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Risk Factors for Depression Among Middle-Aged to Older People Living With HIV in Lima, Peru

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Abstract

Introduction: Depression is prevalent among aging people living with HIV (PLWH) worldwide. We sought to identify depression risk factors among a group of middle-aged and older PLWH in Lima, Peru.

Materials and Methods: We assessed risk factors for depression among PLWH over age 40 receiving care in an HIV clinic in Lima, Peru. The Patient Health Questionnaire-9 (PHQ-9) was administered. We performed descriptive statistics and logistic regression analyses.

Results: Mean age was 51.7 ± 7.7 years with 15.3% females. One-quarter of participants had depression with higher frequency in females. Risk factors that significantly increased the risk of depression included female sex (adjusted prevalence ratio [aPR] = 2.19 [95%CI 1.07-4.49]), currently smoking (aPR = 2.25 [95%CI 1.15-4.43]), and prior opportunistic infection (aPR = 2.24 [95%CI 1.05-4.76]).

Discussion: Our study demonstrates that PLWH who are female, current smokers, or had an opportunistic infection have higher risk of depression. Identifying PLWH at-risk for depression is key to early mental health interventions.

Keywords

depression, people living with HIV, Peru, Latin America, risk factors, Patient Health Questionnaire-9

Plain Language Summary

Factors affecting depression in older people with HIV in Peru

Introduction: Depression is common in older people living with HIV (PLWH) worldwide. We identified depression risk factors among a group of middle-aged and older PLWH in Lima, Peru. **Materials and Methods:** We assessed risk factors for depression among PLWH over age 40 receiving care in an HIV clinic in Lima, Peru. The Patient Health Questionnaire-9 (PHQ-9) was administered. **Results:** Mean age was 51.7 ± 7.7 years with 15.3% females. One-quarter of participants had depression with higher frequency in females. Risk factors that significantly increased the risk of depression included female sex (adjusted prevalence ratio [aPR] = 2.19 [95%CI 1.07-4.49]), currently smoking (aPR = 2.25 [95%CI 1.15-4.43]), and prior opportunistic infection (aPR = 2.24 [95%CI 1.05-4.76]). **Discussion:** Our study demonstrates that PLWH who are female, current smokers, or had an opportunistic infection have higher risk of depression. Identifying PLWH at-risk for depression is key to early treatment or interventions that can improve mental health in PLWH in Peru.

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Introduction

Depression is one of the most prevalent and disabling mental health disorders with 280 million people estimated to live with depression worldwide, making depression the second leading cause of morbidity globally.[1] Studies have shown that depression is prevalent, yet under-characterized, in low-to-middle-income countries (LMICs).[2-4] Known risk factors associated with depression globally, include female sex, lower educational level, and unemployed status.[5,6] Depression is also associated with T-lymphocyte activation,[7] increase in cytokine production[8-10] and HIV receptor expression,[11] which may also play a role in modulating HIV disease in people living with HIV (PLWH).

In 2022, more than 38 million people worldwide were living with HIV,[12] a number expected to increase over time, particularly in LMICs. Depressive disorder can be 2 to 3 times higher among PLWH (22%-45%),[13] compared with people who do not have HIV (3%-17%).[3] One systematic review of PLWH in east Africa estimated the frequency of depression to be between 30% and 48%, varying by country and individual characteristics.[14] Among PLWH, factors that increase the risk of depression include social stigma, lower absolute CD4 counts and a prior history of opportunistic infections.[15,16] Moreover, depression in PLWH interferes with patients' social, work, and family life, further exacerbating depressive symptoms in PLWH.[17] Several factors related to HIV, including social stigma, fear of persecution, or social isolation that may contribute to depression in HIV, yet the effect of risk factors for depression among aging PLWH in many LMICs, including in Peru, has not been studied.

