Association of delayed HIV diagnosis or ART initiation with risk of age-associated dementia

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BACKGROUND

- Recent studies have reported that older adults with HIV are at elevated risk of age-associated dementia despite antiretroviral therapy (ART).
- We investigated the hypothesis that delayed HIV diagnosis or delayed initiation of ART could contribute to greater risk of developing dementia later in life.

METHODS

Population and setting

- ≥50-year-old people with HIV
- Kaiser Permanente (KP) healthcare systems in three U.S. regions - Northern California, Southern California, & Mid-Atlantic States (Maryland, Virginia, Washington, D.C.)
- Study period: January 1, 2000 to December 31, 2023
- Inclusion criteria: ≥1 documented ART prescription fill, ≥1 year of health plan enrollment, no prior dementia diagnosis.

Study design and data collection

- Retrospective cohort
- Exposure: For each participant, the lowest pre-ART CD4 count was identified. Low CD4 count (i.e., <200 cells/µl) was used as a proxy for delayed HIV diagnosis or delayed ART initiation.
- Outcome: Incident dementia, identified using ICD codes.
- Covariates: Data were collected on demographics, history of smoking, frequency of outpatient visits (measure of healthcare utilization), and ICD-coded diagnoses of substance use disorders, depression, diabetes, hepatitis C infection, and cardiovascular disease. HIV data included date of first known HIV infection, CD4 cell counts, HIV RNA levels, and ART prescription fills.

Data sources

- KP electronic health records (EHR)
- KP regional HIV registries and Diabetes registries

Analyses

- The association of low CD4 count with incident dementia was evaluated using Fine-Gray subdistribution hazard models to account for the competing risk of death, with age as the time scale and adjustment for covariates.

Delayed HIV diagnosis and delayed ART initiation are associated with greater risk of age-associated dementia

RESULTS

- The study included 21,354 people with HIV (mean age 54 years at start of follow-up, 87% men, 46% White, 23% Black, 21% Hispanic, 4% Asian, 6% other/unknown race/ethnicity.
- All study participants were on ART (i.e., at least 1 documented ART prescription fill).
- At start of follow-up, mean CD4 count was 570 cells/µl (SD: 327 cells/µl), 78% had undetectable HIV RNA (<200 copies/ml), and the mean duration of HIV infection was 12 years (SD: 9 years).
- 30% had a pre-ART CD4 count <200 cells/µl.
- At start of follow-up, 41% had a history of smoking, 29% had depression, 13% had diabetes, 10% had a history of hepatitis C infection, and 6% had cardiovascular disease.

Table 1. Risk of incident dementia in people with HIV, by level of pre-ART CD4 count.

	Hazard ratio for incident dementia (95% CI)	
Lowest pre-ART CD4 count (cells/µl)	Unadjusted	Adjusted
≥200	**Reference**	**Reference**
<200	**1.56 (1.33-1.83)**	**1.33 (1.12-1.57)**

Adjusted models included terms for sex, race, Census-based neighborhood-level education, ever smoking, substance use disorders, depression, diabetes, hepatitis C infection, cardiovascular disease, KP region, year of HIV diagnosis, HIV RNA level at start of follow-up, and number of outpatient visits in the year before start of follow-up.

- During follow-up (mean 6 years, SD: 6), we observed 618 cases of incident dementia.
- Low pre-ART CD4 count (<200 cells/µl) was associated with greater risk of developing dementia (adjusted hazard ratio: 1.33, 95% CI: 1.12-1.57).

STRENGTHS

- Large population of older adults with HIV on ART.
- Confirmation of ART prescription using pharmacy records linked to EHR.
- Individual-level adjustment for confounding dementia risk factors and related comorbidities using EHR data.
- Extensive capture of HIV measures in KP regional HIV registries.

LIMITATIONS

- Clinical practice changes during the study period (e.g., in timing of ART initiation) may have impacted our results. We adjusted for calendar year of HIV diagnosis to account for some of these effects.
- No data on ART adherence.
- No neuroimaging and cerebrospinal fluid data; therefore, unable to evaluate underlying causes of dementia.

CONCLUSIONS

- Findings suggest that delayed HIV diagnosis and delayed ART initiation are associated with greater risk of developing age-associated dementia.
- These findings emphasize the importance of continuing assertive HIV screening in the community.

ADDITIONAL INFORMATION

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