

## Original Research Article

# Outcome of antiretroviral therapy: a longitudinal study in Nalgonda district, Telangana

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## ABSTRACT

**Background:** India is among the list of countries with highest HIV prevalence. Retention in care is vital to maintain good health and obtain antiretroviral therapy (ART) medicines on time. The objectives of the study were to study the clinico-demographic profile of study population and to study the outcome of ART after one year of treatment initiation.

**Methods:** This is an observational follow up (longitudinal) study done on 142 patients which included all newly diagnosed (diagnosed on or after 1<sup>st</sup> January 2012), sero positive, adult patients, enrolled at an ART centre and started on treatment during the months of December 2012, January 2013, February 2013, using a pre-designed, pre-tested questionnaire. They were visited again a year after ART initiation and outcome was assessed along with determinants of poor outcome.

**Results:** Mortality at the end of one year was 9.15%, rate of loss to follow up (LFU) was 7.6%. Therefore a total of 73.2% cases were retained in care and 26.8% were disengaged from care (LFU and dead) after one year of ART initiation. Risk factors found to have significant association with being disengaged from care were male sex, unmarried/widowed/divorced/separated individuals, lower socio economic status, illiteracy, unskilled occupation, spouse status negative for HIV, presence of addictions like alcoholism, smoking, experience of drug side effects, early WHO clinical stage, presence of opportunistic infections and low CD4 counts.

**Conclusions:** Many of the risk factors are amenable for intervention and may be incorporated to strengthen the programme.

**Keywords:** Outcome of ART, Retained/disengaged from care, HIV

## INTRODUCTION

Globally, HIV is a major global public health issue. At the end of 2015, WHO estimated that 36.7 million (34.0-39.8 million) people were living with HIV. Sub-Saharan Africa remains the most severely affected, with an estimated prevalence of 4.4%.<sup>1</sup>

India has the third largest HIV epidemic in the world. In 2015, the estimated prevalence of HIV in India at 0.26% translates to 2.1 million of people living with HIV (PLHIV). During the same year, there were an estimated 68,000 deaths due to AIDS-related illnesses. The adult prevalence is in the range of 0.3%, of which around 40% are women.<sup>2</sup>

Starting from National AIDS Control Programme (NACP-1) in 1992 to the current NACP-IV, controlling and reversing of the HIV epidemic through key strategies of intensifying and consolidating preventive services, promoting comprehensive care, support and treatment, expanding behaviour change communication, building capacities at all levels and strengthening strategic information management system has been high on the agenda of Government of India.<sup>3</sup>

Initiation of antiretroviral therapy (ART) has caused decline in the incidence of most AIDS defining conditions and mortality. Adequate viral suppression requires strict adherence to antiretroviral therapy for which remaining in care is of vital importance. Hence it is important to know the retention rate of patients in HIV care. The present study endeavours to study the clinico-demographic profile of the study population and to study the outcome of antiretroviral therapy after one year of treatment initiation.

## METHODS

This is an observational follow up (longitudinal) study was done on all newly diagnosed (diagnosed on or after 1<sup>st</sup> January 2012), sero positive, adult patients, enrolled at an ART centre in Telangana state and started on treatment during the months of December 2012, January 2013, February 2013. Pregnant women and acutely ill patients, children (age <15 yrs) and those unwilling to participate in the study were excluded. A sample size of 142 was calculated based on prevalence of non-adherence as 50% (verbal communication by medical officer in charge of the ART centre), absolute precision of 10% was taken. With level of significance of 95% and anticipated loss to follow up and case fatality rate within first year as 20% each. Total patients during study period was 267, of them 96 patients was diagnosed with HIV before 1<sup>st</sup> January 2012 and 26 was pregnant women and 3 was children (age <15 yrs), so total 96+26+3=125 patients were excluded from the patients during study period i.e. 267-125=142. Hence the total sample size of the study was 142.

This study was conducted at an ART centre which is a government-owned facility attached to the district hospital, where ART drugs are provided free of charge. The study was approved by the Institutional Ethics Committee. A pilot study was conducted from 1<sup>st</sup> to 15<sup>th</sup> of October on 30 patients to assess feasibility of the research project, refine questionnaire and establish content validity. First interview and clinical examination was conducted from 1<sup>st</sup> December 2012 to 28<sup>th</sup> February 2013. Follow up interview and clinical examination was conducted from 1<sup>st</sup> December 2013 to 28<sup>th</sup> February 2014 (one year following the first interview). The questionnaire consists of three parts. In first part, socio demographic data was included. The second part captured data on relevant anthropological, behavioural, clinical and laboratory variables. The third part of the

questionnaire was completed 1 year later after the first interview to identify the retention rates. The above data was collected after acquiring written informed consent from the patient. Permission to conduct the study was obtained from the Medical Superintendent of the district hospital to which the ART centre is attached and the District Coordinator of hospital services (DCHS).

