TIMELINESS OF ART INITIATION AMONG HIV-INFECTED PATIENTS WITH TB IN SUB-SAHARAN AFRICA

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Background

Studies have shown that initiating antiretroviral therapy (ART) early during tuberculosis (TB) treatment increases survival among people living with HIV (PLWH).[1-3] In 2010, the World Health Organization (WHO) released guidelines recommending ART initiation as soon as possible within 8 weeks of starting TB treatment, regardless of CD4+ count.[4] Prior guidelines had recommended delaying ART until after 8 weeks of TB treatment for patients with CD4+ count ≥200 cells/μL. Since the release of 2010 guidelines, the proportion of PLWH with TB on ART in the African region has increased from 44% in 2010 to 55% in 2012 .[5] However, few studies have examined the change in time to ART initiation with adoption of the new WHO guidelines in routine service delivery settings.[6]

Methods

We used routinely-collected data from electronic patient-level databases in 74 HIV clinics in Mozambique and Rwanda supported by ICAP-Columbia University. The sample consisted of adult HIV patients newly enrolling in HIV care who were ART-naïve and ART-eligible at enrollment based on the prevailing WHO guidelines during 05/2003-03/2013.

We compared time to ART initiation before vs. after adoption of the 2010 WHO guidelines for ART-eligible patients both with and without TB at enrollment into HIV care. "On TB treatment at enrollment" variable was used to identify patients with TB at enrollment.

We compared patient characteristics before vs. after adoption of guidelines, using chi-square and Wilcoxon rank-sum tests for categorical and continuous variables, respectively. We used stratified Kaplan-Meier survival curves to estimate median days to ART initiation. Patients who were lost to follow-up or died during the pre-ART phase were censored at their last clinic visit date. Generalized Wilcoxon tests were used to compare differences before vs. after adoption of guidelines. We conducted sensitivity analyses to examine whether results were robust to different censoring assumptions.

Results

Patient characteristics: Of a total of 179,086 PLWH enrolled in HIV care, 49,375 (28%) were ART-eligible at enrollment, and 36,508 (74%) of ART-eligible PLWH initiated ART. Of all PLWH, 5,014 (2.8%) had TB at enrollment. Median CD4+ count at enrollment was 142 cells/μL.

In both countries, a higher proportion of PLWH enrolled after (vs. before) adoption of 2010 WHO guidelines were female, ART eligible at enrollment, and had TB. They were also less likely to die or be lost to follow-up during the pre-ART phase. In Rwanda, patients without TB enrolling after (vs. before) adoption of 2010 WHO guidelines had higher CD4+ count (See Table 1 for further country-specific patient characteristics).

Time to ART initiation: Median time to ART initiation for PLWH with TB at enrollment decreased after 2010 WHO guidelines adoption from 55 to 28 days in Mozambique and from 58 days to 43 days in Rwanda (Figures 1a and 1b). The proportion of PLWH with TB at enrollment initiating ART within 8 weeks increased from 69.6% to 82.7% in Mozambique and 57.8% to 68.1% in Rwanda. Accounting for the unequal distribution of death and lost to follow-up before and after adoption of guidelines did not significantly alter the results. Median days to ART initiation are shown in Table 2.

- In Mozambique, PLWH with TB at enrollment had a significantly longer time to ART initiation vs. ART-eligible PLWH without TB prior to 2010 WHO guidelines adoption (p<0.001) but a significantly shorter time to ART initiation after guidelines adoption (p<0.001).
- In Rwanda, PLWH with TB at enrollment had a longer time to ART initiation vs. ART-eligible PLWH without TB both before and after 2010 WHO guidelines adoption (p<0.001).

