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Combined Antiretroviral Treatment Initiation During Hospitalization: Outcomes in South African Adults

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To The Editor:

In Southern Africa there still remain a large number of HIV infected patients who have as yet not accessed combined antiretroviral therapy (cART) [1]. A proportion of these patients present for the first time to medical services with advanced HIV disease as evidenced by WHO staging and/or CD4 T-cell counts of less than 200 cell/mm^3. This group of patients presents unique challenges to clinicians when considering initiating treatment. Co-morbid illnesses, potential drug interactions, drug toxicities, immune reconstitution inflammatory syndrome and high pill-burdens complicate management and must be taken into consideration [2]. In such cases it has been recommended that cART be commenced after treatment for opportunistic infections has commenced, however there is increasing evidence that earlier initiation of cART may lead to reduced morbidity and mortality [3,4]. Prolonged hospitalization of HIV infected patients may require initiation of antiretroviral therapy during the hospital admission.

We undertook a matched case-control study in order to evaluate outcomes in patients commencing cART during hospitalization at a South African academic hospital between 01 January 2004 and 31 March 2008. Controls were selected from patients attending the infectious diseases outpatient department (OPD) during the same time period. OPD controls were matched on WHO stage, sex and age; one control was selected for each case. Patients were categorized as being lost to follow-up if they failed to return to the OPD for a period of 3 months or more.

60 patients who commenced cART during hospitalization were included in the analysis. Of these 48 patients (80%) were admitted with AIDS defining illnesses, the commonest admission diagnoses were Kaposi Sarcoma (7 cases), Tuberculosis (7 cases) and Non-Hodgkins Lymphoma (6 cases). 11 patients died prior to hospital discharge and another 6 prior to follow-up appointment. The median CD4 count in the hospitalized group was 91 cells/mm^3 (Table 1).

Among the OPD control patients the median CD4 count was 64.5 cells/mm^3 (IQR: 23-150). The commonest AIDS defining illnesses in this group were disseminated Tuberculosis (19 cases) and oesophageal candidiasis (11 cases). There was no statistically significant difference between the CD4 counts of the cases and controls (p=0.1567).

In the case-control analysis hospitalized patients had a greater risk of dying (OR= 7.33; 95% CI =2.8–19.23) and were more likely to be lost to follow up (OR=4.07; 95% CI=1.32–12.52).

There were 15 hospitalized patients who remained on cART and had follow up viral load measurements at 12 months. In this group 2 patients had virological failure at 12 months on therapy and this finding was no different among matched OPD control patients (p=0.500).

In the bivariate analysis the time taken to initiate cART, the time on cART prior to discharge and the distance that patients lived from the facility had no statistically significant impact on the risk of death or being lost to follow up.

It was anticipated that there would be higher mortalities among hospitalized patients as these patients were admitted due to the severity and extent of their illnesses. The high risk of loss to follow up in hospitalized patients is noteworthy. It is likely that a proportion of these patients may have died. Previous studies have suggested that up to 50% of patients who are lost to follow up in low resource settings have died [5].

Hospitalized patients who returned for follow-up and remained on cART had favorable treatment outcomes. This is in keeping with results from Latuadda, et al [6], which showed good virological outcomes and adherence in an Italian cohort of patients commencing cART during hospitalization. However both studies are small making it difficult to draw meaningful conclusions from the limited number of patients.

This study demonstrates poor retention in care and high mortality associated with commencing cART in hospitalized patients. However patients who do remain in care have comparable treatment outcomes to those of more clinically stable patients.

An improved system for patient follow-up and earlier initiation of cART is recommended to improve outcomes in hospitalized patients in this setting.

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Table 1

Hospitalized patients initiated on cART (n=60).

Sex:	**Male (n):**	**19**	**(32%)**
	Female (n):	**41**	**(68%)**
Age:		33.8 yrs*	(IQR:28.4–41.1 yrs)
CD4 count:		91 cells/mm^3	(IQR: 51–154 cells/mm^3)
Length of admission:		29 days*	(IQR: 13–43 days)
Time to commence cART:		15 days*	(IQR: 8–28 days)
Time on cART prior to discharge/death:		7 days*	(IQR: 3–18 days)
Loss to follow up (n):		15**	(35%)
Deaths within 1 year on cART (n):		24	(40%)
Time from cART to death:		34 days*	(IQR: 24–86 days)

* Median values reported.

** 43 discharged patients included in the loss to follow up analysis.