Interview and examination were conducted during the OPD hours of ART centre after their examination by medical officer and dispatch of their drugs. It was conducted in complete privacy with the help of ART counselors. ART centre was visited again from 1<sup>st</sup> December 2013 (one year following the commencement of study) to 28<sup>th</sup> February 2014 when patients came for monthly supply of drugs and clinical examination. Outcome after one year was categorised as retention in care, disengagement from care and death as recommended by WHO 'Retention in HIV programme' document 2011.<sup>4</sup> Retention in care includes patients on regular treatment as well as patients who occasionally missed doses (i.e. patients who arrived later than their scheduled day for collection of drugs). Disengaged from care includes cases who were loss to follow up (i.e. patients who did not report to the ART centre for 3 consecutive months despite not having been transferred out to another ART centre). Loss to follow up cases and dead patients were grouped under 'disengaged from care' for the purpose of calculation in the present study. The influence of socio-demographic factors, alcohol intake, CD4 count, BMI on outcome was studied. Determinants of becoming disengaged from care were studied.

The data was entered in Microsoft Office Excel Sheet. The quantitative data was analyzed by using percentages, mean and standard deviation and the association between various qualitative data was analysed by using chi-square test and  $p < 0.05$  was considered as level of significance.

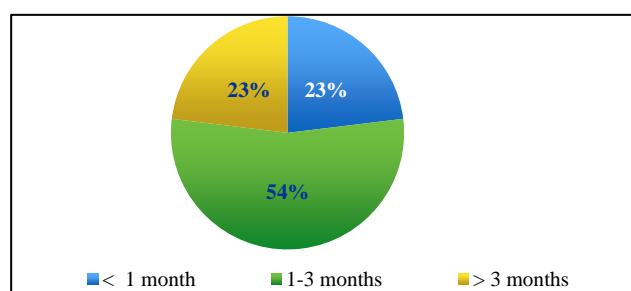
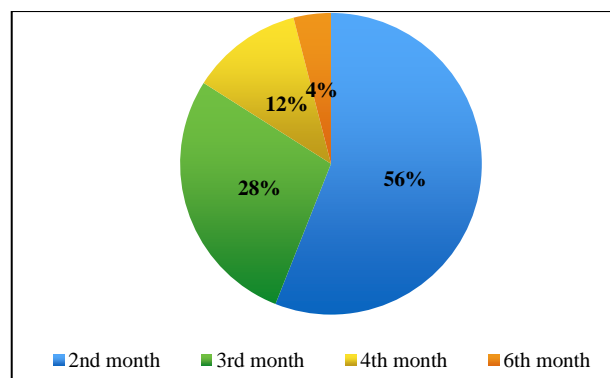
## RESULTS

It was seen from Table 1 that majority 92 (64.8%) were males and 50 (35.2%) were females and 78.88% belonged to economically productive age group (16-45 years). Smaller proportion of the study subjects (21.13%) were seen in more than 45 years age group. The mean age was  $39.33 \pm 10.29$  SD and the range is 18 to 70. Most of the study subjects were married. Most of the subjects were educated between classes 6 and 10 and only a small minority was graduates. A majority of the subjects were skilled labourers and professionals were only 2.8%. Majority belonged to lower middle class, resided in rural areas and belonged to nuclear families.

As seen from Figure 1 that the mortality rate in the present study was found to be 13 (9.15%). Of this, majority 7 (54%) of mortality cases had died between 1 and 3 months. This was followed by 3 (23%) of mortality cases who died within 1 month and more than 3 months respectively.

