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TB:HIV an international prospective observational study

Major Challenges in Clinical Management of TB/HIV Coinfected Patients in Eastern Europe Compared with Western Europe and Latin America

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BACKGROUND

Rates of both TB/HIV coinfection and multidrug-resistant (MDR) TB are increasing in Eastern Europe (EE). Data on the clinical management of TB/HIV coinfected patients are scarce.

AIMS

- To study the clinical characteristics of TB/HIV coinfected patients in Europe and Latin America (LA) at TB diagnosis.
- Identify factors associated with MDR-TB.
- Assess the activity of initial anti-TB treatment regimens given the results of drug-susceptibility tests (DSTs).

METHODS

Characteristics of patients were compared across regions. Risk factors for MDR-TB were identified in logistic regression models. Among patients with DST done within the first month of anti-TB therapy, we linked empiric anti-TB treatment regimens to the DST results and calculated the distribution of patients receiving 0, 1, 2, 3 and ≥ 4 active drugs in each region. If a specific DST result was not available for a given drug, the patient was assumed to be sensitive to this drug; sensitivity analyses restricted to patients with complete resistance results (DST results available for all anti-TB drugs used in the empiric treatment regimen) were also performed.

RESULTS

- 1413 TB/HIV coinfected patients were enrolled from 62 clinics in 19 countries in EE, Western Europe (WE), Southern Europe (SE) and LA from 01/01/2011 to 31/12/2013.
- Significant differences were observed between EE, WE, SE and LA; in EE, TB/HIV patients had poorer exposure to cART, less often a definite TB diagnosis (culture or PCR positive for *M. Tuberculosis)*, and more often MDR-TB compared to other parts of Europe and LA (**Table 1 and 2**).
- A history of injecting drug use, prior anti-TB treatment and living in EE were independently associated with MDR-TB (**Figure 1**).
- For 585 patients with available DST, the empiric anti-TB treatment contained ≥3 active drugs in 66% of patients in EE compared with 90-96% of patients in other regions (**Figure 2a**). Had the patients received empiric therapy with standard therapy (Rifampicin, Isoniazid, Pyrazinamide, Ethambutol (RHZE)), the corresponding proportions would not have changed substantially (**Figure 2b**).
- Large intraregional variations in levels of MDR-TB and use of empiric RHZ-based anti-TB treatment were observed especially in EE, where the proportion of MDR-TB cases ranged from 11 to 59% between countries, and the use of RHZ-based empiric anti-TB treatment ranged from 54% to 96%.

CONCLUSIONS

- Empiric anti-TB therapy in EE was suboptimal, with less than two-thirds of patients receiving three active drugs, and improved compliance with standard RHZE treatment does not seem to be the solution. Improved management of TB/HIV patients requires routine use of DST, empiric anti-TB therapy according to prevailing resistance patterns, and more widespread use of cART.

Table 1

Patient characteristics

		Eastern Europe, N (%)	Western Europe, N (%)	Southern Europe, N (%)	Latin America, N (%)	P-value
Total		844 (100)	152 (100)	164 (100)	253 (100)	
Gender	Female	210 (24.9)	67 (44.1)	45 (27.4)	67 (26.5)	<.0001
Ethnicity	White	773 (95.2)	39 (26.2)	112 (72.3)	47 (19.0)	<.0001
	Black African	0 (0)	94 (63.1)	27 (17.4)	2 (0.8)	
Age	Years, median (IQR)	35 (31 - 40)	37 (32 - 48)	42 (33 - 48)	38 (30 - 45)	<.0001
HIV Risk Group	MSM	12 (1.5)	16 (10.8)	29 (18.2)	80 (32.3)	<.0001
	IDU[1]	502 (63.5)	9 (6.1)	45 (28.3)	33 (13.3)	
	Heterosexual	206 (26.0)	84 (56.8)	44 (27.7)	119 (48.0)	
HIV disease	HIV+ more than 3 months before TB diagnosis	635 (75.2)	82 (54.0)	99 (60.4)	157 (62.1)	<.0001
	CD4 count, median (IQR) (cells/mm³)	107 (35 - 254)	149 (35 - 360)	129 (38 - 315)	96 (35 - 289)	0.12
HIV treatment	cART	140 (16.6)	60 (39.5)	72 (43.9)	89 (35.2)	<.0001
TB Risk Group	IDU	516 (61.1)	14 (9.2)	48 (29.3)	38 (15.0)	<.0001
	In prison in last 2 years	157 (18.6)	4 (2.6)	8 (4.9)	17 (6.7)	<.0001
	Alcohol misuse	202 (23.9)	12 (7.9)	19 (11.6)	73 (28.9)	<.0001
	TB cases in the family	62 (7.4)	9 (5.9)	11 (6.7)	43 (17.0)	<.0001
	Travel/Migration	2 (0.24)	64 (42.1)	29 (17.7)	5 (2.0)	<.0001
	None indicated	183 (21.7)	49 (32.2)	60 (36.6)	43 (17.0)	<.0001
TB Type	Pulmonary	303 (35.9)	27 (17.9)	52 (31.7)	76 (30.2)	<.0001
	Extrapulmonary	59 (7.0)	37 (24.5)	38 (23.2)	60 (23.8)	
	Disseminated	481 (57.1)	87 (57.6)	74 (45.1)	116 (46.0)	
TB in the past	Yes	111 (13.4)	14 (10.1)	21 (14.5)	41 (16.5)	0.36
Current OST[2]	Yes	16 (3.7)	6 (66.7)	21 (48.8)	0 (0)	<.0001

