Poster # ZO - 03

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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 complication of HIV infection and poses many challenges to the clinical management of patients.

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 consecutively enrolled HIV-patients diagnosed with TB between Jan. 2004 and Dec. 2006 in 47 clinics across Europe and Argentina were included in this analysis.

Patients were included in this study if they had either:

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

or

- A clinically-defined diagnosis of TB including clinical features of TB, anti-TB therapy, 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
- 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, median (IQR)	36 (31-43)	37 (31-44)	30 (26-35)	< 0,0001
Origin out of site country %	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	
CD_4 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 recent 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). CD_4 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 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**)

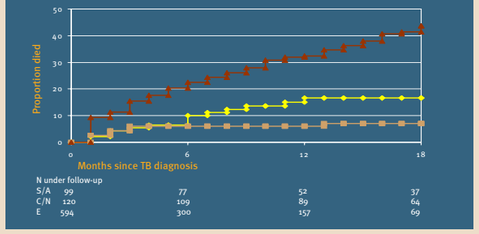
Table 3

Clinical outcomes of HIV/TB patients

	S/A N=99	C/N N=120	E N=599	p
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



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

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