According to The Joint United Nations Programme on HIV/AIDS (UNAIDS), approximately 110 000 individuals in Peru are estimated to live with HIV as of 2022 with 5800 new infections in the year 2022.[18] There are few studies from Peru which have addressed depression in PLWH, mostly focused on young PLWH and lacking information regarding risk factors. Depression was diagnosed in 42% of men who have sex with men and transgender women seeking HIV preventative care in Peru.[19] One qualitative study of PLWH in Lima found that PLWH often sent text messages describing depressive symptoms and sought mental health services particularly during the initial stage of establishing HIV care.[20]

Our prior study[21] reported a depression prevalence of 25% among PLWH age≥40 years receiving care at a large nonprofit clinic in central Lima, Peru. This prevalence is comparable to prior studies among older PLWH in Latin America, ranging from 21.3% to 34.6% in Brazil[22-24] and 15.9% in Mexico.[25] Determining risk factors for depression among PLWH within a particular country is fundamental to prioritizing and targeting therapies to avoid adverse health outcomes, including suicidal ideation, poor adherence to antiretroviral treatment (ART), HIV disease progression, treatment failure, and poor quality of life.[26,27] However, risk factors for depression among middle-aged and older PLWH in Peru are currently unknown. Therefore, we sought to identify sociodemographic and medical risk factors for depression in this group.

Methods and Materials

Study Participants and Procedures in the Original Study

This is a secondary analysis of data from participants previously enrolled in a cross-sectional study on PLWH in Lima, Peru between September 2019 until March 2020.[21] We estimated that the 1145 PLWH over age 40 who seek care at the HIV clinic where enrollment occurred were representative of PLWH living in Peru based on Ministry of Health statistics.[28] Using an expected prevalence of 20% neurocognitive impairment as described in prior studies,[29] we expected 80% power with an enrollment goal of 140 participants with neurocognitive impairment.

The inclusion criteria of the parent study included: men and women aged 40 years or older, record of a positive enzyme-linked immunoassay and western blot tests in their medical chart who had been receiving ART therapy for at least 1 month, Peruvian-born, native Spanish speakers, at least 6 years of schooling (primary school), and the ability and willingness to participate in the study and provide informed consent were recruited from a large HIV clinic in Lima, Peru. Exclusion criteria included: self-reported history of non-HIV-related neuromedical comorbidities that may cause neurocognitive impairment (ie, non-HIV-related neurological disorder that led to neurocognitive impairment [eg, epilepsy or stroke], psychotic disorders [schizophrenia or bipolar disorder], brain injury with loss of consciousness for more than 30 minutes without return to premorbid baseline, current, and lifetime substance use disorder according to the *Diagnostic and Statistical Manual of Mental Disorders*-5 [DSM-5]). For the current secondary analysis of the parent study data, we included all participants who were enrolled in the parent study and who met the inclusion/exclusion criteria as described.

All participants completed the Patient Health Questionnaire (PHQ)-9 to screen for depression. The PHQ-9 Spanish version used in this study had been previously validated in Spanish for use in Peru (Supplemental File).[30,31] The standard cutoff score to identify any depression (mild, moderate, or severe) is 5 or above.[31] Other study participant and procedures from the original study are described in detail elsewhere.[21]

Statistical Analyses

Descriptive statistics were computed with means (standard deviations [SD]) or medians (interquartile ranges [IQRs]) for all continuous variables. Frequencies and percentages were computed for categorical data. The frequency of depressive symptoms was defined based on previously determined cutoff scores for depression using the PHQ-9 (5 or above vs <5).[30] Two-by-two comparisons between depression status groups (depression vs no depression) were completed using t-test or Pearson correlation. Univariable (without adjustment for covariates) and multivariable regression analyses were performed

using generalized linear model with link log and family Poisson to obtain unadjusted and adjusted prevalence ratios (PR). Multivariable analyses were adjusted for the following covariates: sex, age, current alcohol use, current smoker, years with HIV diagnosis, current absolute CD4 count, plasma HIV viral load, prior opportunistic infection, current efavirenz use, and adherence to ART. Collinearity between the covariates for the final model was assessed using the regression collinearity diagnostics, which calculates condition indices and variance decomposition proportions. A $P < .05$ was considered statistically significant. All statistical analyses were performed using the STATA (College Station, TX, USA).

