Poster #1000

CROI 2008

Characteristics and clinical outcome of patients with HIV-associated tuberculosis (HIV/TB) in Europe and Argentina

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BACKGROUND

Tuberculosis (TB) is globally the most common serious complication of HIV infection and poses many challenges to the clinical management.

OBJECTIVES

- To establish a cohort of HIV/TB coinfected patients
- To compare regional differences in clinical characteristics and outcomes of patients with HIV/TB coinfection.

METHODS

895 consecutive HIV-patients diagnosed with TB between 1/2004 and 12/2006 in 47 clinics across Europe and Argentina were included in this analysis.

Patients were included in this study if they had either:

- confirmed diagnosis of TB: documented by either positive smear, culture, nucleic acid amplification test or histology

or

- clinically-defined diagnosis of TB: clinical features of TB, anti-TB therapy administrated and TB diagnosis not subsequently ruled out.

Information collected included:

- Demographic data,
- Previous TB diagnosis,
- Clinical presentation of current TB disease,
- Microbiological characterisation of the TB infection, including resistance to anti-TB drugs and laboratory assessments,
- Anti-TB treatment
- Clinical outcome of the TB disease, and
- Data on underlying HIV-infection

Demography, clinical characteristics and outcomes of HIV/TB patients were compared across regions of residence. The following countries participated in the study:

- Argentina/Southern Europe (A/S): Argentina, Italy, Spain (N=151, 14 clinics)
- Central/Northern Europe (C/N): France, Denmark, Switzerland, United Kingdom (N=130, 21 clinics)
- Eastern Europe (E): Belarus, Latvia, Romania, Russia, Ukraine (N=614, 12 clinics)

Table 1

Characteristics of HIV/TB patients in Europe and Argentina

At TB diagnosis	A/S N=151	C/N N=130	E N=614	*p*
Gender, male, %	64	47	72	< 0,0001
Age, years, median (IQR)	36 (31-43)	37 (31-44)	30 (26-35)	< 0,0001
Origin, other than country of site, %	19	69	2	< 0,0001
Ethnicity, non-Caucasian,%	49	64	1	< 0,0001
HIV risk factor, IDU, %	19	9	62	< 0,0001
TB risk factor, %[1]				< 0,0001
IDU	39	14	80	
Prison	7	2	24	
Alcohol	24	3	36	
Recent exposure to TB	32	9	14	
TB symptoms duration, %				
< 1 month	31	25	23	< 0,0009
1-3 months	51	42	43	
> 3 months	14	14	23	
CD4 cell count, cells/µl, median (IQR)	155 (64-306)	149 (81-300)	209 (83-472)	0.0017
Confirmed diagnosis of TB, %[2]	81	86	70	< 0,0001
- by microscopy only, %	27	8	20	0.015
Known HIV+ ≥ 1 month prior TB,%	68	64	71	0.32

[1] % out of patients with known risk factor for TB (N=754)
[2] TB diagnosis confirmed by either microscopy, culture, PCR or histology

Table 2

Anti-tuberculosis and antiretroviral therapies

	S/A	C/N	E	*p*
Initial TB treatment: N =	146	130	583	
4 1st line drugs, %	74	83	26	< 0,0001
3 1st line drugs, %	17	12	41	< 0,0001
> 1 2nd line drugs, %	13	12	63	< 0,0001
Streptomycin, %	45	6	55	< 0,0001
Any Antiretroviral therapy (ART): N=	122	119	149	
% on ART ≥ 1 month prior to TB	31	39	8	<0.0001
Median (IQR) time on ART, months	34 (9-73)	54 (23-88)	22 (4-46)	0.0030
% on ART at 6 month after TB, Kaplan-Meier (95% CI)	68 (58-77)	81 (72-90)	23 (19-27)	<0.0001

RESULTS

Patient Characteristics

- Large regional differences in patient characteristics were noted (**Table 1**)
- Patients in E were almost exclusively Caucasian and born locally, more often had injection drug use (IDU) as risk factor for HIV (62%) and TB (80%), and were younger. Prison and alcohol abuse were also common risk factors for TB acquisition in E whereas resent exposure to TB played an important role in TB acquisition in A/S. Patients in C/N more often were non-Caucasian and originated from countries where TB was endemic
- TB was diagnosed ≤1 month of HIV diagnosis in 29-36% (p=0.32). CD4 cell count at the time of TB diagnosis was higher in patients from E. In C/N, a higher proportion of TB diagnosis was confirmed (i.e. by microscopy, PCR, culture or histology), and TB diagnosis less frequently relied on smears for acid-fast-bacilli
- The duration of TB-related symptoms for was similar across the 3 regions
- Conventional 1st-line TB treatment regimens (rifampin, isoniazid, pyrazinamide, ethambutol) were frequently used in C/N and A/S. Patients in E started anti-TB treatment with 3 1st line drugs more commonly and had a 2nd line drug added to the initial regimen: in 55% of cases it was Streptomycin (**Table 2**)
- Antiretroviral treatment (ART) was used significantly less in E, both prior to and concurrent with TB treatment (**Table 2**)

Follow-up and clinical outcome

- Median (IQR) follow-up time since the date of TB diagnosis was 13 (2-25), 18 (12-28) and 6 (2-12) months in A/S, C/N and E respectively
- The proportion of patients with a successful outcome (cure or completion of TB treatment) was lower, and the proportion who died was substantially higher in E compared to the other regions (**Table 3, Figure 1**)

CONCLUSIONS

- HIV-infected patients who developed TB across regions of Europe and Argentina differed by their demographical and clinical characteristics
- Marked differences in outcome of HIV/TB coinfected patients were noted across the regions. Mortality rate was significantly higher in Eastern Europe compared with Argentina/Southern Europe and Central/Northern Europe
- Differences in patient demographics, access to combination antiretroviral therapy, TB drug-susceptibility and use of rifampicin-based TB therapy may have contributed to the observed differences in outcome
- There is an urgent need to further understand why these differences exist and how outcome of HIV/TB in Eastern Europe can be improved
- One of the study limitations was that there could be a potential differences in patients characteristics and outcomes within a region

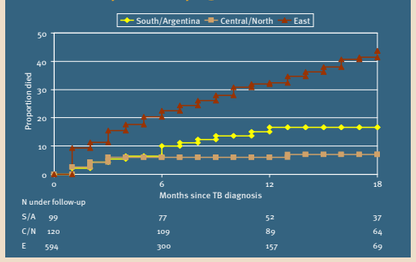
Table 3

Clinical outcomes of HIV/TB patients

	S/A	C/N	E	*p*
N	99	120	599	
Cure/ Treatment completed, %	67	87	47	< 0,0001
Treatment Failure, %	2	2	5	0.204
Defaulted/interrupted treatment, %	5	3	4	0.817
Lost to Follow-up, %	11	2	14	0.0007
Died, %	15	7	31	< 0,0001

Figure 1

Kaplan-Meier progression to death



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