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Title

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Permalink

Journal

ISSN

Authors

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et al.

Publication Date

DOI

Peer reviewed

Association of Pain and Pain Medication Use with Multiple Characteristics of Older People Living with HIV

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Abstract

People living with HIV (PLWH) experience chronic pain that may impact function. Gaps in knowledge exist for factors that impact pain and pain medication use in older (age 50+) PLWH. Data for this study were obtained from the Aging with Dignity, Health, Optimism and Community (ADHOC) cohort, an observational study of older PLWH from 10 clinics across the United States. Participants self-reported socioeconomic, psychosocial, and health factors via an online questionnaire. Of 1,051 participants, 66% reported pain. In a multivariable regression model, multimorbidity and tobacco use were associated with a greater likelihood of experiencing pain, whereas being male, black, and having higher cognitive function were associated with a lower likelihood of experiencing pain. Of the 696 participants who reported pain, 46% reported using pain medication. In a multivariable regression model, pain medication use was associated with multimorbidity and with lower income. Recognition of the factors associated with pain and pain medication use in this vulnerable population may lead to strategies that mitigate negative health outcomes.

Keywords: older adults, HIV, pain, multimorbidity

Introduction

CHRONIC PAIN IMPACTS up to 85% of people living with HIV (PLWH).[1–5] The high prevalence is due to direct and indirect effects of HIV (i.e., direct HIV toxicity and secondary toxicity of antiretroviral therapy on the central and peripheral nervous systems)[6–9] and is magnified by co-occurring psychosocial factors such as depression,[10] stress,[11] past trauma,[12] social isolation,[13] and substance use.[14] These co-occurring factors also contribute to increased risk for prescription opiate misuse and overdose mortality,[15–17] and to maladaptive coping (avoidance, thought suppression, and catastrophizing)[18–22] that negatively modify the pain experience. The medical management of pain increases in complexity as older PLWH (≥50 years) accumulate age-associated painful comorbidities such as osteoarthritis. Additionally, non-opiate medications used for pain (i.e., skeletal muscle relaxants, NSAIDS) have side effects that increase risks for falls, delirium, and gastrointestinal bleeding that may further worsen the health of older PLWH.[23–27]

To identify specific psychosocial and clinical factors associated with chronic pain and pain medication use, an online registry (Aging with Dignity, Health, Optimism & Community, ADHOC) of older PLWH that collects patient-reported outcome measures (PROMs), including psychosocial and socioeconomic data, was utilized.

Methods

Study design

ADHOC is a longitudinal cohort study that collects data on PLWH over the age of 50 using an online questionnaire. The questionnaire includes information on sociodemographic factors, activities and interests, HIV diagnosis and status, health care use and satisfaction, antiretroviral therapy, comorbid medical conditions, health and well-being, substance use, and sexual practices. Validated PROMs are collected where appropriate. PROMs are "standardized, validated questionnaires completed by patients to measure their perceptions of their functional well-being and health status."[28]

ADHOC began collecting data on the cohort in October 2017 and continues to collect follow-up data on an annual basis. For this cross-sectional analysis, baseline data collected between October 2017 and July 2019 were used.

The ADHOC study protocol was approved by the Ethical and Independent Review Services (E&I #17130) and the

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UCSD Institutional Review Board (IRB). Written informed consent was collected from all participants.

Participants

To be eligible for ADHOC, participants must have an HIV-1 or −2 infection and be at least 50 years of age. Participants are primarily identified during visits to clinical practices providing care for HIV. These clinics are located in California, Florida, Illinois, North Carolina, Texas, Washington DC, Washington State, and Wisconsin, and encompass both university-based and private practices.

Assessment of pain and pain medications

As part of the questionnaire, participants were asked to report whether they had been diagnosed with specific medical conditions. Participants were instructed that ''diagnosed means the condition was confirmed by a medical professional.'' Within the pain conditions category, participants were asked whether they had been diagnosed with back pain, hip pain, joint pain, or muscle pain, and were also instructed to write in chronic pain conditions that were not listed. Each time a participant indicated they had a pain condition, they were asked, ''Have you taken prescribed medication for this condition in the last 4 weeks? [Yes/No].''