Results

We included data from 139 PLWH. The large majority were male (84.7%) with a mean age of 51.7 years. Nearly 70% of participants had more than 12 years of education, and 6.6% were currently unemployed. One-quarter of PLWH had depression (Table 1). Current smokers had a statistically significantly higher frequency of depression compared with nonsmokers. No differences were found in depression frequency by demographic variables, current alcohol use, nor HIV characteristic variables, including current efavirenz use, time with HIV diagnosis, HIV viral load, nor current CD4 count.

In an unadjusted regression analysis, female sex was associated with depression (PR: 1.84; 95% CI: 1.01-3.38). Those who were retired had a higher likelihood of depression compared to those who were currently employed (PR: 2.36; 95% CI: 1.15-4.82). In addition, those who were current smokers were nearly twice as likely to be depressed as those who did not smoke (PR: 1.92; 95% CI: 1.06-3.45). Adherence to ART was associated with 50% less depression compared to those with poor adherence (defined as taking ART <95% of the time) (Table 2).

In the adjusted model, factors that remained statistically significantly associated with depression included: female sex (adjusted PR [aPR]: 2.19; 95% CI: 1.07-4.49), current smoker (aPR: 2.25; 95% CI: 1.15-4.43), and a history of any non-central nervous system (CNS) opportunistic infection (aPR: 2.24; 95% CI: 1.05-4.76). Current efavirenz use was associated with a lower prevalence of depression (aPR: 0.38; 95% CI: 0.16-0.90). No association was observed for CD4 count >500 copies/mL nor detectable HIV viral plasma (Table 2).

Discussion

We present the first study of depression risk factors among a middle-aged and older group of PLWH in Peru and one of the few in Latin America. We found that female sex, currently smoking and having had a prior opportunistic infections were associated with an increased frequency of depression among middle-

Table 1. General Characteristics of PLWH Evaluated in a Single Center in Lima, Peru (N = 139).

	PLWH (N = 139)	
	N, Mean	%, SD
Demographics		
Age (years)	51.7	7.7
Female sex	22	15.3
Educational level, <12 years	60	41.7
Employment type		
Currently working	120	87.0
Retired	9	6.5
Unemployed	9	6.6
Civil Status		
Single	93	66.9
Married or domestic partnership	46	33.1
Social or Psychiatric Factors		
Depression (PHQ-9≥5)	35	25.2
Current alcohol use	68	47.2
Current smoker	24	16.7
HIV Disease Characteristics		
HIV Duration (years)	8.87	12.7
CD4 count, current	553.5	346.5
CD4 count, <500 copies/ml	55	42.9
Plasma HIV viral load detectable[+]	18	14.3
Prior non-CNS opportunistic infection[a]	43	29.9
Efavirenz, current use	91	63.2
Not currently on ART	14	9.7

[+]Mean and SD.

[a]Prior opportunistic infection included any history of: candidiasis, Kaposi's sarcoma, cytomegalovirus, or *pneumocystis* pneumonia.

Abbreviations: ART, antiretroviral treatment; CNS, central nervous system; IQR, interquartile range; OR, odds ratio; PHQ-9, Patient Health Questionnaire-9; PLWH, people living with HIV; SD, standard deviation.

Table 2. Unadjusted and Adjusted PR for Depression Risk Factors Among People Living With HIV in a Single Center in Lima, Peru (N = 139).

