Original Article

Predictors of Mortality among HIV Patients on HAART in an ART Centre – A Retrospective Study

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ABSTRACT
Introduction: The primary goal of highly active antiretroviral therapy (HAART) is to reduce mortality and morbidity rates among HIV-infected people, and to improve their quality of life. As of May 2015, a total of 8, 69,576 HIV/AIDS patient are receiving free Antiretroviral Therapy (ART), in our country despite which, there has been high HIV prevalence and mortality in certain areas. The objective of this retrospective study was to determine the factors associated with mortality in patients on ART under routine programme conditions in an ART centre in Southern Odisha. **Methods:** Data of HIV positive patients under HAART in the ART centre during April 2014 to March 2015 time period were collected and analysed for various demographic variables, clinical profile and mortality. **Results:** A total of 956 patients were under HAART during the study period, of which 204 (21.33 %) expired. Even though in majority of patients who died [193 (94.6%)] ART was initiated early; only 56 (27.45%) were under regular treatment; 73 (35.8%) had missed (irregular) doses, 75 (36.8%) were lost to follow up (LFU). Majority (88.24%) of the deaths occurred in the first six months of therapy in patients who had associated tuberculosis or some other AIDs related complications. **Conclusion**: The study reveals poor survival during the study period in spite of no delay in ART initiation. The increasing number of missed dose cases and LFU cases early after initiation of therapy suggests immediate need to intensify the patient retrieval and counselling services in this region.
Key words: Early ART, low CD4 count, HIV, co-infections, mortality, lost to follow- up cases

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INTRODUCTION

The primary goal of highly active antiretroviral therapy (HAART) is to reduce mortality and morbidity rates among HIV-infected people, and to improve their quality of life. The National AIDS Control Organization (NACO) of India has been providing free antiretroviral (ARV) drugs since 2004. According to a press release by the Ministry of Health and Family Welfare, Government of India, on 30th July, 2015, the amount spent on procurement of (Antiretroviral) ARV Drugs by National Aids Control Organization (NACO) during the year 2014-15 was 513.60 crores. A high prevalence of this dreaded disease has been reported in certain eastern states of our country in spite of investment of crores of rupees by the Government for treatment and awareness programmes. As of May 2015, a total of 8, 69,576 HIV/AIDS patient are receiving free Antiretroviral Therapy (ART), in 510 Antiretroviral Therapy (ART) centres and 1068 Link Antiretroviral Therapy (LAC) in our country. The present study was conducted in an ART centre located in Southern Odisha, which is functional since October 2006. The centre provides services like counselling, free HIV testing, free CD 4 count, free treatment / referral for management of opportunistic infections, along with supply of free ART medicine to HIV patients. But in spite of all these measures, Ganjam district under this ART Centre has high HIV prevalence in contrast to the National Prevalence showing a steady decline. Over 1,310 people have lost their lives on account of AIDS while a significant number of people are living with HIV (According to reports of Orissa State AIDS Control Society (OSACS) – by Express News Service – published 15th July 2014). Though a large number of patients have access to HAART through National Programme, there is paucity of data to document the outcome of ART in terms of survival or its determinants. A study done in a centre from the north showed a mortality of 12 per cent at two years[1] and a retrospective cohort analysis from another ART centre showed mortality rate at one year to be 7.66 deaths/100 patient-years with > 50 per cent of the deaths occurring during the first three months of ART initiation[2], Age, sex, educational status, place of residence, WHO clinical stage, CD4, haemoglobin, nutrition, functional status, and opportunistic infections have been associated with mortality among patients on ART.[3] Strengthening adherence and measures to curtail loss to follow up are important challenges for the ART roll-out programme in India.[4] Regular assessment of associated risk factors

and record keeping of the mortality data among patients on HAART is important to determine the effectiveness and impact of the ART program. An understanding of the prognostic factors in high-risk individuals will pave way for tailored follow up and better-targeted interventions, and thus improve survival. In this context, the present study was done to identify the factors associated with mortality in HIV-infected patients taking HAARTs in an ART centre in Southern Odisha.