Assessment of other variables

Covariates identified *a priori* that might influence pain and pain medication use were selected from the ADHOC online questionnaire. Variables included age, gender, race/ethnicity, education level, sexual orientation, annual household income in US dollars, employment status, living alone, multimorbidity, HIV viral load, ART adherence, tobacco use, recreational drug use, alcohol use measured by The Alcohol Use Disorders Identification Test (AUDIT-C),[29] social well-being and cognitive function measured by The Functional Assessment of HIV Infection (FAHI),[30] quality of life measured by the PozQoL,[31] depression and anxiety measured by The Patient Health Questionnaire-4 (PHQ-4),[32] loneliness measured by the Three-item Loneliness Scale,[33] interpersonal support measured by the Interpersonal Support Evaluation List-12,[34] resilience measured by the Connor-Davidson Resilience Scale,[35] and stigma measured by the Internalized AIDS-Related Stigma Scale.[36] Good ART adherence was defined as taking 95% or more of prescribed ART medication. Hazardous drinking was defined as having a score of 4 or more for men and having a score of 3 or more for women on the AUDIT-C.[29] Screening positive for anxiety was defined as having a score of 3 or more on the PHQ-4 anxiety subscale, and screening positive for depression was defined as having a score of 3 or more on the PHQ-4 depression subscale.[32] Results for the Poz-QoL, the Three-item Loneliness Scale, ISEL-12, CD-RISC, and the Internalized AIDS-Related Stigma Scale were treated as continuous variables. Multimorbidity was defined as reporting six or more chronic conditions, in addition to HIV. Categories of comorbidities captured in ADHOC for this analysis included bone and joint, cancer, cardiovascular, GI and liver, hormonal, kidney/genitourinary, lung, mental health, and neurologic conditions.

Statistical analyses

Cross-sectional analyses of the relationship between pain and selected covariates, as well as between pain medication use and selected covariates among participants who reported at least one pain condition, were performed using data from 1,051 ADHOC participants. Bivariate analyses were conducted using Student's t-tests for continuous variables, and chi-square tests for categorical variables. Pearson's correlation coefficients were also determined for each variable. Given that this analysis was exploratory, we did not correct for multiple comparisons. A multivariate logistic regression model was developed to investigate predictors of pain using backward elimination. Only variables that were associated with pain at $p < .20$ in the bivariate analyses were used in the regression. Using the same backward elimination approach, a second multivariate logistic regression model was developed to investigate predictors of pain medication use. Variables in the regression model were classified as significant at $p < .05$. Statistical analyses were performed using Stata 15.1 (Stata Corporation, College Station, TX).

Results

Characteristics of older PLWH in ADHOC

Among the 1,051 participants enrolled in ADHOC, the mean age of participants was 60.2 ± 6.1 years, with a range of 50–89 years. Fifty-six percent of participants were between 50 and 59 years old, and 44% were 60 years old or older (Table 1). The majority of participants were male (85%), gay, lesbian, or bisexual (83%), and white (69%). Forty-eight percent had at least a 4-year college education, and 57% had an annual household income of less than $50,000. Sociodemographic assessments showed that 57% were single and 37% lived alone. From a clinical perspective, 94% had an undetectable HIV viral load, 86% adhered to their HIV medication regimen 95% of the time or more, and 58% had six or more comorbidities. The average time since HIV diagnosis was 21.4 ± 9.0 years. Behavioral items from the survey showed that 26% of participants reported hazardous drinking and 29% used recreational drugs. Twenty-one percent of the population reported depression, 21% reported anxiety, and 14% reported both.

