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MAJOR ARTICLE

Undiagnosed Cognitive Impairment and Impact on Instrumental Activities of Daily Living Among People With HIV Infection in Primary Care

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Background. Little is known about the prevalence of undiagnosed cognitive impairment and its impact on instrumental activities of daily living (IADL) among people with HIV (PWH) in primary care.

Methods. PWH were recruited from an integrated health care setting in the United States. PWH were eligible for recruitment if they were ≥50 years old, taking antiretroviral therapy (ie, ≥1 antiretroviral therapy [ART] prescription fill in the past year), and had no clinical diagnosis of dementia. Participants completed a cognitive screen (St. Louis University Mental Status exam) and a questionnaire on IADL (modified Lawton-Brody).

Results. Study participants (n = 47) were mostly male (85.1%), 51.1% White, 25.5% Black, 17.0% Hispanic, and the average age (SD) was 59.7 (7.0) years. Overall, 27 (57.5%) participants were categorized as cognitively normal, 17 (36.2%) as having mild cognitive impairment, and 3 (6.4%) as having possible dementia. Of the 20 participants with mild cognitive impairment or possible dementia, 85.0% were men, the average age (SD) was 60.4 (7.1) years; 45.0% were White, 40.0% were Black, 10.0% were Hispanic, and 30.0% reported difficulty with at least 1 IADL. Most (66.7%) attributed difficulty with IADL primarily (33.3%) or in part (33.3%) to cognitive problems.

Conclusions. Undiagnosed cognitive impairment is frequent among ART-treated PWH, with possible elevated risk among Black PWH, and may be accompanied by difficulty with IADL. Efforts are needed to optimize identification of factors contributing to cognitive and IADL difficulties among ART-treated PWH in primary care.

Keywords. activities of daily living; aging; cognitive impairment; dementia; everyday functioning; function.

Cognitive impairment is common in people with HIV infection (PWH) and may adversely affect everyday activities [1]. Data from observational research cohorts estimate that 30%–50% of PWH have some degree of cognitive impairment, but little is known about the prevalence of cognitive and functional impairments among PWH engaged in primary care and taking antiretroviral therapy (ART) [2–8]. Recent electronic health record (EHR)–based studies in primary care settings report elevated risk of diagnosed dementia among PWH [9–11]. However, EHR-based analyses typically underestimate the prevalence of cognitive impairment and dementia as providers do not routinely assess cognition, and patients may not recognize or report cognitive problems until they substantially impact everyday life [12, 13]. Among PWH, cognitive issues may not be prioritized given other important clinical goals such as achieving HIV suppression and limited time to address multiple concerns during clinic encounters. To better understand cognitive impairment among ART-treated PWH in primary care and complement recent retrospective EHR-based analyses of diagnosed dementia [9, 10], we conducted a cross-sectional study to estimate the prevalence of undiagnosed cognitive impairment and associated difficulties with instrumental activities of daily living (IADL) in a diverse sample of PWH.

METHODS

We recruited a sample of PWH at Kaiser Permanente Northern California (KPNC), an integrated health care system in the United States; participants were recruited between March 2020 and June 2022 (with periodic suspension due to the coronavirus disease 2019 [COVID-19] pandemic). Inclusion criteria mirrored those from prior EHR-based studies in the same setting [9, 10]. PWH were eligible for recruitment if they were ≥50 years old, taking ART (defined as ≥1 ART

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prescription fill in the past year), and had no prior clinical diagnosis of dementia recorded in the EHR. PWH recruited for this study were simultaneously being recruited for another study that aimed to evaluate substance use and mental health (PIs: Silverberg/Satre, U01AA026230), but substance use and mental health status were not inclusion criteria for either study. Target enrollment was 50 participants. Study participation consisted of a brief cognitive screen, a questionnaire about IADL, and a questionnaire about depressive symptoms. The study protocol was approved by the KPNC Institutional Review Board. Study participants were provided with a study information form before agreeing to participate, and a waiver of documented informed consent was received as no identifying information was collected with study questionnaires.

Cognition

Cognitive status was assessed using the St. Louis University Mental Status (SLUMS) exam, which was administered in-person by trained staff [14]. The SLUMS exam was chosen for this study given its ease of administration and scoring based on level of education [15, 16]. Cognitive status was scored numerically from 1 to 30 and categorized as normal, mild cognitive impairment, or possible dementia, with thresholds differing by high school completion status (yes/no) [14]. Prior clinical diagnosis of mild cognitive impairment was ascertained from the EHR.

