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Latent tuberculosis infection and associated risk factors among people living with HIV and HIV-uninfected individuals in Lithuania

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BACKGROUND

People living with HIV (PLHIV) with latent tuberculosis infection (LTBI) are at increased risk for tuberculosis (TB) reactivation compared to HIV-negative population.
Lithuania belongs to the 18 high-priority TB countries in the European region.

PURPOSE

To compare the prevalence of LTBI and LTBI-related risk factors between PLHIV and HIV-negative population.

METHODS

A cross-sectional study was conducted in three geographically distinct Lithuanian Infectious Diseases centres in Vilnius, Klaipeda and Siauliai from 08/2018 to 05/2022.
PLHIV 18-65 years of age, first seen in an HIV centre after 01/2012, and the comparison group made up of HIV-negative population, frequency matched to PLHIV by age and gender, were included in the study.
Participants were tested for LTBI using interferon-gamma release assay (IGRA) followed by tuberculin skin test (TST) in Vilnius and with IGRA only – in Klaipeda and Siauliai.
A structured questionnaire was completed by study participants to determine LTBI related risk factors.
The primary outcome was evaluated by the presence of LTBI diagnosed with positive IGRA.
Statistical analysis: logistic regression was used to assess the factors associated with LTBI. Cohen's kappa was used to determine IGRA and TST agreement.

RESULTS

- 390 PLHIV and 443 HIV-uninfected individuals enrolled, median age 41 (IQR 36-48) and 43 (IQR 36-50), 69.7% and 65.5% male, respectively (**Table**).
- In the PLHIV group, median CD4 count was 475 (IQR 268.5-672.5) cells/µl, 60.6% of patients had undetectable (<200 copies/ml) viral load and 67.4% had started ART at time of LTBI test.
- The prevalence of LTBI defined by positive IGRA among PLHIV was higher compared to HIV-negative population (17.9% vs. 11.1%, OR 1.62, 95%CI 1.16-2.28, p=0.005).
- The rate of positive TST among PLHIV and HIV-negative population was 22/242 (9.1%) vs. 24/197 (12.2%), p=0.29, respectively.
- Concordance between IGRA and TST was fair: kappa=0.2 (95%CI 0.07-0.40).
- In multivariable analyses, association with intravenous drug use (ORa 2.45, 95%CI 1.09-5.49, p=0.03) in PLHIV and a history of contact with a TB patient (ORa 3.08, 95%CI 1.26-7.53, p=0.01) in HIV-uninfected individuals were the only significant associations with LTBI (**Figure**).

LIMITATIONS

The limitation of this study is related to the relatively small sample size which may limit power to assess factors associated with LTBI.

CONCLUSIONS

The prevalence of LTBI among PLHIV in Lithuania is higher compared to HIV-uninfected population and European average.
The association with IVDU in PLHIV emphasizes the need for integrated HIV/HCV/TB and substance abuse treatment to provide patient-centred care.
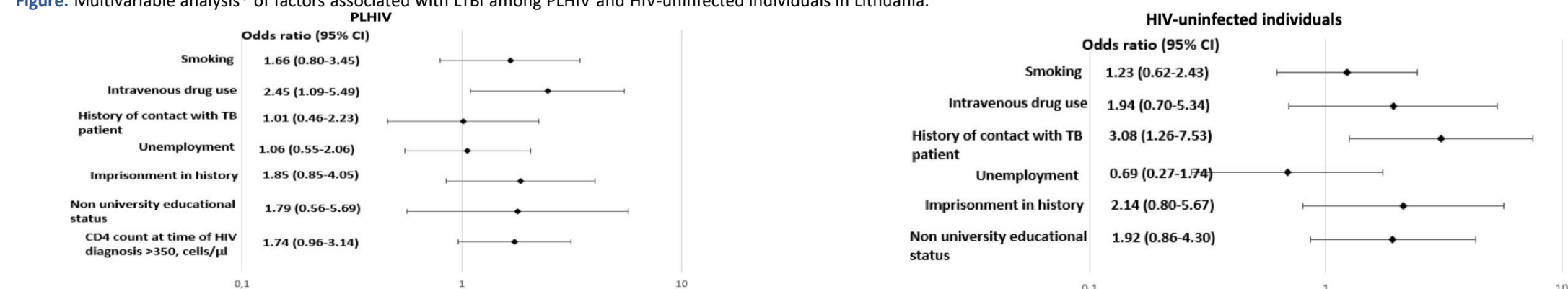
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Table. Sociodemographic and clinical characteristics of study participants (n=833)