**Table 1: Distribution of study subjects based on socio demographic profile (n=142).**

Variables	Males (n=92) No. (%)	Females (n=50) No. (%)	Total (n=142) No. (%)
<b>Age (in years)</b>			
15- 25	04 (2.8)	04 (2.8)	08 (5.6)
26-35	33 (23.2)	23 (16.2)	56 (39.4)
36-45	34 (23.9)	14 (9.7)	48 (33.8)
≥46	21 (14.8)	09 (6.3)	30 (21.1)
<b>Marital status</b>			
Married	72 (50.7)	41 (28.9)	113 (79.6)
Unmarried	04 (2.8)	04 (2.8)	08 (5.6)
Widowed/ divorced/ separated	16 (11.3)	05 (3.5)	21 (14.8)
<b>Education</b>			
Illiterate	32 (22.5)	08 (5.6)	40 (28.2)
Upto 5 <sup>th</sup> class	27 (19.0)	13 (9.2)	40 (28.2)
6 <sup>th</sup> to 10 <sup>th</sup> class	29 (20.4)	28 (19.7)	57 (40.1)
Intermediate	01 (0.7)	01 (0.7)	02 (1.4)
Graduate	03 (2.1)	00 (0.0)	03 (2.1)
<b>Occupation</b>			
Unskilled	33 (23.2)	08 (5.6)	41 (28.9)
Semi skilled	06 (4.2)	10 (7.0)	16 (11.3)
Skilled	50 (35.2)	31 (21.8)	81 (57.0)
Professional	03 (2.1)	01 (0.7)	04 (2.8)
<b>Socio-economic status (as per modified B.G. Prasad classification)</b>			
Upper high	02 (1.4)	05 (3.5)	07 (4.9)
High	20 (14.1)	23 (16.2)	43 (30.3)
Upper middle	23 (16.2)	07 (4.9)	30 (21.1)
Lower middle	36 (25.4)	10 (7.0)	46 (32.4)
Poor	11 (7.7)	05 (3.5)	16 (11.3)
<b>Place of residence</b>			
Rural	67 (47.2)	39 (27.5)	106 (74.6)
Urban	25 (17.6)	11 (7.7)	36 (25.4)
<b>Type of family</b>			
Nuclear family	82 (57.7)	43 (30.3)	125 (88.0)
Joint family	08 (5.6)	05 (3.5)	13 (9.2)
Three generation	02 (1.4)	02 (1.4)	04 (2.8)

**Figure 1: Distribution of study subjects based on time duration between ART initiation and mortality (n=13).****Figure 2: Distribution of study subjects based on time duration between ART initiation and becoming loss to follow up (n=25).**

It was seen from Figure 2 that out of a total of 25 loss to follow up cases, 14 cases (56%) were lost in the 2nd month followed by 7 cases (28%) lost in 3rd month, 3 cases (12%) in 4th month and 1 case (4%) in 6th month.

**Table 2: Reasons for disengaging from care among loss to follow up patients (n=25)\*.**

Reasons	No. (%)
Depression/disinterest to live with HIV diagnosis	09 (60.0)
Financial difficulty	07 (46.7)
Side effect of drugs	06 (40.0)
Pill burden due to opportunistic infections	05 (33.3)
Others	05 (33.3)

(\* Multiple response).

It was seen from Table 2 that out of a total of 25 LFU, 10 cases could not reach at the address provided by them. At least three home visits were undertaken before indicating that a patient was not available. Surrogate interviews were not permitted, however house hold members assisted the patient in recalling information. Out of 25 loss to follow up cases (LFU), only 15 patients could be reached at address provided by them. Multiple responses were obtained for the above question. Depression or disinterest to live with HIV diagnosis was the most common reason.

It was observed from Table 3 that males were at higher risk of having poorer outcomes compared to females, Unmarried/widowed/divorced/separated subjects, lower socio economic status, illiteracy and unskilled nature of occupation were at higher risk of having poorer outcomes. It was found that sero discordant couples (couples where one spouse is positive and another is negative) were 7.75 times more at risk of having poor outcome compared to sero concordant couples (couples where both are positive).

**Table 3: Socio demographic factors related to disengagement from care.**

Socio demographic factors	X <sup>2</sup> value	P value
<b>Male</b>	5.03	0.0018
<b>Unmarried/widowed/divorced/separated</b>	3.46	0.0045
<b>Low socio economic status</b>	3.62	0.0015
<b>Illiterate</b>	34.29	0.0001
<b>Unskilled occupation</b>	16.49	0.0001
<b>Negative status of spouse for HIV</b>	7.75	0.0002

**Table 4: Patient related factors associated with disengagement from care.**

Variables	X <sup>2</sup> value	P value
<b>Alcoholic</b>	12.06	0.0001
<b>Smoker</b>	11.67	0.0001
<b>Drug side effects</b>	29.54	0.0001
<b>4th stage HIV</b>	0.49	0.03
<b>Presence of opportunistic infections</b>	7.08	0.0001
<b>CD4 count &lt;200</b>	2.31	0.045

It was seen from Table 4 that patients who were alcoholics, smokers and those who experience drug side effects were at greater risk of poor outcomes. We found that patients in stage 4 disease are more likely to have better outcomes than patients in other clinical stages. Presence of opportunistic infections, CD4 counts less than 200 were found to be associated with poorer outcome.

