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Causes of death in HIV/TB coinfected patients
Results from the HIV/TB collaborative study

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BACKGROUND

Results from the HIV/TB study showed an estimated 1-year mortality rate of 33% in Eastern Europe compared with 7-14% in Western Europe and Argentina (**Figure 1**). Other factors, significantly associated with increased death rate were: initiation of TB treatment with regimens not containing 3 main anti-TB drugs (rifampicin, isoniazid and pyrazinamide (RHZ)), resistance to at least rifampicin, and absence of cART.

OBJECTIVES

To assess and compare causes of death (COD) in HIV/TB patients across regions.

METHODS

The CoDe procedure (http://www.chip.dk/CoDe) was used to ascertain underlying and immediate COD.

- **Underlying COD** was defined as a disease/condition which "initiated the train of morbid events leading directly or indirectly to death" (WHO ICD10)
- **Immediate COD** was a disease/condition directly causing death. The immediate COD could be the same as underlying COD
- **Immediate COD** was used as endpoint for the present analysis

Consecutive HIV-infected patients diagnosed with definite, probable or presumptive TB between 2004 and 2006 were included in the analyses. The analyses were restricted to patients who had died within 12 months of TB diagnosis and for whom CoDe forms were available. COD for patients from Eastern Europe (EE) were compared to COD for patients from Western Europe and Argentina (WEA)[1]. Within regions, CODs were also stratified by the interval between TB diagnosis and time of death (< 3 months, 3-12 months).

RESULTS

Of the 1,074 patients in the HIV/TB study, 200 (19%) died within one year of TB diagnosis (158 in EE, 42 in WEA). CoDe forms were available for 167 (83%) patients (EE=142, WEA=25). COD was based on post-mortem findings in 104 (62%). Patient characteristics at the time of TB diagnosis are presented in **Table 1**. In EE, patients who died were more likely to have been diagnosed with extrapulmonary or disseminated TB and prior AIDS events, and to be infected with drug-resistant *Mycobacteria* strains, they had lower CD4 cell counts, and they were less likely to have been on cART at the time of TB diagnosis compared to those who were still alive at 1 year.

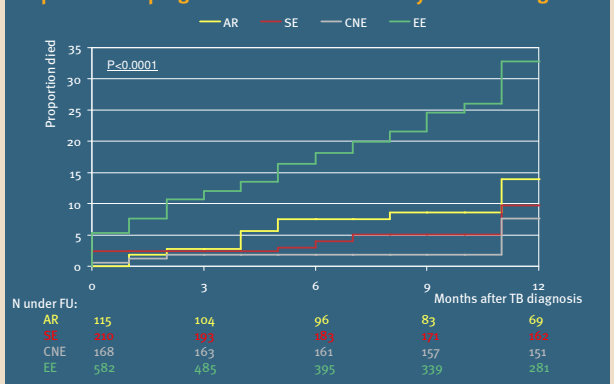
Overall, TB was the COD in 113 (68%) patients, with death resulting from TB-sepsis/multi-organ failure in 33 (29%) and TB-meningitis or TB brain in 28 (25%) (**Figure 2**). TB was the immediate COD in 108 (76%) of patients in EE and 5 (20%) in WEA (p<0.001). In WEA, non-infectious comorbidities, AIDS-defining conditions other than TB and non-opportunistic infections were relatively common COD (**Figure 3**). TB progression remained the main COD for patients in EE regardless of whether they died shortly after TB diagnosis (<3 months) or later (3-12 months). Although the numbers for WEA were small, there is an indication that if patients in WEA had survived the first 3 months, they were more likely to die from non-TB-related CODs (**Figure 3**).

SUMMARY

HIV/TB patients in EE were more likely to die within 12 months of TB diagnosis compared to patients in WEA, and these deaths were more often due to TB than in patients from WEA. There is an urgent need to reduce mortality in HIV/TB patients. Earlier TB diagnosis, prompt introduction of optimal TB treatment (which may require the addition of second line agents to 4-drug first line therapy) may limit inflammation and progressive dissemination of TB, while earlier initiation of cART may further contribute to reducing the risk of death.

