HIV-ASSOCIATED TB IN A LOW BURDEN COUNTRY: IS SCREENING FOR LATENT TB STILL NEEDED?

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INTRODUCTION

Combination antiretroviral therapy (cART) reduces the risk of developing tuberculosis (TB) in persons with HIV both in low and high TB burden countries.

Nonetheless, some studies suggest that this risk may remain above that of background HIV-uninfected populations. It is not clear whether in low TB burden countries the recommendation of guidelines to screen and treat for latent TB infection (LTBI) all persons with newly diagnosed HIV infection is presently justified.

MATERIAL AND METHODS

We analyzed data of persons enrolled in the ICONA cohort in 2006-2017 in Italy (a low TB incidence country, 6.6 cases per 100,000 in 2016) diagnosed with HIV within 6 months of enrolment. We considered cases of TB occurring up to December 2017 and diagnosed at first presentation or during follow-up.

Factors associated with presenting with TB at the time of HIV diagnosis (± 3 months) were identified by multivariable logistic regression.

Incidence rates of TB from the time of starting cART were calculated, and Poisson regression model was used to identify factors associated with the incidence of TB in the study population.

RESULTS

We included in this analysis 7,533 persons with HIV; of them 57% were males and 71.1% were born in Italy. Among foreign born persons, area of origin was: Sub Saharan Africa 35%, Latin America 27% and Eastern Europe 17%.

Overall, 123 TB cases occurred in the study population, the vast majority (84%) being diagnosed at the time of HIV diagnosis (Fig 1).

TB at HIV diagnosis. The risk of being diagnosed with TB decreased in individuals diagnosed with HIV in more recent time periods while it increased significantly for those diagnosed at more advanced levels of immunosuppression and for foreign born individuals (Tab.1)

Figure1. Timing of onset of TB in HIV-infected individuals in relation to the date of diagnosis of HIV infection and the date of starting cART

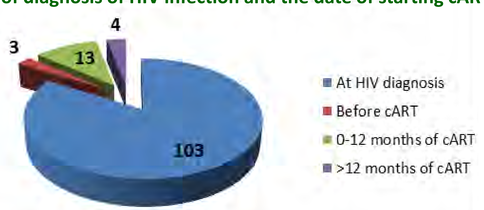

Table 1. Factors associated with presenting with TB at the time of HIV diagnosis

Characteristics	TB (N=103)	Not TB (N=7430)	OR of TB: Unadjusted OR (95% CI)	p-value	OR of TB: Adjusted* OR (95% CI)	p-value
Place of birth				<0.001		<.001
Italy	24 (23.3%)	5335 (71.8%)	1		1.00	
Other	79 (76.7%)	2095 (28.2%)	8.38 (5.29, 13.27)		5.70 (3.24, 10.04)	
CD4 count				<0.001		<.001
350+	14 (16.3%)	3055 (49.9%)	1		1.00	
201-350	14 (16.3%)	1230 (20.1%)	2.48 (1.18, 5.23)		2.05 (0.97, 4.37)	
0-200	58 (67.4%)	1842 (30.1%)	6.87 (3.82, 12.35)		4.85 (2.64, 8.93)	
Period of HIV diagnosis				0.100		0.033
2006-2009	17 (16.5%)	859 (11.6%)	1		1.00	
2010-2013	42 (40.8%)	2666 (35.9%)	0.80 (0.45, 1.41)		0.59 (0.31, 1.11)	
2014-2018	44 (42.7%)	3905 (52.6%)	0.57 (0.32, 1.00)		0.43 (0.23, 0.81)	

*Adjusted for all factors included in table and for mode of HIV transmission, age, sex and education – Logistic regression analysis

TB among persons on cART. Seventeen cases of TB occurred over 19,757 person-years of follow-up (PYFU) for an overall incidence of 0.86 per 1,000 PYFU (95%CI: 0.50 - 0.13) among persons on cART. Incidence rates tended to be lower among persons born in Italy, and the highest incidence was recorded among foreign born persons starting cART at low CD4 cells count (Fig. 2). In multivariable analysis the risk of developing TB significantly decreased after the first 12 months of cART, while it was significantly higher for foreign born persons (Tab,2).

Figure2. TB incidence rates among persons on cART by place of birth and CD4 cells count

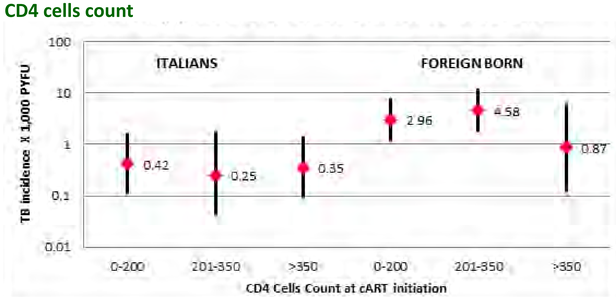

Table 2. Factors associated with the occurrence of TB after starting cART

Characteristics	N. TB	PYFU	Relative Rates of developing TB: Rates x 1,000 PYFU (95% CI)	Unadjusted RR (95% CI)	p-value	Adjusted* RR (95% CI)	p-value
Place of birth							
Italy	7	15947	0.44 (0.21, 0.92)	1		1.00	
Other	10	3810	2.62 (1.41, 4.88)	5.98 (2.28, 15.71)	<0.001	5.03 (1.39, 18.18)	0.014
CD4 count at cART							
350+	3	6783	0.44 (0.14, 1.37)	1		1.00	
201-350	5	4810	1.04 (0.43, 2.50)	2.35 (0.56, 9.83)	0.242	2.26 (0.52, 9.76)	0.274
0-200	6	6091	0.98 (0.44, 2.19)	2.23 (0.56, 8.91)	0.257	1.73 (0.41, 7.35)	0.458
Duration of ART, months							
0-3	4	1988	2.01 (0.76, 5.36)	1		1.00	
4-12	9	3887	2.32 (1.20, 4.45)	1.15 (0.35, 3.74)	0.815	0.94 (0.28, 3.23)	0.925
12+	4	13882	0.29 (0.11, 0.77)	0.14 (0.04, 0.57)	0.006	0.12 (0.03, 0.57)	0.008

*Adjusted for all factors included in table and for sex, age, mode of HIV transmission, current calendar period, education – Poisson regression model

CONCLUSIONS

- More than 80% of the cases of TB in our study were diagnosed at the time of HIV diagnosis, although the risk of presenting with TB significantly decreased over time. These case cannot be prevented by screening for and treating LTBI.
- Incidence rate of TB among persons on cART is higher during the first year of treatment. Most of these cases may reflect either IRIS/unmasking or still incomplete immune reconstitution. Incidence of TB during cART remains higher than in general population.
- Foreign born persons are at increased risk of presenting with TB and of developing TB during cART.
- Promoting early HIV diagnosis and immediate initiation of cART appear to be the most important interventions to further decrease the risk of HIV-associated TB in a low TB burden country.
- Additional prevention efforts should be focused on persons born in high TB burden countries and on those diagnosed with HIV at low CD4 level.
- The effectiveness of screening and treatment of LTBI among persons with HIV from low TB burden countries and with less advanced immunosuppression should be reevaluated.

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