[1]IDU = Intravenous Drug Use.
[2]OST = Opioid Substitution Therapy. The denominator is IDU (HIV) risk group. 81 individuals (of those who were IDU's) had missing data on OST status.

Table 2

TB diagnostic status, empiric treatment regimens and drug resistance patterns

		Eastern Europe, N (%)	Western Europe, N (%)	Southern Europe, N (%)	Latin America, N (%)	P-value
Diagnosis	Definite	395 (46.8)	108 (71.1)	118 (72.0)	101 (39.9)	<.0001
	Probable	115 (13.6)	12 (7.9)	9 (5.5)	90 (35.6)	
	Presumptive	334 (39.6)	32 (21.1)	37 (22.6)	62 (24.5)	
Treatment[1]	RHZ-based	592 (71.3)	132 (87.4)	140 (86.4)	227 (89.7)	<.0001
Resistance	Tested	288 (34.1)	92 (60.5)	105 (64.0)	84 (33.2)	<.0001
	None Detected	123 (42.7)	82 (89.1)	96 (91.4)	62 (73.8)	<.0001
Tested for at least RH	Susceptible to RH	117 (48.2)	60 (90.8)	81 (91.0)	45 (73.7)	<.0001
	R resistant/ H susceptible	2 (0.8)	0 (0)	0 (0)	3 (4.9)	0.02
	R susceptible/ H resistant	27 (11.1)	3 (4.6)	5 (5.6)	4 (6.6)	0.004
	Resistant to RH (MDR-TB)	97 (39.9)	3 (4.6)	3 (3.4)	9 (14.8)	<.0001

[1]R = Rifampicin, H = Isoniazid, Z = Pyrazinamide

Figure 1

Factors associated with MDR-TB in multivariable logistic regression analysis

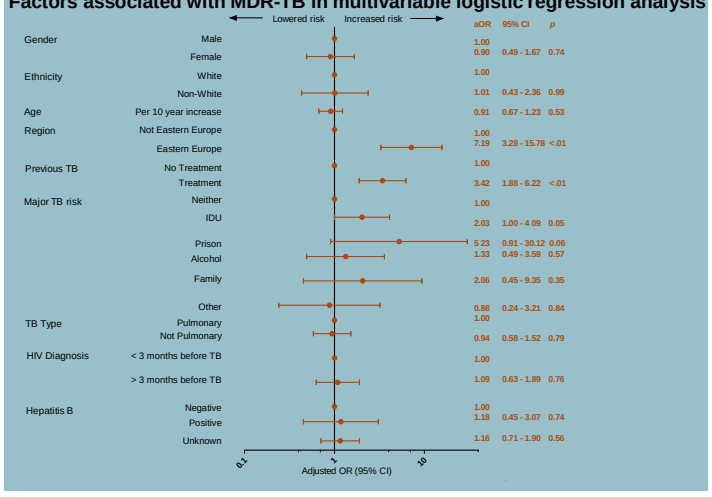

Figure 2a and 2b

Susceptibility of empiric anti-TB treatment (2a) and hypothetical susceptibility presuming RHZE had been initiated (2b)

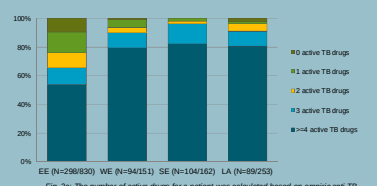

Fig. 2a: The number of active drugs for a patient was calculated based on empiric anti-TB therapy and DST results within the first month of therapy (available for 585/1396 patients)

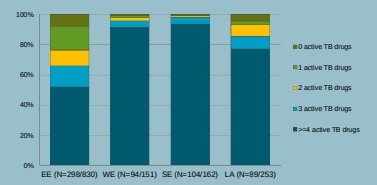

Fig. 2b: The number of active drugs in the empiric anti-TB treatment regimen, assuming RHZE had been initiated in all subjects (available for 585/1396 patients)

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SEVENTH FRAMEWORK PROGRAMME

EuroCoord