Factors associated with pain

Overall, 66% ($n = 696$) reported one or more of the pain conditions evaluated (Fig. 1). Regarding demographic factors, bivariate analyses showed that pain was associated with an annual household income less than $50,000 ($\chi^2 = 13.63$, $p < .001$), and unemployment ($\chi^2 = 25.22$, $p < .001$) (Table 2 and Supplementary Table S1).

From a behavioral and clinical perspective, bivariate analyses showed that pain was associated with having six or more medical conditions ($\chi^2 = 117.82$, $p < .001$), tobacco use ($\chi^2 = 5.71$, $p = .017$), and low or no alcohol use ($\chi^2 = 4.17$, $p = .041$) (Table 2).

With regard to psychosocial factors, pain was associated with anxiety ($\chi^2 = 15.70$, $p < .001$), depression ($\chi^2 = 6.84$, $p = .009$), a high degree of loneliness ($t = -3.07$, $p = .002$), lower resilience ($t = 3.03$, $p = .003$), lower quality of life ($t = 5.67$, $p < .001$), lower social well-being ($t = 2.32$, $p = .021$), and lower cognitive function ($t = 5.57$, $p < .001$) (Table 2).

TABLE 1. CHARACTERISTICS OF OLDER PEOPLE LIVING
WITH HIV IN AGING WITH DIGNITY, HEALTH, OPTIMISM,
AND COMMUNITY

Characteristic	N (%)
Age	
50–59	590 (56%)
60+	461 (44%)
Gender	
Male	896 (85%)
Female, transgender, other	155 (15%)
Sexual orientation	
Gay, lesbian, bisexual	869 (83%)
Straight, heterosexual	182 (17%)
Race/ethnicity	
White	727 (69%)
Black	212 (20%)
Hispanic/Latino	92 (9%)
Education	
Less than college	545 (52%)
College graduate	317 (30%)
Graduate school or more	189 (18%)
Annual household income	
Less than $50,000	555 (57%)
$50,000 or more	415 (43%)
Relationship status	
Single	603 (57%)
In a relationship	448 (43%)
Live alone	
Yes	385 (37%)
No	666 (63%)
Viral load	
Undetectable	972 (94%)
Detectable	59 (6%)
Antiretroviral therapy adherence	
Good adherence (defined as >=95%)	894 (86%)
Issues with adherence (<95%)	145 (14%)
Number of comorbid conditions	
Less than six	438 (42%)
Six or more	613 (58%)
Alcohol use	
Hazardous drinker	276 (26%)
Nonhazardous- or nondrinker	775 (74%)
Recreational drug use	
Yes	295 (29%)
No	717 (71%)
Screen positive for depression	
Yes	220 (21%)
No	831 (79%)
Screen positive for anxiety	
Yes	218 (21%)
No	833 (79%)

A multivariate logistic regression model was constructed and included multimorbidity, tobacco use, annual household income, anxiety, depression, alcohol use, employment status, resilience, quality of life, social well-being, cognitive function, age, gender, race/ethnicity, loneliness, and interpersonal support. After backward elimination, the model showed that being male (odds ratio [OR] = 0.50 95% confidence interval [CI] = 0.26–0.94), being black (OR = 0.47, 95% CI = 0.26–0.83),

and having higher cognitive function (OR = 0.83, 95% CI = 0.75–0.92) decreased the odds of experiencing pain (Table 3). Having six or more conditions (OR = 3.40, 95% CI = 2.11–5.51) and use of tobacco (OR = 1.99, 95% CI = 1.08–3.67) increased the odds of having a pain-related condition.

Factors associated with pain medication use

Among older PLWH with pain, 46% (n = 320) reported using pain medications (Fig. 1). Regarding demographic factors, bivariate analyses showed that pain medication use was higher among heterosexuals (χ^2 = 5.21, p = .022) and blacks (χ^2 = 8.82, p = .003) (Table 4 and Supplementary Table S2). Pain medication use was lower among men (χ^2 = 16.30, p < .001). Lower education levels (χ^2 = 17.30, p < .001), annual incomes less than $50,000 ($\chi^2$ = 37.69, p < .001), and unemployment (χ^2 = 36.60, p < .001) were also associated with pain medication use.

