People Living With HIV Diagnosed Late Provide Source of HIV Infection to Other With Recent Diagnosis

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BACKGROUND

- Late presentation remains an important hurdle in the management and prevention of HIV infection. In the WHO European Region, 52.4% of people presented late in 2023 (ECDC, HIV/AIDS Surveillance in Europe, 2024). In Greece, in 2023, the proportion of those diagnosed late was 63.7% (NPHO, HIV/AIDS Surveillance in Greece, 2024).
- Our **aim** was to investigate the potential source of infection among people living with HIV (PLHIV) with different stages of diagnosis, using in addition to the traditional definition for late diagnosis, the time interval between HIV acquisition and diagnosis dates.

METHODS

- The study sample consisted of 3,093 HIV-1 subtype A1 and B sequences from a period with dense sampling in Greece.
- Analysis was performed on 2,385 sequences with pairwise genetic distances ≤ 0.015 substitutions/site found within molecular transmission clusters (MTCs) consisting of > 10 sequences (large clusters). Pairwise genetic distances were estimated using the Tamura-Nei nucleotide substitution model (MEGA X). Characteristics of PLHIV whose sequences were analysed are presented in Table 1.
- 2,194 PLHIV were categorized according to the CD4 count or presence of an AIDS-defining condition at diagnosis (advanced disease: CD4 < 200 cells/μl or clinical AIDS, late: 200 ≤ CD4 ≤ 350 cells/μl, non-late: CD4 > 350 cells/μl).
- Treatment-naïve PLHIV were categorized according to the time from HIV infection to diagnosis (recent: subtype A: 0.05-1.31, subtype B: 0.09-1.09, intermediate: A: 1.32-2.68, B: 1.10-2.41, late: A: 2.69-11.54, B: 2.42-11.87 years).
- HIV infection date was estimated by molecular clock analysis (Bayesian birth-death models, BEAST v1.8.0). HIV diagnosis date was approximated by the date of the first sample obtained for HIV-RNA / genotypic resistance testing.
- HIV transmissions among PLHIV with different diagnosis status were estimated by a modified statistical phylogeography method (maximum parsimony, PAUP*4.0).

Late diagnosis not only *complicates* the management of HIV-1 infection but also serves as a *source* of *new* HIV-1 *transmissions*. Our findings emphasize the critical *importance* of *early diagnosis* in controlling the spread of the virus

RESULTS

- For subtype A1, analysis using the estimated infection dates revealed that among PLHIV with recent diagnosis, the mean number of infections originated from PLHIV with late and intermediate diagnosis, were 35.7 (11%) and 32.8 (10%), respectively (Figure 1A, Figure 2).
- For those diagnosed late, only 21.3 (6.7%) and 18.5 (5.8%) of infections were from PLHIV with intermediate and early diagnosis (Figure 2).
- Similarly for subtype B, a proportion of infections among PLHIV with recent (13%) and intermediate (17.5%) diagnoses originated from PLHIV with late status (Figure 1A, Figure 2).
- Statistical phylogeography confirmed that late presenters were a significant source of HIV transmission to PLHIV from other groups.
- Analysis using CD4 counts showed consistent results for both subtypes (Figure 1B).
- Late and advanced disease groups provided a significant source of infections to other groups.
- Non-late presenters were not a significant source of HIV transmission to those with late presentation and advanced disease.