Objective:

1. To analyse the mortality outcome of the HIV-infected patients on antiretroviral treatment in ART Centre.
2. To identify the determinants associated with mortality among the HIV-infected patients on antiretroviral treatment in ART Centre.

SUBJECTS AND METHODS

It was a retrospective study conducted in October 2015 in the ART centre of MKCG Medical College, Berhampur, Ganjam, and Odisha. The study was approved by the Institutional Ethics Committee. Following necessary approvals, data was collected from the ART medical record register. The study population included all HIV positive patients, and on HAART in the ART centre (as per Revised NACO guidelines 2009) during April 2014 to March 2015.[5] Relevant information of patients who were under HAART during April 2014- March 2015 were collected from record since the date of initiation of HAART. Utmost care was taken to maintain the confidentiality of the documents. Information with regard to demographic characteristics, number of deaths, cause of death, duration since initiation of ART, adherence to treatment, CD4 values at the time of death was collected from ART register and retrospective analysis of various parameters associated with death was carried out.

Statistical analysis: The extracted data was presented as frequency with their respective percentages for categorical variables. The main outcome variable was death and the time of its occurrence during the one year period. The predictor variables used in the analysis were gender, CD4 count; ART drugs intake status (Regular/ Missed/ LFU), delay in ART initiation and presence of co-infections. Chi-square test was used to find out any significant association between the above variables. The above analyses were performed on exclusion of the LFU cases. $P < 0.05$ was considered to be statistically significant. (IBM SPSS Statistics 20.0 software)

RESULTS

A total of 956 patients were under HAART during the study period (April 2014- March 2015), of whom 204 (21.33 %) expired. This mortality figure includes patients who were on ART since last 9 years (Figure1). Baseline characteristics of the deceased cases (Table-1) revealed that the proportion of death among male persons (68.14%) was higher compared to females (27.94%) and 14-59 years age group (95.09%) were most commonly affected. Death rate was also high in persons belonging to low socio-economic status (73.03%) and agriculture/unskilled workers (38.72%).

Clinical characteristics (Table-2) showed that among the 204 patients who had died, in 193 (94.6%) patients, ART- was initiated without any delay according to the NACO Guidelines. In majority of patients the CD4 count was <250 cells/cmm (<100 cells/cmm 35.29%, and 100-250 cells/cmm 37.74%) at the last follow up. It was observed that in 91(44.60%) of cases the cause of death was due to TB related severity, 68 (33.33%) cases due to AIDs related severity and 13 (6.37%) were because of other diseases (pneumonia, Hepatitis C, candidiasis, herpes, diabetes, ischaemic heart disease) related severity. The average life span [post diagnosis] of a HIV patient with tuberculosis (TB) was found to be 223.23 days and in a patient with CD4 count ≤100, 161.68 days. With regard to history of
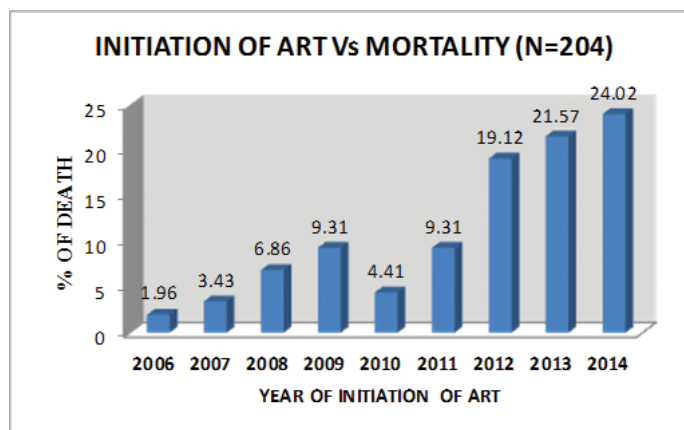

Figure 1: Year of initiation of ART among cases that died between 2014-15

Table 1: Baseline characteristics of the Death Cases (N=204)

