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 administered 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=430, 21 clinics)
- Eastern Europe (E): Belarus, Latvia, Romania, Russia, Ukraine (N=614, 12 clinics)

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). 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 smear for acid-fast-bacilli.
- The duration of TB-related symptoms was similar across the 3 regions
- Conventional 1st line TB treatment regimens (rifampicin, isoniazid, pyrazinamide, ethambutol) were frequently used in C/N and A/S. Patients in E started anti-TB treatment with a 3 line drugs more commonly and had a 2nd line drug added to the initial regimen in 53% of cases it was Streptomycin (Table 1).
- Antituberculosis treatment (ART) was used significantly less in E, both prior to and concurrent with TB treatment (Table 1).

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 (2-11) months in E, C/N and A/S 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 demographic and clinical characteristics.
- Marked differences in outcome of HIV/TB coinfection 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 anti-TB and antiretroviral therapies, TB drug-susceptibility and use of rifampicin-based TB therapy may have contributed to the observed differences in outcomes.
- 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.