From a behavioral and clinical perspective, bivariate analyses showed that pain medication use was associated with having six or more medical conditions (χ^2 = 47.85, p < .001) and low or no alcohol use (χ^2 = 5.91, p = .015) (Table 4).

With regard to psychosocial factors, bivariate analyses showed that pain medication use was associated with anxiety (χ^2 = 11.72, p = .001), depression (χ^2 = 16.42, p < .001), loneliness (t = −2.46, p = .014), lower interpersonal support (t = 2.58, p = .010), lower quality of life (t = 3.92, p < .001), and lower cognitive function (t = 2.45, p = .015) (Table 4).

A multivariate logistic regression model was constructed and included tobacco use, multimorbidity, annual household income, anxiety, alcohol use, employment status, resilience, quality of life, cognitive function, gender, sexual orientation, race/ethnicity, education level, depression, loneliness, and interpersonal support. After backward elimination, this model showed that multimorbidity (OR = 2.48, 95% CI = 1.34–4.59) and an annual household income less than $50,000 (OR = 4.17, 95% CI = 2.22–7.84) increased the odds of pain medication use.

Discussion

This cross-sectional study of older PLWH evaluated the associations between pain and pain medication use and multiple factors, including demographics, HIV-related factors, multimorbidity, substance use, mental illness, loneliness, social isolation, and resilience. To our knowledge this is the first study to evaluate the relationship between these factors and pain *specifically* in older PLWH. Of note was the association of multimorbidity with both pain and pain medication use, a factor that remained significant in both multivariate logistic regression models. This strong association may suggest that HIV-related, non-AIDS conditions (i.e., arthritis and neuropathy) are contributing to the experience of pain. Alternatively, this association could simply reflect the complex medical nature of older PLWH (i.e., clustering of diseases) due to excess inflammation and other psychosocial factors.[37–39] Regardless, this finding underscores the importance of overlapping multiple chronic conditions in older PLWH. From a clinical perspective, when treating pain in an older person with HIV, it is important to consider the impact of an intervention on pain and other chronic conditions and overall function.[40]
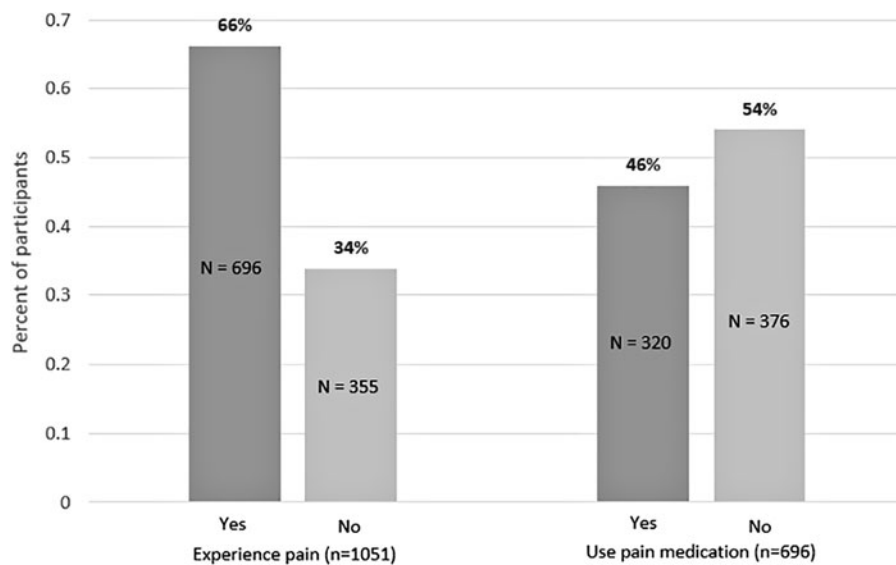
FIG. 1. Self-reported pain, and self-reported pain medication use among participants who reported pain.