IADL

Difficulty with IADL was assessed via a self-administered questionnaire. IADL included housekeeping, managing finances, buying groceries, cooking, transportation, using the telephone, doing laundry, managing medications, and maintaining performance at work. The questionnaire was based on the Lawton-Brody IADL Scale [17]. As we expected study participants to be relatively young and not yet retired (although all at least 50 years old), the questionnaire was modified to include a question about ability to maintain attention and finish tasks at work, as done in other HIV cohorts [18]. Participants were also asked whether difficulty with IADL was primarily due to cognitive problems, physical problems, or both.

Depressive Symptoms

Depressive symptoms were assessed via a self-administered Patient Health Questionnaire (PHQ-2) given its accuracy, efficiency, and utility in screening for depression in HIV clinics [20, 21]. The PHQ-2 consists of the first 2 items of the PHQ-9: (1) feeling down, depressed, or hopeless and (2) little interest or pleasure in doing things [19]. Depression was defined as a score of 3 or higher, consistent with prior studies [20–22].

Analyses

Descriptive analyses were conducted examining cognition, IADL (presence and attribution), and depressive symptoms in the overall sample and among participants with any cognitive impairment (ie, mild cognitive impairment or possible dementia according to the SLUMS exam). The likelihood of cognitive and IADL impairments was compared within sex and race/ethnicity categories using χ^2 tests. Fisher exact tests were used when cell sizes were <10. Analyses were conducted in Stata 18 (StataCorp, College Station, TX, USA).

RESULTS

In total, 59 eligible individuals were approached for participation in the study, and 47 agreed to participate. Participants were mostly male (85.1%), the average age (SD) was 59.7 (7.0) years, 97.9% reported completing high school, and 78.7% were not yet retired. Participants were 51.1% White, 25.5% Black, 17.0% Hispanic, 4.3% Asian or other race, and 2.1% unknown race. Individuals who declined to participate were slightly older (63.5 years) but comparable in terms of sex (83.3% male), education level (91.7% completed high school), and race/ethnicity (58.3% White, 25% Black, and 16.7% Hispanic). Overall, 27 (57.5%) participants were categorized as cognitively normal, 17 (36.2%) as having mild cognitive impairment, and 3 (6.4%) as having possible dementia. None of these participants had a prior diagnosis of mild cognitive impairment in the EHR.

Of the 20 participants with any cognitive impairment (ie, mild cognitive impairment or possible dementia), 85.0% were men; the mean age (SD) was 60.4 (7.1) years; 45.0% were White, 40.0% were Black, and 10.0% were Hispanic; 80.0% were not yet retired; and 30.0% reported difficulty with at least 1 IADL. Though a large proportion of participants with cognitive impairment were men (reflecting the overrepresentation of men in the sample), the likelihood of cognitive impairment among men was not different than among women (relative risk [RR], 1.00 and 1.01, respectively; $P = .99$). The likelihood of having cognitive impairment was elevated among Black participants (with vs without cognitive impairment; RR, 2.70; $P = .09$), but not among White participants (RR, 0.81; $P = .56$), Hispanic participants (RR, 0.45; $P = .44$), or participants of Asian or other race (RR, 0.68; $P = 1.0$).

Among participants with any cognitive impairment (n = 20), difficulty with IADL was reported for housekeeping (20.0%), working (18.8%), doing laundry (10.0%), managing finances (5%), doing groceries (5%), managing medications (5%), and cooking (5%) (Figure 1). None of these participants reported difficulty with transportation or using their phone. Most (66.7%) reported that difficulty with IADL was due primarily (33.3%) or in part (33.3%) to cognitive problems. All 3 of the women with cognitive impairment reported difficulty with IADL, compared with 17.6% (3 out of 17) of the men with

