIDS Control Organization. Operational Guidelines for ART Centres. New Delhi: Ministry of Health and Family Welfare (Govt of India); 2008; p. 65.
- National AIDS Control Organization and Central TB Division. Intensified TB/HIV package for NACP & RNTCP Programme Managers & Supervisors at State and District level. New Delhi: Ministry of Health and Family Welfare (Govt of India); 2009; p. 31.
- Sharma SK, Dhooria S, Prasad KT et al. Outcomes of antiretroviral therapy in a northern Indian urban clinic. *Bull World Health Organ* 2010;88:222–6.
- Marins JR, Jamal LF, Chen SY et al. Dramatic improvement in survival among adult Brazilian AIDS patients. *AIDS* 2003;17:1675–82.
- Stringer JSA, Zulu I, Levy J et al. Rapid scaleup of antiretroviral therapy at primary care sites in Zambia: feasibility and early outcomes. *JAMA* 2006;296:782–93.
- Ghate M, Deshpande S, Tripathy S et al. Mortality in HIV infected individuals in Pune, India. *Indian J Med Res* 2011;133:414–20.
- Teja VD, Sudha T, Lakshmi V. Causes and pattern of mortality in HIV-infected hospitalized patients in a tertiary care hospital: a fourteen year study. *Indian J Med Sci* 2007;61:555–61.
- Rajasekaran S, Jeyaseelan L, Raja K et al. Increase in CD4 cell counts between 2 and 3.5 years after initiation of antiretroviral therapy and determinants of CD4 progression in India. *J Postgrad Med* 2009;55:261–6.
- The antiretroviral therapy in lower income countries (ART-Linc) collaboration; ART cohort collaboration (ART-CC) groups. Mortality of HIV-1- infected patients in the first year of antiretroviral therapy: comparison between low-income and high-income countries. *Lancet* 2006;367:817–24.
- Steward WT, Bharat S, Ramakrishna J et al. Stigma is associated with delays in seeking care among HIV-infected people in India. *J Int Assoc Provid AIDS Care* 2012;12:103–9.
- Mojumdar K, Vajpayee M, Chauhan NK et al. Late presenters to HIV care and treatment, identification of associated risk factors in HIV-1 infected Indian population. *BMC Public Health* 2010; 10:416.
- National AIDS Control Organization and Population Council. Factors Affecting Enrolment of PLHIV into ART Services in India. New Delhi: Ministry of Health and family welfare; 2010.
- van der Sande MA, Schim van der Loeff MF, Aveika AA et al. Body Mass Index at time of HIV diagnosis: a strong and independent predictor of survival. *J AIDS* 2004;37:2
- Paton N, Sangeetha S, Earnest A et al. The impact of malnutrition on survival and the CD4 count response in HIV-infected patients starting antiretroviral therapy. *HIV Med* 2006;7:323–30.
- Tang AM, Forrester J, Spiegelman D et al. Weight loss and survival in HIV-positive patients in the era of highly active antiretroviral therapy. *J Acquir Immune Defic Syndr* 2002;31:230–6.
- Grobler L, Siegfried N, Visser ME et al. Nutritional interventions for reducing morbidity and mortality in people with HIV. *Cochrane Database Syst Rev* 2013;28;2:CD004536.
- Sarna A, Pujari S, Sengar AK et al. Adherence to antiretroviral therapy and its determinants amongst HIV patients in India. *Indian J Med Res* 2008;127:28–36.

- 30 WHO. Retention in HIV programmes: defining the challenges and identifying solutions: meeting report, 13–15 September 2011. Geneva: World Health Organization; 2012.
- 31 Brinkhof MW, Pujades-Rodriguez M, Egger M. Mortality of patients loss to follow-up in antiretroviral treatment programmes in resource-limited settings: systematic review and meta-analysis. *PLoS One* 2009;4:e5790.
- 32 Brinkhof MW, Spycher D, Yiannoutsos C et al. Adjusting mortality for loss to follow-up: analysis of five ART programmes in Sub-Saharan Africa. *PLoS One* 2010;5 (11) :e14149.