SL. No.	Characteristics	Number	%
01	**Age (years)**		
	< 14	08	3.92
	14-59	194	95.09
	≥ 60	02	0.98
02	**Sex**		
	Male (Adult)	139	68.14
	Female (Adult)	57	27.94
	Male/female (Child)	08	3.92
03	**Educational status**		
	Primary school (1-5th standard)	98	48.04
	Matriculation	85	41.66
	Graduation	21	10.29
04	**Occupation**		
	Agriculture/unskilled worker	79	38.72
	Driver/sweeper	37	18.14
	Service	11	5.39
	Business	27	52.94
	Unemployed/housewife	45	22.05
	Student	5	2.45
05	**Socio-economic status**		
	High	2	0.98
	Average	53	25.98
	Low	149	73.03
06	**Residency**		
	Rural	135	66.17
	Urban	69	33.82

drug intake, 56 (27.45%) were under regular treatment; 73 (35.8%) had missed (irregular) doses, 75 (36.8%) were lost to follow up (LFU). LFU was defined as a patient not taking an ART refill for ≥ 3 months from his/her last visit to the ART Centre for refill and not categorised as 'dead' or 'transferred-out'. Among the patients who were on regular ART (n= 56), majority of patients were adherent to treatment (35.71, 100% and 28.57,

Table 2: Death analysis of On-ART patients in ART Centre

S.N.	Parameters study	Key Variables		Incidence (%)
01	Cause of death (n=204)	TB	TB related severity	91 (44.60)
			LFU (≥ 3 months)	18 (8.82)
			AIDS related severity	68 (33.33)
			Other diseases related severity	13 (6.37)
			Drug toxicity	04 (1.96)
			LFU (≥ 3 months)	06 (2.94)
			Cause not known	04 (1.96)
02	Drug intake (n=204)	Regular		56 (27.45)
		Irregular (Missed)		73 (35.8)
		LFU		75 (36.8)
03	Regular patients- cause of death [n=56]	TB		17 (30.35)
		AIDS Severity/Related infection		11 (19.64)
		Other disease		03(5.35)
		Drug toxicity		05 (8.92)
		Delay of ART Initiation/ART failure		09 (16.07)
		Cause not known		11 (19.64)
04	Delay of ART Initiation (n=204)	1-2 months		2 (0.98)
		2-6 months		3 (1.47)
		More than 6 months		6 (2.94)
		Not delayed		193 (94.6)
05	CD4 range (n=204)	≤ 100		72 (35.29)
		100-250		77 (37.74)
		250-350		27 (13.25)
		≥ 350		28 (13.73)
		No CD4 test result		11 (5.39)
06	Adherence to ART (n=56)	< 75%		13 (23.21)
		76- 95 %		7 (12.50)
		95-99%		16 (28.57)
		100 %		20 (35.71)
07	Average Life span of HIV patient (Days) (n=204)	With TB		223.23
		$CD_4 ≤ 100$		161.68
		100-350		527.06
		≥ 350		703.72

95-100%). Cause of death amongst regular patients, was mostly due to tuberculosis 17(30.35%) and AIDs related severity 11(19.64 %).

But the number of deaths was highest 51 (24.02%), in patients who had initiated ART, in the same year (2014). During this period, in 49 out of 51 cases there was no delay in ART (96.07%), but important observation was that only 22 cases (43.13%) were on regular doses. Forty-one patients (80.39%) had CD4 count <250 and twenty-one (41.17%) persons had associated co-infections with an equal number of cases (41.17%) showing no adherence to treatment. Chi-square analysis showed a significant association between year of initiation of ART, gender, CD4 count and adherence to treatment. (Table-3) Further odds ratio (OR) with confidence interval (CI) was computed to find out if the above factors are determinants of mortality among patients on ART which revealed that

these variables were not the predictors of mortality in the present study. (Table-4)

