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Title: TB incidence in HIV infected patients who are started on antiretroviral therapy in a South African mining population

Background and objectives:

Antiretroviral therapy (ART) was initiated in eligible miners within an industrial programme setting. TB incidence following antiretroviral initiation was measured and risk factors for TB incidence are described. First-line ART was zidovudine, lamivudine and efavirenz, and criteria for ART initiation were CD4 below 250 cells/ml; a WHO stage 4 condition; or a WHO stage 3 condition and CD4 count <350 cells/ml.

Methods:

We retrospectively analysed routine data from patients at ART initiation. TB cases were ascertained from the company TB database that collects all cases that are started on TB treatment.

Results: 1363 miners (mean age 41.9y; 96% males, %WHO stage and %VL group) were followed up after ART initiation for incidence of TB. During followup (2413 person years(py), median followup 1.56y), 257 patients developed TB with an incidence was 10.64 per 100 person years(py). TB incidence was increased with decreasing lower as baseline CD4 count at ART initiation increased: CD4 count (cells/mm³) <50: 14.4/100py; 51-200:12.94/100py; 201-250: 9.24/100py; >250: 6.03/100py. TB incidence was also highest in the first 45 days after ART initiation (26.06/100py) and but reduced declined with increasing duration of treatment to following that as follows: 45-90days 14.92/100py, 91 – 180days 11.22/100py, 181 – 360days 8.85/100py, 361 – 540 days 5.69/100py and 540-720 days: 4.09/100pys. On the univariate analysis, risk factors found to be associated with increased TB incidence were CD4 count at baseline (P<0.001), baseline viral load (P<0.001) and WHO stage baseline(p<0.001). On the multivariate analysis, WHO stage (P=0.04) and baseline viral load (P<0.01) emerged as the independent risk factors.

Conclusions: TB incidence in patients starting ART on ART is remains still extremely high, even after 2 years of treatment, but does reduce with higher CD4 counts at baseline and after the first three months on treatment. The high incidence immediately following ART is probably due to immune reconstitution syndrome. All patients should be screened for TB before starting ART. TB incidence could be further reduced by concomitant isoniazid preventive therapy.

Additional comments:

Either censor follow up when patients stop ART (preferred for this abstract) or include FU after ART stopped and describe this in the methods and results sections.

You should mention all risk factors evaluated in the abstract, eg age group, prior TB history, gender and prior IPT use and stopped ART if you include in this abstract.

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Table 4: Risk factors for TB incidence after initiation of ART

		TB cases (first-time cases)	Total FU time (PYrs)	TB episodes Rate/100Py	95%CI
Overall		257	2414	10.65	9.42 – 12.03
Sex	Male	255	2368	10.77	9.52 – 12.17
	Female	2	45	4.42	1.11 – 17.67
Age – grouped	<30	9	140	6.43	3.34 – 12.36
	30-39	63	543	11.60	9.06 – 14.85
	40-49	123	1171	10.51	8.80 – 12.54
	≥ 50	62	560	11.07	8.63 – 14.20
CD4 count at baseline	≤ 50	42	291	14.40	10.64 – 19.48
	51-200	135	1043	12.94	10.93 – 15.32
	201-250	32	346	9.24	6.53 – 13.07
	>250	36	597	6.03	4.35 – 8.36
Treatment stopped	No	140	1478	9.47	8.03 – 11.18
	Yes	117	936	12.50	10.43 – 14.99
Previous TB	Yes	79	668	12.00	9.63 – 14.97
	No	178	1756	10.14	8.75 – 11.74
Baseline Viral load	<10 000	21	365	5.75	3.74 – 8.81
	10000-100000	97	981	9.89	8.10 – 12.06
	>100000	90	580	15.5	12.62 – 19.07
INH started	No	256	2402	10.66	9.43 – 12.05
	Yes	1	12	8.32	1.17 – 59.04
WHO stage baseline	1	13	170	7.63	4.43 – 13.14
	2	18	256	7.03	4.43 – 11.15
	3	121	831	14.55	12.18 – 17.39
	4	32	249	12.84	9.09 – 18.17
Time after starting ART	<45 days	81	311	26.06	20.96 – 32.39
	45 – 90 days	42	281	14.92	11.03 – 20.19
	91 – 180 days	56	499	11.22	8.64 – 14.58
	181 – 360 days	35	396	8.85	6.35 – 12.32
	361 – 540 days	18	316	5.69	3.59 – 9.04
	540 – 720 days	25	611	4.09	2.77 – 6.06

Univariate and multivariate analysis was done and detailed results are shown in Appendix 3. The following factors are independent risk factors for developing TB after ART initiation: Viral load at baseline (P<0.01) and WHO stage (P=0.04).

Table 5. Univariate and Multivariate analysis of TB incidence in patients who were started on ART

		Univariate analysis		Multivariate analysis	
		Hazard Ratio (HR)	95% CI	Hazard Ratio (HR)	95% CI
Age – grouped	<30	1.00	P=0.33	1.00	P=0.69
	30-39	1.83	0.91 – 3.67	1.18	0.49 – 2.83
	40-49	1.71	0.87 – 3.36	0.92	0.40 – 2.13
	≥ 50	1.67	0.83 – 3.37	0.95	0.40 – 2.26
CD4 count at baseline	≤ 50	1.00	P<0.001	1.00	P=0.27
	51-200	0.85	0.60 – 1.20	1.19	0.73 – 1.97
	201-250	0.62	0.39 – 0.99	0.89	0.45 – 1.74
	>250	0.42	0.27 – 0.66	0.79	0.43 – 1.47
Baseline Viral load	<10 000	1.00	P<0.001	1.00	P<0.01
	10000-100000	1.66	1.03 – 2.66	1.06	0.63- 1.79
	>100000	2.51	1.56 – 4.04	1.49	0.87 – 2.56
WHO stage baseline	1	1.00	P<0.001	1.00	P=0.04
	2	0.94	0.46 – 1.92	1.10	0.49 – 2.45
	3	2.06	1.16 – 3.65	2.12	1.09 – 4.12
	4	1.77	0.93 – 3.38	2.10	1.00 – 4.41