TABLE 2. BIVARIATE ANALYSIS OF ASSOCIATIONS BETWEEN PAIN AND VARIOUS CHARACTERISTICS AMONG OLDER PEOPLE LIVING WITH HIV

	Pain		No pain		χ^2	t	p-value
	No.	%	No.	%			
Annual household income					13.63	—	<.001
Less than $50,000	397	61	158	49			
$50,000 and greater	250	39	165	51			
Currently employed					25.22	—	<.001
Yes	292	42	207	58			
No	404	58	148	42			
Number of comorbidities					117.82	—	<.001
Less than six	208	30	230	65			
Six or more	488	70	125	35			
Current smoker					5.71	—	.017
Yes	142	20	51	14			
No	554	80	304	86			
Hazardous drinking					4.17	—	.041
Yes	169	24	107	30			
No	527	76	248	70			
Anxiety					15.70	—	<.001
Yes	169	24	49	14			
No	527	76	306	86			
Depression					6.84	—	.009
Yes	162	23	58	16			
No	534	77	297	84			
	Mean	SD	Mean	SD			
Loneliness	5.7	2	5.3	2.1	—	−3.07	.002
Resilience	6.3	1.5	6.5	1.5	—	3.03	.003
Quality of life	3.6	0.74	3.9	0.73	—	5.67	<.001
Social well-being	19.6	8.0	20.8	8.0	—	2.32	.021
Cognitive function	8.4	2.7	9.9	2.3	—	5.57	<.001

Hazardous drinking was measured using the AUDIT-C. Anxiety and depression were measured using the PHQ4. Loneliness was measured using the 3 Item Loneliness Scale, where higher scores indicate greater loneliness (range 3–9). Resilience was measured using the CD-RISC, where higher scores indicate greater resilience (range 0–8). Quality of life was measured using the PozQoL, where higher scores indicate higher quality of life (range 1–5). Social well-being was measured using the FAHI Social, where higher scores indicate higher social well-being (range 0–32). Cognitive function was measured using the FAHI Cognition, where higher scores indicate higher cognitive function (range 0–12).

TABLE 3. LOGISTIC REGRESSION ANALYSIS SHOWING FACTORS STATISTICALLY SIGNIFICANTLY CORRELATED WITH PAIN AMONG OLDER PEOPLE LIVING WITH HIV

Covariate	OR	SE	z	p-value	95% CI
Male	0.50	0.16	−2.16	.031	0.26–0.94
Black	0.47	0.14	−2.57	.010	0.26–0.83
6 or more conditions	3.40	0.83	5.02	<.001	2.11–5.51
Tobacco use	1.99	0.62	2.21	.027	1.08–3.67
Cognition	0.83	0.042	−3.59	<.001	0.75–0.92

OR = Odds ratio; 95% CI = 95% confidence interval. Pseudo $R^2 = 0.15$. Cognitive function was measured using the FAHI Cognition, where higher scores indicate higher cognitive function (range 0–12).

This study provides a unique look into unexplored factors associated with pain and pain medication use in an older PLWH population. For example, unemployment and lower annual household income were positively associated with pain and pain medication use, highlighting the association between social adversity and pain in older PLWH. The cross-sectional nature of this study prevents us from better understanding causal relationships between pain and lower socioeconomic status, but one previous prospective study in a HIV-seronegative cohort suggested that lower socioeconomic status in childhood and adulthood contributes to the development of pain syndromes.[41] Factors in that study that contributed to the development of pain syndromes included poor adult mental health, psychological distress, and adverse life events, all of which are common in older PLWH.[42]

TABLE 4. BIVARIATE ANALYSIS OF ASSOCIATIONS BETWEEN PAIN MEDICATION USE AND VARIOUS CHARACTERISTICS AMONG OLDER PEOPLE LIVING WITH HIV

