Short-term impacts of a change in ART initiation threshold for patients co-infected with TB in Johannesburg, South Africa

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ABSTRACT

Introduction: Recent studies showed earlier antiretroviral therapy (ART) initiation in patients co-infected with tuberculosis (TB) leads to reduced mortality. On April 1st, 2010 South Africa changed its HIV treatment guidelines to initiate patients with TB at CD4 counts < 350 cells/mm^3, up from <200 cells/mm^3. We evaluated short-term impacts of the guideline change by comparing treatment outcomes for co-infected patients before and after the policy change at the Themba Lethu Clinic, in Johannesburg, South Africa.

Methods: We compared treatment outcomes among 330 co-infected patients initiated on ART between April 2009-March 2010 (pre-period) to 356 patients initiated between April 2010-March 2011 (post-period). TB-HIV co-infection was defined as any episode of pulmonary TB 3 months prior to 30 days after ART initiation. We compared rates of death or loss to follow-up (LTF) over the first six months on ART. We then adjusted for age, sex and ART regimen using logistic regression. LTF was defined as three months late for a scheduled visit. Our primary outcome is death or LTF combined as deaths are more likely to be distinguished from LTF in the pre-period.

Results: Of the 686 TB/HIV co-infected patients 48.5% were female. They had a median age of 36.5 (31.5-42.9) years at ART initiation and a median follow-up of 11.2 person-months. Due to changes in the 2010 treatment guidelines, 86% of patients initiated d4T-3TC-EFV as their first ART regimen in the pre-period, while 75% initiated TDF-3TC-EFV in the post-period. The mean CD4 count at ART initiation was 81.5 cells/mm^3 in the pre-period and 100.3 cells/mm^3 in the post-period (mean difference 18.8 cells/mm^3; 95% CI: 5.1-32.6). Of all ART patients, 13.2% patients were co-infected with TB in the pre-period compared to 12.8% in the post-period. 180 patients died or were LTF after a median of 5.1 (IQR: 3.9-9.0) person-months. After adjustment for age, sex and ART regimen, the odds of death or LTF within 6 months of ART initiation was unchanged in the post-period compared to the pre-period (OR=0.75; 95%CI: 0.40-1.40).

Conclusions: While early outcomes for TB patients were similar pre- and post- policy change, our data suggest that initiating CD4 counts have begun to increase. If this trend continues it could lead to better outcomes for co-infected patients.

BACKGROUND AND OBJECTIVES

Recent observational studies and randomized trials have demonstrated that earlier initiation of antiretroviral therapy (ART) in patients co-infected with tuberculosis (TB) can lead to reduced rates of mortality. However, while encouraging, to achieve the benefits of earlier treatment in co-infected patients, patients with HIV and TB will need to present for antiretroviral therapy with higher CD4 counts.

On April 1st, 2010 South Africa changed its HIV treatment guidelines to initiate patients with TB at CD4 counts <350 cells/mm^3, up from <200 cells/mm^3. While the change has now been implemented, it is not clear if this change will lead to treatment of co-infected patients at higher CD4 counts or lead to improved treatment outcomes and survival.

We evaluated the short-term impacts of South Africa's change in HIV treatment guideline for TB/HIV co-infected patients by comparing characteristics at treatment initiation and treatment outcomes for co-infected patients in the year before and the year after the policy change at the Themba Lethu Clinic, in Johannesburg, South Africa.

METHODS

This study was conducted at the Themba Lethu HIV clinic in Johannesburg, South Africa, a clinic which has initiated over 13,000 patients on antiretroviral therapy.

Patients at Themba Lethu are managed according to South African National Treatment Guidelines.

Study Population

TB/HIV co-infection was defined as any episode of pulmonary TB three months prior to 30 days after ART initiation.

We included all TB/HIV co-infected patients who initiated ART at Themba Lethu between April 2009 and March 2011. Patients were followed until the earliest of death, loss to follow-up or completion of 6 months of follow-up.

We compared treatment outcomes among co-infected patients initiated on ART between April 2009-March 2010 (pre-period) to patients initiated between April 2010-March 2011 (post-period).