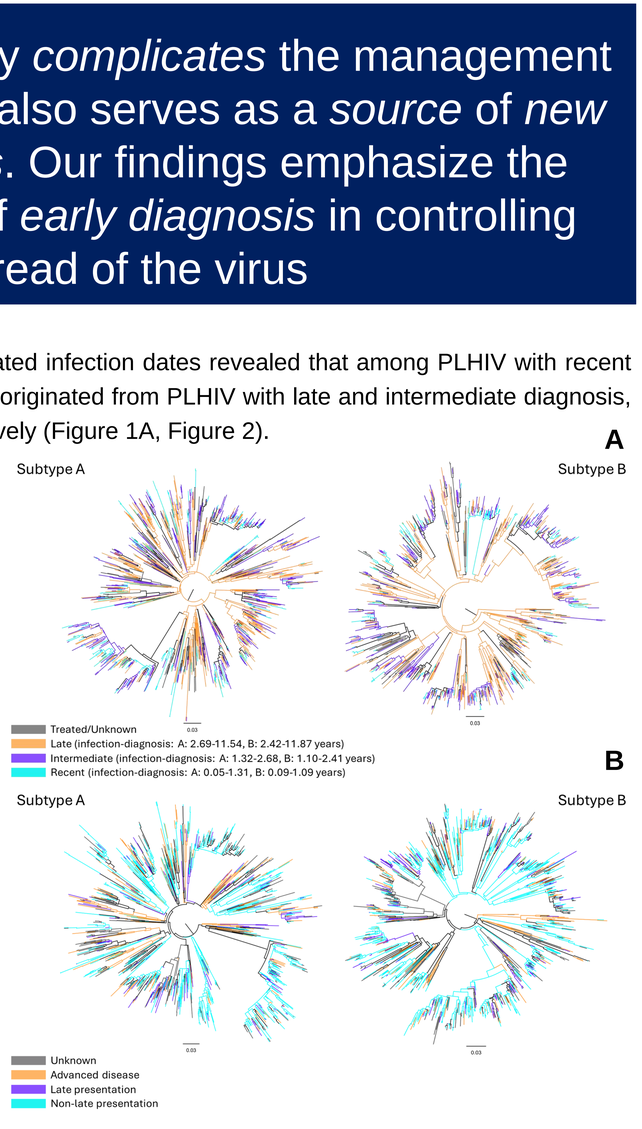


Figure 1 *Unrooted maximum likelihood phylogenetic trees estimated by RAxML v8.2.10 using HIV-1 sequences of subtypes A1 and B with an estimated pairwise genetic distance ≤ 0.015 substitutions/site found within large molecular transmission clusters. Sequences are marked in different colors according to the diagnosis status of PLHIV which was based on* ***A.*** *time from HIV acquisition to diagnosis;* ***B.*** *CD4 count or presence of an AIDS-defining condition at diagnosis.*

Table 1 *Characteristics of people living with HIV (PLHIV) infected with HIV-1 subtype A1 or B whose sequences were included in analysis (n=2,385).*

Characteristic		Subtype A1 (n=1,229)	Subtype B (n=1,156)
Antiretroviral therapy (ART) (n, %)			
	Untreated	1,117 (90.9)	997 (86.3)
	Treated[1]	96 (7.8)	88 (7.6)
	Unknown	16 (1.3)	71 (6.1)
Age (median, IQR[2])[3]		34.8 (28.6, 44.2)	32.9 (27.8, 39.6)
Sex (n, %)			
	Male	1,073 (87.3)	1,057 (91.4)
	Female	93 (7.6)	60 (5.2)
	Unknown	63 (5.1)	39 (3.4)
Mode of HIV acquisition (n, %)			
	Heterosexuals	199 (16.2)	107 (9.3)
	PWID[4]	90 (7.3)	122 (10.5)
	MSM[5]	824 (67.0)	837 (72.4)
	Other	6 (0.5)	9 (0.8)
	Unknown	110 (9.0)	81 (7.0)

[1]PLHIV on ART at genotypic resistance testing; [2]IQR, interquartile range; [3]Based on 1,149 available observations for A1 and 1,101 for B; [4]PWID, people who inject drugs; [5]MSM, men who have sex with men

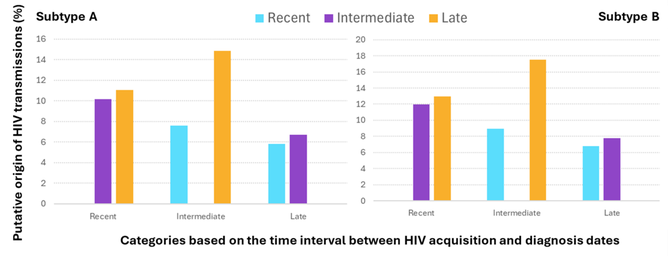


Figure 2 *HIV-1 transmissions among PLHIV with different diagnosis status for subtypes A1 and B. PLHIV were categorized into different groups according to the time interval between HIV acquisition and diagnosis dates.*

CONCLUSIONS

- ✓ Using two different definitions for late diagnosis, we showed that PLHIV diagnosed at a late stage provide a source of infection to those diagnosed earlier, in Greece.
- ✓ Our study highlights that early diagnosis, besides the beneficial effect for the disease prognosis, would significantly mitigate onward HIV transmission.
- ✓ This underscores the need to enhance HIV testing strategies in Greece to ensure earlier diagnosis and timely treatment initiation.

ADDITIONAL KEY INFORMATION

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