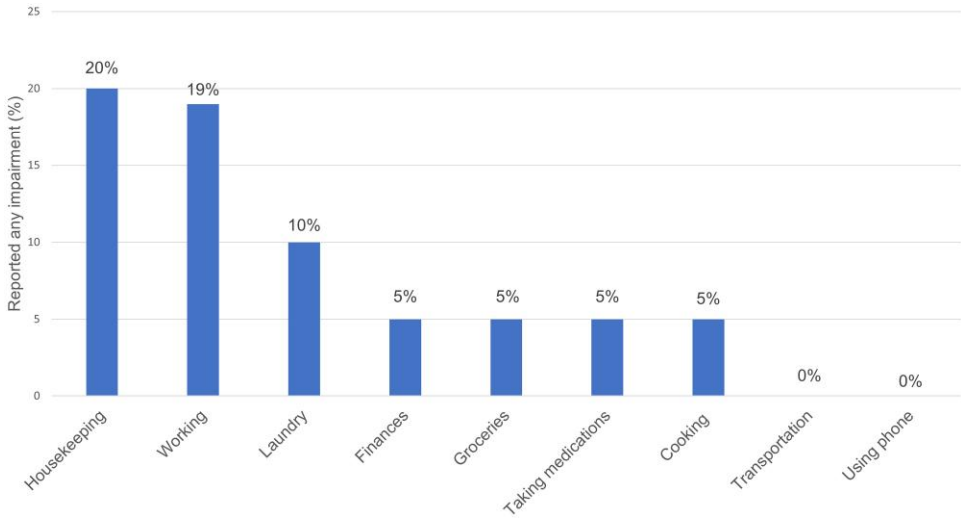

Figure 1. Self-reported difficulty with IADL among PWH with any cognitive impairment (n = 20). Calculation of difficulty at work excluded 4 participants who were retired. Abbreviations: IADL, instrumental activities of daily living; PWH, people with HIV.

cognitive impairment. Black participants with cognitive impairment were more likely to report difficulty with IADL (62.5%) than those who were White (11.1%). None of the participants who were Hispanic, Asian, or other race/ethnicity and who had cognitive impairment reported difficulty with IADL.

Difficulty with IADL was also reported by 9 PWH who were categorized as having normal cognition. Like participants with cognitive impairment, most (66.7%) attributed difficulty with IADL primarily (55.6%) or in part (11.1%) to cognitive problems. Possible depression was identified in 3 (15.8%) participants with any cognitive impairment, in 3 (20.0%) participants who reported any difficulty with IADL, and in 2 participants (33.3%) with both cognitive impairment and difficulty with IADL.

DISCUSSION

In a sample of ART-treated PWH who had no prior clinical diagnosis of mild cognitive impairment or dementia, cognitive impairment was common (42.6%). Undiagnosed cognitive impairment was more than twice as likely among Black PWH and was frequently accompanied by self-reported difficulty with IADL (62.5%). Our data also suggest that women with cognitive impairment may be more likely to have difficulty with IADL than men with cognitive impairment, a finding that should be explored in larger studies. Overall, most participants (66.7%) who had difficulty with IADL reported that the difficulties were attributable at least in part to cognitive problems. PWH with cognitive impairment were on average 60 years old. These findings add to recent EHR-based analyses from this same setting that found that PWH were diagnosed with age-associated dementia on average 10 years earlier than their HIV-uninfected peers and remained at 58% elevated risk of dementia after adjustment for confounding sociodemographic and clinical factors [9, 10].

This study contributes knowledge on undiagnosed cognitive impairment and its potential impact on everyday functioning among a diverse sample of ART-treated PWH in a US health care system. It extends prior studies reporting high frequency of cognitive impairment among PWH conducted in observational research cohorts or among PWH with advanced HIV disease, immunodeficiency, or taking older ART regimens with possible suboptimal HIV suppression [4, 23–28]. It also adds to the literature on cognitive impairment among PWH taking modern ART regimens, including a study of cognitive impairment in 290 PWH age ≥50 years (80% of whom were on ART) participating in a clinical trial of HIV and aging, which also reported high prevalence of cognitive impairment (34.5% using the global deficit score and 30.0% using Frascati criteria) but only included Black and White participants in the United Kingdom and Ireland [29].