Characteristic		PLHIV with LTBI (n=70), n (%)	PLHIV without LTBI (n=320), n (%)	Crude OR (95%CI)	P-value	HIV-uninfected individuals with LTBI (n=49), n (%)	HIV-uninfected individuals without LTBI (n=394), n (%)	Crude OR (95%CI)	P-value
Gender	Male	50 (71.4)	222 (69.4)	1.10 (0.62-1.95)	0.735	35 (71.4)	255 (64.7)	1.36 (0.71-2.62)	0.353
	Female	20 (28.6)	98 (30.6)			14 (28.6)	139 (35.3)		
Age	≤40 years	37 (52.9)	153 (47.8)	1.22 (0.73-2.05)	0.445	18 (36.7)	164 (41.6)	0.81 (0.44-1.51)	0.512
	>40 years	33 (47.1)	167 (52.2)			31 (63.3)	230 (58.4)		
Educational status	Not University	66 (94.3)	243 (75.9)	5.23 (1.85-14.81)	0.002	40 (81.6)	258 (65.5)	2.34 (1.10-4.97)	0.027
	University	4 (5.7)	77 (24.1)			9 (18.4)	136 (34.5)		
Unemployment	Yes	41 (58.6)	108 (33.8)	2.78 (1.64-4.71)	<0.001	7 (14.3)	54 (13.7)	1.05 (0.45-2.46)	0.912
	No	29 (41.4)	212 (66.2)			42 (85.7)	340 (86.3)		
History of contact with TB patient	Yes	11 (15.7)	44 (13.8)	1.17 (0.57-2.40)	0.669	8 (16.3)	27 (6.8)	2.65 (1.13-6.22)	0.025
	No, unknown	59 (84.3)	276 (86.2)			41 (83.7)	367 (93.2)		
Imprisonment in history	Yes	46 (65.7)	96 (30.0)	4.47 (2.58-7.74)	<0.001	12 (24.5)	31 (7.9)	3.80 (1.80-8.02)	<0.001
	No	24 (34.3)	224 (70.0)			37 (75.5)	363 (92.1)		
Hepatitis, yes vs. no	Anti-HCV positive (n=534)	44 (75.9)	85 (34.8)	5.88 (3.05-11.34)	<0.001	20 (64.5)	88 (43.8)	2.33 (1.06-5.13)	0.035
	HBsAg positive (n=487)	3 (5.2)	9 (3.7)	1.41 (0.37-5.39)	0.614	2 (10.5)	27 (16.2)	0.61 (0.13-2.81)	0.530
Smoking	Yes	58 (82.9)	186 (58.1)	3.48 (1.80-6.74)	<0.001	23 (46.9)	126 (31.9)	1.88 (1.03-3.43)	0.039
	No	12 (17.1)	134 (41.9)			26 (53.1)	268 (68.1)		
Intravenous drug use, ever vs. never	Ever	50 (71.4)	104 (32.5)	5.19 (2.94-9.17)	<0.001	10 (20.4)	28 (7.1)	3.35 (1.52-7.41)	0.003
	Never	20 (28.6)	216 (67.5)			39 (79.6)	366 (92.9)		
Alcohol abuse	Yes	6 (8.6)	25 (7.8)	1.11 (0.44-2.81)	0.832	3 (6.1)	15 (3.8)	1.65 (0.46-5.91)	0.443
	No	64 (91.4)	295 (92.2)			46 (93.9)	379 (96.2)		
CD4 count at time of HIV diagnosis, ≤350 vs. >350 (cells/mm³) (n=364)	≤350	26 (41.3)	182 (60.3)			-	-	-	-
	>350	37 (58.7)	120 (39.7)	2.16 (1.24-3.75)	0.006	-	-	-	-
CD4 count at time of IGRA test, ≤350 vs. >350 (cells/µl) (n=383)	≤350	18 (25.7)	115 (36.6)			-	-	-	-
	>350	52 (74.3)	199 (63.4)	1.67 (0.93-2.99)	0.085	-	-	-	-
HIV RNA at time of HIV diagnosis, copies/ml (n=336)	<200	8 (13.6)	24 (8.6)			-	-	-	-
	≥200	51 (86.4)	254 (91.4)	0.60 (0.26-1.42)	0.245	-	-	-	-
HIV RNA at time of IGRA test, copies/ml (n=378)	<200	41 (58.6)	188 (60.8)			-	-	-	-
	≥200	29 (41.4)	121 (39.2)	110 (0.65-1.86)	0.726	-	-	-	-

Figure. Multivariable analysis* of factors associated with LTBI among PLHIV and HIV-uninfected individuals in Lithuania.

PLHIV — Odds ratio (95% CI):
- Smoking: 1.66 (0.80-3.45)
- Intravenous drug use: 2.45 (1.09-5.49)
- History of contact with TB patient: 1.01 (0.46-2.23)
- Unemployment: 1.06 (0.55-2.06)
- Imprisonment in history: 1.85 (0.85-4.05)
- Non university educational status: 1.79 (0.56-5.69)
- CD4 count at time of HIV diagnosis >350, cells/µl: 1.74 (0.96-3.14)

HIV-uninfected individuals — Odds ratio (95% CI):
- Smoking: 1.23 (0.62-2.43)
- Intravenous drug use: 1.94 (0.70-5.34)
- History of contact with TB patient: 3.08 (1.26-7.53)
- Unemployment: 0.69 (0.27-1.74)
- Imprisonment in history: 2.14 (0.80-5.67)
- Non university educational status: 1.92 (0.86-4.30)

*Only variables with p-value <0.10 in any of the two univariable analyses were included into multivariable analysis, except for hepatitis C, because of its close association with intravenous drug use, and CD4 count available only for PLHIV