Figure 1

Kaplan- Meier progression to death within 1 year of TB diagnosis



Podlekareva et al. AIDS 2009

Table 1

Baseline characteristics of HIV/TB patients

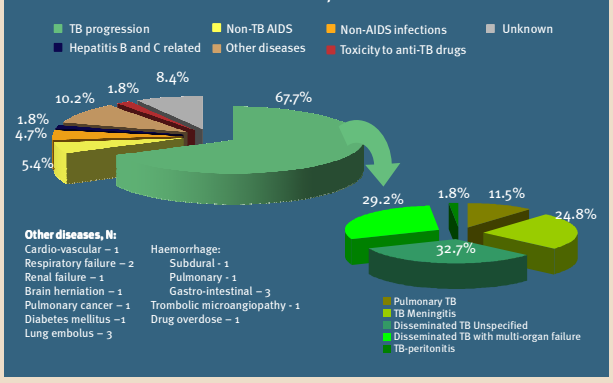
At TB diagnosis	Eastern Europe			Western Europe and Argentina		
	Dead	Alive	p	Dead	Alive	p
Total N	142	440		25	467	
%						
Gender: male	78.1	69.3	0.042	64.0	63.6	0.968
Origin: same as centre	95.1	95.5	0.850	60	50.3	0.346
HCV positive	52.8	43.6	0.056	20.0	16.7	0.592
TB risk factor: IDU	86.1	78.4	0.058	40.0	27.6	0.229
alcohol	38.0	33.1	0.309	10.0	15.4	0.751
MDR-TB*	44.0	23.8	0.004	5.9	2.5	0.380
RHZ-based initial treatment	37.3	46.8	0.048	84.0	82.7	1.000
Prior AIDS	26.8	14.1	<0.001	32.0	32.3	0.972
TB location: expulm/diss	80.3	58.4	<0.001	80.0	64.7	0.116
On cART at TB, % of HIV+	2.3	10.2	0.005	21.7	27.2	0.568
Median (IQR)						
Age, years	30 (27-34)	30 (26-35)	0.995	40 (33-46)	37 (32-43)	0.247
CD4 cell count, cells/µl	94 (39-231)	268 (127-509)	<0.001	80 (32-200)	140 (53-280)	0.071

*MDR-TB cases including cases with resistance to at least rifamycin. Numbers indicate % of those with resistance test performed (N: EE 50 and 202; WEA 17 and 244 for dead and alive patients respectively)

Figure 2

Causes of death among HIV/TB patients died within 12 months of TB diagnosis

N = 167

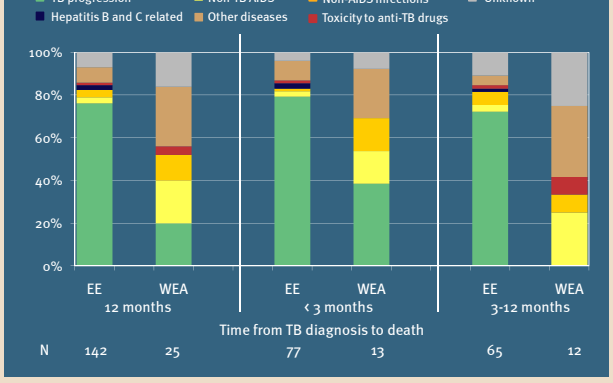


Other diseases, N:
Cardio-vascular – 1
Respiratory failure – 2
Renal failure – 1
Brain herniation – 1
Pulmonary cancer – 1
Diabetes mellitus –1
Lung embolus – 3

Haemorrhage:
Subdural - 1
Pulmonary - 1
Gastro-intestinal – 3
Trombolic microangiopathy - 1
Drug overdose – 1

Figure 3

Causes of death among HIV/TB patients died within 12 months of TB diagnosis according to the time of death



[1]Eastern Europe (EE): Belarus, Latvia, Romania, Russia, Ukraine;
Western Europe and Argentina (WEA): France, Denmark, Switzerland, United Kingdom, Italy, Spain, Argentina

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