	Use pain meds		No pain meds		χ^2	t	p-value
	No.	%	No.	%			
Gender					16.30	—	<.001
Male	249	78	335	89			
Female/transgender/other	71	22	41	11			
Sexual orientation					5.21	—	.022
Gay, lesbian, or bisexual	252	79	321	85			
Straight/heterosexual	68	21	55	15			
Race/ethnicity: White					11.43	—	.001
Yes	205	64	285	76			
No	115	36	91	24			
Race/ethnicity: Black					8.82	—	.003
Yes	76	24	56	15			
No	244	76	320	85			
Education level					17.30	—	<.001
Less than college	193	60	169	45			
College grad	86	27	129	34			
Graduate school grad	41	13	78	21			
Annual household income					37.69	—	<.001
Less than $50,000	222	74	175	50			
$50,000 and greater	78	26	172	50			
Currently employed					36.60	—	<.001
Yes	95	30	197	52			
No	225	70	179	48			
Number of comorbidities					47.85	—	<.001
Less than six	54	17	154	41			
Six or more	266	83	222	59			
Hazardous drinking					5.91	—	.015
Yes	64	20	105	28			
No	256	80	271	72			
Anxiety					11.72	—	.001
Yes	97	30	72	19			
No	223	70	304	81			
Depression					16.42	—	<.001
Yes	97	30	65	17			
No	223	70	311	83			
	Mean	SD	Mean	SD			
Loneliness	5.9	2.1	5.5	2.0	—	−2.46	.014
Interpersonal support	3.1	0.69	3.2	0.69	—	2.58	.010
Quality of life	3.5	0.8	3.7	0.7	—	3.92	<.001
Cognitive function	8.0	2.7	8.8	2.6	—	2.45	.015

Hazardous drinking was measured using the AUDIT-C. Anxiety and depression were measured using the PHQ4. Loneliness was measured using the 3 Item Loneliness Scale, where higher scores indicate greater loneliness (range 3–9). Interpersonal support was measured with the ISEL-12, where higher scores indicate more social support (range 1–4). Quality of life was measured using the PozQoL, where higher scores indicate higher quality of life (range 1–5). Cognitive function was measured using the FAHI Cognition, where higher scores indicate higher cognitive function (range 0–12).

Previous research in other populations found similar results to findings in this study. For example, heavy alcohol use has been associated with less pain and pain medication use (i.e., self-medication), while anxiety has been associated with higher rates of pain and pain medication use.[1,43] As was the case in previous studies, substance use (with the exception of tobacco) in older PLWH was not associate with pain.[44,45] Finally, previous studies demonstrated that men are significantly less likely than women to take pain medications.[46]

This study has several limitations. Because it was not originally designed to evaluate the impact of pain, the cohort lacks granular measures of pain and of pain impact on function. These limitations prevent us from evaluating associations between pain severity and different types of pain. Similarly we did not capture information about the specific pain medications used, which could range from acetaminophen to opioids. Women made up only 15% of the cohort, which may affect generalizability of study findings. In addition, multimorbidity was characterized purely using counts of conditions, as opposed to using established comorbidity measures like the Charlson, Elixhauser or Veterans Aging Cohort Study scores.[42,47,48] Also, the cross-sectional nature of this study limits the ability to determine directionality or causality between associated factors. Finally, while many of the findings in this study of older PLWH, such as higher self-reported pain among those with multimorbidity, are consistent with findings from the literature in older general populations without HIV, a detailed comparison of these populations was beyond the scope of this study.[49]

Overall, this study highlights the complexity of pain in older PLWH. Many factors identified, such as socioeconomic status and multimorbidity, will be difficult to change. However other factors, such as, anxiety, depression, social isolation, and smoking, may represent targets for future interventions. Focusing on improving chronic pain management should be a priority due to the known impact of chronic pain on physical[50] and cognitive function[51] and subsequent independence in this vulnerable population.

Supplementary Material

Supplementary Table S1
Supplementary Table S2

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