The high prevalence of cognitive impairment in our study population (42.6%) is consistent with prior literature reporting that many PWH experience cognitive issues, occurring as early as middle age and despite well-controlled HIV infection [2–7]. Although our study population was restricted to PWH with evidence of ART dispensation in the EHR, we were not able to measure HIV RNA or CD4+ T-cell levels on the day of cognitive and IADL screening. Therefore, participants who had cognitive impairment may have been those who were nonadherent to ART at the time of assessment. Regarding comparability of our study to others, we note several important considerations. First, cognitive assessment was done using a brief cognitive screen used in clinical practice to identify individuals who

may require further evaluation. Cognitive status assigned therefore does not correspond to the subtypes of HIV-associated neurocognitive disorders (HANDs) diagnosed in research settings following full neuropsychological and functional assessment [30]. Second, comparability of cognitive impairment prevalence across studies is generally limited as there is no widely used and validated cognitive screening tool for ART-treated PWH, though this is an active area of research [31–34]. Previously validated brief cognitive tests for PWH were designed for detection of more severe cognitive deficits and are no longer suitable for use in ART-treated PWH [34, 35]. The SLUMS exam was normed in a general geriatric population and has not been validated in PWH, so it may be less sensitive to cognitive impairments among our relatively younger and relatively highly educated (ie, 97.9% high school education or greater) HIV-infected study population, resulting in underestimation of cognitive impairment. However, prior studies indicate that the SLUMS exam is superior in detecting dementia in its early stages compared with other brief cognitive assessments such as the Mini-Mental State Examination (MMSE) [15, 16]. Lastly, comparability to other studies may be limited since we excluded PWH previously diagnosed with dementia and/or not taking ART.

Most PWH attributed difficulty with IADL to cognitive problems, consistent with other studies reporting that severity of cognitive impairment positively correlates with objective measures of functional impairment [23, 24, 36, 37]. Some people with *normal* cognition reported difficulty with IADL, and most of them attributed it to cognitive problems. This may be because people who were less cognitively impaired were more aware of having difficulty with everyday activities. Another explanation is that the SLUMS exam was insensitive to cognitive deficits among PWH, thus misclassifying some PWH as cognitively normal [29]. Use of a subjective IADL instrument based on self-report instead of an objective assessment may also have contributed to potential misclassification of functional status. Few PWH screened positive on the PHQ-2. Therefore, comorbid depression at the time of cognitive and IADL assessment was unlikely to have substantially affected participants' responses.

As PWH are living to older ages on ART, cognitive impairment and age-associated dementia are important emerging health concerns [38–41]. Cognitive impairment has significant clinical implications because it is associated with poor retention in HIV care, reduced ART adherence, lower quality of life, and increased all-cause mortality, all of which threaten the significant advances in HIV health and survival made in recent decades [42, 43]. Treatment failure among cognitively impaired PWH could also jeopardize progress in the "Ending the HIV Epidemic" Initiative, an effort led by the US Department of Health and Human Services to end the persistent national HIV epidemic by 2030 [44]. By identifying IADL difficulty among older PWH with undiagnosed cognitive impairment and potential disparities by race/ethnicity and sex, this study contributes to ongoing discussions regarding the value and utility of clinical cognitive screening in this population [27, 34, 45]. Brief cognitive and IADL screenings could potentially be used to proactively identify PWH requiring more focused care including intervention on contributing causes (eg, polypharmacy, substance use), more attention to ART adherence, assistance with managing comorbidities, and referral to support services. Limitations of this study include (1) the small sample size (n = 47), (2) primarily male (85%) and employed (79% not yet retired) study sample, which could limit generalizability, (3) self-report of IADL and depressive symptoms, (4) lack of longitudinal measurement, and (5) lack of data on behavioral and clinical risk factors for cognitive impairment, such as treatable psychiatric conditions or other causes of cognitive impairment including traumatic brain injury or past prolonged loss of consciousness. Due to COVID-19 pandemic–related suspensions in recruitment, the enrollment target of 50 participants was not reached. Strengths of the study include assessment of both cognitive and functional status, capture of cognitive impairment related to work, assessment of depression, and restriction of participation to PWH on ART.

CONCLUSIONS

Undiagnosed cognitive impairment is frequent among ART-treated PWH engaged in primary care, with possible higher risk among Black PWH, and may be accompanied by difficulty with IADL. Cognitive impairment among younger PWH of working age could adversely impact employment, independence, and quality of life. Efforts are needed to optimize identification of factors contributing to cognitive and IADL difficulties among ART-treated PWH and investigate potential racial, ethnic, and/or sex disparities.

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