Treatment Outcomes

The primary outcomes for this analysis were defined as:

- CD4 count at ART initiation – We defined baseline CD4 count as 6 months before to 7 days after ART initiation
- Mortality - Death is ascertained through linkage with the national vital registration system.
- Loss to follow-up (LTF) – Loss is defined as ≥3 months late for the last scheduled appointment

Statistical Methods

- To determine whether the policy change for TB/HIV co-infected patients resulted in earlier treatment initiation for TB/HIV co-infected patients we compared median baseline CD4 counts between cohorts.
- We then compared differences in rates of death or loss to follow-up (LTF) over the first six months on ART.
- Results of comparisons in differences in death/loss to follow-up were adjusted for age, sex and ART regimen at ART initiation using logistic regression.

RESULTS

Cohort Description

- 330 co-infected patients initiated on ART between April 2009-March 2010 (pre-period) to 356 patients initiated between April 2010-March 2011 (post-period).
- Patients were similar with respect to age and sex in the pre and post periods.
- At ART initiation, patients in the pre-period were more likely to have a CD4 count <50 (41.2% vs. 30.9%).
- In the post period, patients were much more likely to be in a tenofovir based regimen due to changes in the treatment guidelines (75.3% vs. 6.7%).

Characteristics at ART Initiation

Variable	Exposure	April 2009-March 2010 (pre-period N =330)	April 2010-March 2011 (post-period N=356)
Sex	Male	175 (53.0%)	178 (50.0%)
	Female	155 (47.0%)	178 (50.0%)
Age at ART	18 – 29	58 (17.6%)	59 (16.6%)
Initiation	30 – 34	92 (27.9%)	82 (23.0%)
	35 – 39	68 (20.6%)	78 (21.9%)
	40 – 44	49 (14.8%)	64 (18.0%)
	45+	63 (19.1%)	73 (20.5%)
CD4 at ART Initiation	Median (IQR)	60 (26 – 118)	72 (30 – 151)
(cells/mm^3)	Missing	10 (3.0%)	62 (17.4%)
	0 – 49	136 (41.2%)	110 (30.9%)
	50 – 99	82 (24.8%)	74 (20.8%)
	100 – 199	72 (21.8%)	73 (20.5%)
	200 – 349	28 (8.5%)	32 (9.0%)
	350+	2 (0.6%)	5 (1.4%)
First ART Regimen	d4T-3TC-EFV	284 (86.1%)	61 (17.1%)
	TDF-3TC-EFV	22 (6.7%)	268 (75.3%)
	Other	24 (7.3%)	27 (7.6%)
Outcome at 6 Months	Alive	272 (82.4%)	297 (83.4%)
	Dead or LTF	50 (15.2%)	45 (12.6%)
	Transferred	8 (2.4%)	14 (3.9%)

Predictors of Death or Loss to Follow-up

Characteristic	Dead or LTF/N (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Pre/Post Guidelines Change			
April 2009 – March 2010	50/330 (15.2%)	Reference	Reference
April 2010 – March 2011	45/356 (12.6%)	0.81 (0.53-1.25)	0.75 (0.40-1.40)
Sex			
Female	42/333 (12.6%)	Reference	Reference
Male	53/353 (15.0%)	1.22 (0.79-1.89)	1.20 (0.77-1.86)
Median Age			
≤36.5	46/345 (13.3%)	Reference	Reference
>36.5	49/341 (14.4%)	1.09 (0.71-1.68)	1.10 (0.71-1.70)
First ART Regimen			
d4T-3TC-EFV	48/345 (13.9%)	Reference	Reference
TDF-3TC-EFV	37/290 (12.8%)	0.91 (0.57-1.43)	1.12 (0.57-2.18)
Other	10/51 (19.6%)	1.51 (0.71-3.21)	1.66 (0.75-3.65)

Outcomes

- In crude analyses, we found little association with time period and overall attrition (death or loss to follow-up), HR post vs pre: 0.81; 95% CI: 0.53-1.25.
- After adjustment the association was similar, HR: 0.75; 95% CI: 0.40-1.40, but again with wide confidence intervals making it difficult to draw strong conclusions.
- Male sex and a non-standard ART regimen were associated with increased attrition

CONCLUSIONS

While early outcomes for TB patients were similar pre- and post- policy change, our data suggest that initiating CD4 counts have begun to increase. If this trend continues it could lead to better outcomes for co-infected patients.

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