DISCUSSION

One of the predictors of mortality most commonly reported[6-11] is the time of enrolment into the ART care. Ignorance about the disease and screening programmes, social stigma and discrimination, large scale migration are some reasons why in our setup patients report to the ART centre in advanced stages of disease. The present study showed that, during the year 2014-15, the mortality in patients on ART was high among those initiated on treatment the same year compared to those initiated on treatment during the previous nine years. We have not

Table 3: Factors associated with mortality of patients on ART(excluding LFUs) [n=129]

Variables	N [%]	[2,] P-value
Sex		
Male [adult]	90 [69.76]	83.23, 0.001
Female [adult]	35 [27.13]	
Male/female [Children]	4 [3.10]	
Drug intake		
Regular	56 [43.41]	2.24, 0.134
Missed doses	73 [56.58]	
ART initiation		
Delayed	5 [3.87]	109.77, 0.001
Not delayed	124 [96.12]	
CD4 Count		
<250	99 [76.74]	36.92, 0.001
>250	30 [23.25]	
Co- infection		
Present	61 [47.28]	0.38, 0.538
Absent	68 [52.71]	
Adherence to treatment		
Non-Adherent	35 [27.13]	26.98, 0.001
Adherent	94 [72.86]	

Table 4: Determinants of mortality of patients on ART(excluding LFUs) [N=129

Variables	Non-adherent N (%)	Adherent N (%)	OR [C.I]	p-value
Sex				
Male [adult]	25 (71.42)	65 (69.14)	0.84 [0.35-2.03]	0.82
Female [adult]	10 (28.57)	25(26.59)		
Male/female [Children]	0 (0)	4 (4.25)		
Drug intake				
Regular	13 (37.14)	43 (45.74)	0.70 [0.31-1.5]	0.42
Missed doses	22 (65.85)	51 (54.25)		
ART initiation				
Delayed	1(2.85)	4 (4.25)	0.66 [0.07-6.13]	1.0
Not delayed	34 (97.14)	90 (95.74)		
CD4 Count				
<250	18 (51.42)	31 (32.97)	1.65 [0.61-4.47]	0.35
>250	11(35.35)	39 (41.48)		
Co- infection				
Present	13 (37.14)	48 (51.06)	0.56 [0.25-1.25]	0.17
Absent	22 (65.85)	46 (48.93)		

shown the data about the time of imitation of ART to the number of deaths in the same years, for 2006 to 2013. However, according to this study, though there was no delay in ART treatment (2014-2015), 88.24% of the deaths occurred in the first six months of therapy, indicating a very high early mortality in our patients. There are some studies showing that, patients starting HAART in resource-poor settings have increased mortality rates in the first months on therapy, compared with those in developed countries.[12] Several other studies in the developed and low- and middle-income countries also demonstrated that that the survival of HIV-infected patients on ART depends on sex, age, viral load, CD4 count, total lymphocytes, body mass index (BMI) or bodyweight (kg), WHO clinical stage, co-trimoxazole preventive therapy (CPT), haemoglobin, adherence, and nutritional support.[13, 14] Male sex was an important risk factor associated with mortality in this study, which has also been reported by another study from our country.[15] It was observed that in majority of patients the cause of death was due to TB related severity or AIDs related severity corroborating with other literatures, which report that the risk of death in co-infected individuals is twice that of HIV infected individuals without TB, even when CD4 cell count and antiretroviral therapy are taken into account.[16] Further, strict adherence to ART has been associated with a higher chance of survival of HIV infected patients.[17, 18] Most important finding in our study was a high lost to follow up cases (36.8%) and patients with missed / irregular doses (35.8%) which were also documented in other studies from India.[19, 20] Most LFU also occurred within first three months and these patients also had significantly low CD4 count. Even though many studies as cited above, have proved male sex, low CD4 count, co-infections, adherence to HAART, or other factors to be associated with mortality we could not predict them to be associated with mortality in the present study because of the limitations like analysis of death cases of only one year duration and exclusion of LFU cases from the analysis. To conclude, poor survival in spite of early ART initiation, a number of missed dose cases and LFU cases as revealed from the present study suggests immediate need to intensify the patient retrieval and counselling services in this region.

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