PE3/62

TB:HIV

Delayed diagnosis of tuberculosis in persons living with HIV in Eastern Europe: associated factors and effect on mortality

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Introduction

- 10 million people diagnosed with tuberculosis (TB) globally in 2019 - 8.2% with HIV (PLWH) (1) (2).
- Delayed diagnosis of TB leads to more severe disease presentation, increased morbidity and mortality (3, 4)
  - Even more distinct effect in PLWH (5).
- HIV/TB-coinfections still a major challenge in many Eastern European countries (6).
  - a one-year mortality up to 27%
  - 79% of those deaths directly attributable to TB

Objectives

- Describe the prevalence of delayed diagnosis
- Analyze factors associated with delayed diagnosis
- Quantify the effect of delayed diagnosis on survival in PLWH.

Methods

- Prospective observational cohort study (TB:HIV study)
  - Baseline was defined as the date of TB treatment initiation, follow-up censored at 24 months
- Adult PLWH with TB diagnosis from 21 HIV and TB clinics in Belarus, Estonia, Georgia, Latvia, Lithuania, Poland, Romania, Russia and Ukraine
  - Jan 1, 2011 and Dec 31, 2013
- Delayed diagnosis = "symptom duration" (≥ 1 months vs. < 1 months) prior to diagnosis based on self-reporting

Results

Factors associated with delayed diagnosis

740 patients from Eastern Europe - 480 (64.9%) with diagnostic delay (≥1 month)

Factors associated with delayed diagnosis in the multivariable analysis (Table 1)

- Age ≥50 years
- Injecting Drug Use (IDU)
- Being ART treatment naïve at TB diagnosis
- Disseminated TB
- Weight loss
- Conversely, a previous TB diagnosis was associated with earlier diagnosis.

Organ systems affected associated with delayed diagnosis

- genitourinary
- lymphatic TB

		Total (n = 740)	< 1 month (n = 260)	≥ 1 month (n = 480)	OR (95% CI)	Adjusted OR (95% CI)
Age	Age 16 – 49	694 (93.8)	250 (96.2)	444 (92.5)	Ref	Ref
	Age ≥ 50	46 (6.2)	10 (3.8)	36 (7.5)	2.62 (1.21 – 5.66)	2.51 (1.18 – 5.32)
Exposure Group (HIV)	MSM (yes vs no)	10 (1.4)	5 (1.9)	5 (1.0)	0.54 (0.15 – 1.87)	
	IDU (yes vs no)	422 (57.0)	132 (50.8)	290 (60.4)	1.48 (1.09 – 2.00)	1.66 (1.21 – 2.29)
	Heterosexual (yes vs no)	183 (24.7)	72 (27.7)	111 (23.1)	0.79 (0.56 – 1.11)	
Treatment history (HIV)	ART naive at TB diagnosis*	558 (75.4)	176 (67.7)	382 (79.6)	1.86 (1.32 – 2.63)	1.77 (1.24 – 2.54)
	Cotrimoxazole at TB diagnosis	273 (36.9)	84 (32.3)	189 (39.4)	1.36 (0.99 – 1.87)	1.25 (0.89 – 1.74)
Previous TB	yes vs no	99 (13.4)	46 (17.7)	53 (11.0)	0.58 (0.38 – 0.89)	0.60 (0.38 – 0.95)
Clinical Presentation of TB	Pulmonary	239 (32.3)	101 (38.9)	138 (28.8)	Ref	Ref
	Extrapulmonary	54 (7.3)	23 (8.9)	31 (6.5)	0.99 (0.54 – 1.79)	0.83 (0.44 – 1.55)
	Disseminated	447 (60.4)	136 (52.3)	311 (64.8)	1.67 (1.21 – 2.32)	1.56 (1.10 – 2.19)
TB symptoms	Cough (yes vs no)	501 (67.7)	188 (72.3)	313 (65.2)	0.72 (0.52 – 0.99)	0.72 (0.51 – 1.02)
	Fever (yes vs no)	636 (86.0)	227 (87.3)	409 (85.2)	0.84 (0.54 – 1.31)	
	weight loss (yes vs no)	445 (60.1)	133 (51.2)	312 (65.0)	1.77 (1.3 – 2.42)	1.63 (1.18 – 2.24)

Table 1. Baseline characteristics associated with delayed diagnosis

Effect of delayed diagnosis on mortality

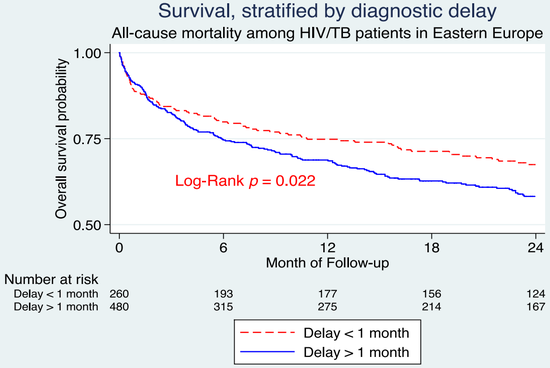

Figure 1. Kaplan-Meier survival estimates by diagnostic delay (< 1month versus ≥1 month)

All-cause mortality at 24 months: 262 (35.4%) deaths

- 80 (30.8%) in the early diagnosis group
- 182 (37.9%) in the late diagnosis group

Cox-proportional hazards model

- **36% increased risk of death** with a delayed TB diagnosis (HR 1.36; 95%CI 1.04–1.77)
- **adjusted HR 1.27 (95% CI 0.95–1.70)**
- adjusted for gender, known HIV+, CD4 cell count, prior AIDS, alcoholism, clinical presentation, TB symptoms (fever, weight loss), chest x-ray, MDR-TB, type of diagnosis, treatment with at least three active drugs, stratified by Center

Limitations

- Selection bias – those undiagnosed with TB or HIV due to early death not included.
- Circularity for delayed diagnosis; disseminated disease or weight loss can be risk factors but also consequences of delayed diagnosis.
- Identical dates of TB diagnosis and treatment initiation: not able to calculate the health care delay (diagnosis to treatment initiation).
- Health care has improved since data collection in 2013.

Conclusion

- Two thirds of PLWH with TB in Eastern Europe had a delayed TB diagnosis: higher risk of death
- Need for optimization of the current TB diagnostic cascade and HIV care
- Health care planners and policy: strengthen diagnostic capacity
- Clinicians: pay special attention to patient groups identified as being at higher risk for delayed TB diagnosis.
- Future research: focus on developing more effective diagnostic interventions to reduce delayed diagnoses.

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Declaration of interest :
Nothing to declare.

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