Figure 1a: Time to ART initiation among PLWH with TB in Mozambique

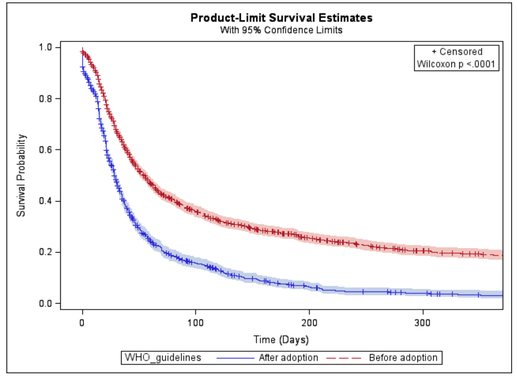

Figure 1b: Time to ART initiation among PLWH with TB in Rwanda

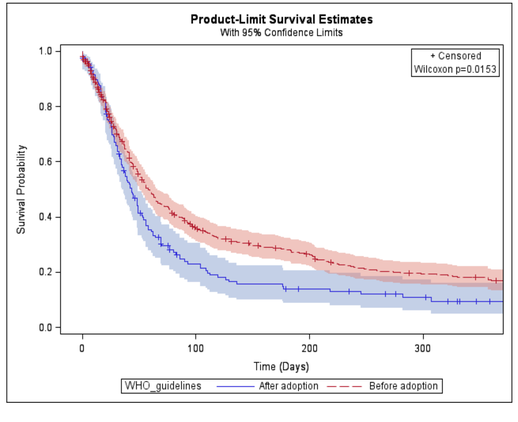

Table 1: Patient Characteristics

	Mozambique			Rwanda		
	Before adoption	After adoption	p-value	Before adoption	After adoption	p-value
Number of sites	32	33		40	40	
Number of patients enrolled	108,122	35,374		29,674	5,916	
Median (IQR) age	32 (26-40)	30 (25-39)	<0.0001	37 (31-44)	35 (29-44)	<0.0001
Proportion female, of enrolled	56.0%	59.2%	<0.0001	57.5%	54.5%	0.0120
Number ART eligible patients	29,169	10,313		7,692	2,201	
Proportion ART eligible, of enrolled	27.0%	29.2%	<0.0001	25.9%	37.2%	<0.0001
Number of patients with TB	2,806	1,539		509	160	
Proportion TB, of enrolled	2.6%	4.4%	<0.0001	1.7%	2.7%	<0.0001
Number of patient initiating ART	20,553	7,219		6,787	1,949	
Proportion on ART, of ART eligible	70.5%	70.0%	0.3765	88.3%	88.6%	0.6840
Median (IQR) CD4+ count (cells/μL)	141 (70-216)	147 (73-147)	0.0651	129 (72-185)	207 (116-289)	<0.0001
% missing	13.0%	14.6%		1.5%	0.6%	
Patients with TB	196 (95-370)	202 (86-395)	0.9809	155 (60-294)	129 (46-304)	0.2958
% missing	43.6%	49.6%		7.1%	5.0%	
Patients without TB	139 (69-210)	144 (72-212)	0.2716	128 (72-183)	211 (122-289)	<0.0001
% missing	9.7%	8.5%		1.1%	0.2%	
Proportion pre-ART lost to follow-up, of ART eligible	25.4%	8.8%	<0.0001	3.0%	1.2%	<0.0001
Proportion pre-ART deaths, of ART eligible	2.2%	1.1%	<0.0001	4.1%	1.5%	<0.0001

Table 2: Median Days to ART initiation (IQR)

	Mozambique			Rwanda		
	Before adoption	After adoption	p-value	Before adoption	After adoption	p-value
ART-eligible PLWH without TB	33 (17-76)	36 (20-68)	0.8946	23 (14-42)	23 (13-43)	0.9981
ART-eligible PLWH with TB*	55 (23-209)	28 (15-59)	<0.0001	58 (25-205)	43 (23-86)	0.0153

*After adoption, all PLWH with TB were ART-eligible.

Conclusion

In this large cohort, adoption of 2010 WHO TB/HIV guidelines was associated with a shorter time to ART initiation for PLWH with TB in Mozambique and Rwanda. The results suggest a change in clinical practice occurred in conjunction with adoption of new guidelines. However, as date of TB treatment initiation was not available, time from TB treatment initiation to ART initiation was not assessed. While, the apparent impact of the WHO guidelines is encouraging, further efforts are needed to more promptly initiate ART for eligible PLWH, particularly those with TB.

References

1. Karim 2010, 2. Havlir 2011, 3. Blanc 2011, 4. Antiretroviral Therapy for HIV Infection In Adults and Adolescents 2010, 5. WHO Global Tuberculosis Report 2013, 6. Vijayan 2013

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