## DISCUSSION

Retention rate at the end of one year was 73.2% and disengagement from care i.e. mortality and LFU together were 26.76%. Similarly study done by Kumarasamy et al found that at the end of one year, the retention rate was 75% and disengagement rate was 25%.<sup>5</sup> Study done by Sharma et al found that retention rate at the end of two year was 69.4% and LFU and mortality together made up 30.6% cases.<sup>6</sup> Another study done by Rai et al found that retention rate at the end of 3 years was 57% and LFU and mortality together constituted 43%.<sup>7</sup> In our study, it was found that age had no statistically significant association with outcome. Similarly studies by Sharma et al and Kumarasamy et al which found no association between age and outcome.<sup>5,6</sup>

A statistically significant association was found between gender male and becoming disengaged. This may be because women have child rearing responsibilities and hence have to take care of themselves. This is in agreement with the results of study done by Rai et al which found that males were at a greater risk of having poor outcomes compared to females (OR=2.8).<sup>7</sup> Study done by Thakore et al also found a statistically significant

relationship between gender male and poor outcome.<sup>8</sup> There was a statistically significant relationship between being widowed/divorced/separated/unmarried and bad outcome. The emotional support provided by marriage may act as a facilitator for staying in care. Similar findings were also obtained by Thakore et al.<sup>8</sup> and Alvarez et al.<sup>9</sup>

Our study found that an association between low economic-status and bad outcomes. Thus, financial assistance to attend care centers, compensation for loss of daily wages etc. may be contemplated in the programme. This study found a significant association between being illiterate and becoming disengaged from care. Similar observations were found in studies done by Thakore et al and Kalichman et al.<sup>8,10</sup> We found unskilled nature of occupation to be associated with disengagement from care. Similar finding were obtained in study done by Sharma et al and Thakore et al.<sup>6,8</sup> This is probably because unskilled labours are mostly daily wage workers and cannot afford to forego daily wages to attend the care center. Present study found that patients whose spouse was sero negative for HIV were more at risk of having poor outcomes compared to patients whose spouses were also sero positive. Similarly a study done by Ware et al found that sero discordant establishes couples, as the HIV-negative partner reacts with anger, fear and sadness to the implication of infidelity represented by HIV infection.<sup>11</sup> Present study found that patients with addictions of alcoholism and smoking were more likely to be disengaged from care. Similar results were found in study done by Kalichman et al.<sup>10</sup> Probably because addictions are known to be responsible for poor self care and diversion of financial resources. This area is amenable for intervention such as inclusion of de addiction programmes in HIV care. An association was found between experiencing adverse drug effects and disengagement. Similar results were found in studies done by Sarna et al and Cauldbeck et al.<sup>12,13</sup>

Our study found that stage-4 clinical HIV patients were more likely to remain in care. These findings were similar to those of study done by Agu et al where it was found that of stage-4 patients were least likely to disengage from care probably because feeling of wellbeing among patients in earlier stages could be a barrier to remain in care.<sup>14</sup> This finding are in contrast with findings of a study done by Teja et al where higher HIV stage was related to disengagement from care.<sup>15</sup> We found that patients having opportunistic infections were more likely to disengage from care. This was in agreement with findings of study done by Ghate et al.<sup>16</sup> There was a statistically significant association between low CD4 counts and adverse outcomes. These findings were in agreement with those of study done by Alvarez et al and Ghate et al.<sup>11,16</sup>

## CONCLUSION

The study subjects were majorly male, married, educated between 6 to 10th class, belonging to economically



productive age group of 16 to 45, skilled workers, belonging to lower middle class of nuclear families. Mortality at the end of one year was 9.15%, rate of loss to follow up (LFU) was 7.6%. Therefore a total of 73.2% cases were retained in care n 26.8% were disengaged from care (LFU and dead) after one year of ART initiation. Risk factors found to have significant association with poor outcome were male sex, unmarried/widowed/divorced/separated individuals, lower socio economic status, illiteracy, unskilled occupation, spouse status negative for HIV, presence of addictions like alcoholism, smoking, experience of drug side effects, early WHO clinical stage, presence of opportunistic infections and low CD4 counts. Many of these are preventable and therefore are amenable to intervention.

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