	Unadjusted PR	95% CI	*P*-value	Adjusted PR[a]	95% CI	*P*-value
Demographics						
Sex						
Male	Ref.			Ref.		
Female	1.84	1.01-3.38	**.049**	2.19	1.07-4.49	**.030**
Age (years)						
40-49	Ref.			Ref.		
50-59	1.01	0.53-1.89	.997	1.24	0.58-2.68	.580
≥60	1.16	0.51-2.64	.717	1.58	0.66-3.78	.308
Educational level (years)						
≥12	Ref.			NA		
<12	1.61	0.91-2.86	.105			
Current employment type						
Employed	Ref.			NA		
Retired	2.36	1.15-4.82	**.019**			
Unemployed	1.49	0.76-2.89	.242			
Civil status						
Single	Ref.			NA		
Married or domestic partnership	0.71	0.36-1.38	.313			
Social factors						
Alcohol use						
No	Ref.			Ref.		
Yes	1.30	0.70-2.21	.466	0.96	0.47-1.94	.898
Current smoker						
No	Ref.			Ref.		
Yes	1.92	1.06-3.45	**.030**	2.25	1.15-4.43	**.018**
HIV characteristics						
Year of HIV diagnosis	1.02	0.98-1.06	.438	0.96	0.89-1.03	.209
CD4 count						
<500 copies/mL	Ref.			Ref.		
≥500 copies/mL	1.80	0.90-3.57	.099	1.69	0.82-3.50	.155
Plasma HIV viral load						
Undetectable	Ref.			Ref.		
Detectable	1.22	0.54-2.76	.628	1.76	0.66-4.70	.258
Prior non-CNS opportunistic infection[b]						
No	Ref.			Ref.		
Yes	1.73	0.98-3.05	.057	2.24	1.05-4.76	**.037**
Efavirenz, current use						
No	Ref.			Ref.		
Yes	0.63	0.36-1.11	.115	0.38	0.16-090	**.027**
Adherence to ART						
No	Ref.			Ref.		
Yes	0.55	0.31-0.99	**.050**	0.79	0.36-1.72	.547

[a]Multivariable analyses were adjusted for the following covariates: sex, age, current alcohol use, current smoker, years with HIV diagnosis, current absolute CD4 count, plasma HIV viral load, prior opportunistic infection, current efavirenz use, adherence to ART.
[b]Prior opportunistic infection included any history of: candidiasis, Kaposi's sarcoma, cytomegalovirus, or *pneumocystis* pneumonia.
Abbreviations: 95% CI, 95% confidence interval; ART, antiretroviral treatment; CNS, central nervous system; PR, prevalence ratio; Ref., reference; SD, standard deviation.
Bold text, $P < .05$ (significant).

aged and older PLWH in our study. We also found that current efavirenz use was associated with a lower depression frequency.

In our study, women living with HIV had higher rates of depression than men living with HIV (41% compared with 22% in men). Global trends similarly reflect these sex inequalities with a preponderance of female adults having depression (odds ratio [OR] 1.95) throughout adulthood with a peak depression incidence in adolescence (OR 3.02).[32] Factors that influence this higher depression risk in women in the general population are multifactorial with an intersecting effect of literacy and poverty rates, intimate-partner violence, contraception use, perinatal depression, and comorbid medical conditions.[32] South American countries carry the highest depression prevalence in the world with women being disproportionately burdened too.[2,33]

In Latin America, few studies have focused on sex disparities in mental health outcomes among PLWH. One study from Mexico,[25] and another from Brazil[24] reported female sex as a risk factor for depression, similar to our findings. We

found one study from 2008 of 78 young Peruvian women living with HIV reported 68% had depression, and identified that food insecurity, missing an appointment with their healthcare provider in the past 30 days, high HIV-associated stigma and low social support were risk factors for depression.[34] Literature from other LMICs has elucidated factors that may increase depression among females with HIV. For example, one study from Tanzania of pregnant women with HIV found that being single, food insecurity and shame associated with having HIV were factors that increased risk of depression.[35] In Zimbabwe, intimate partner violence was identified as a risk factor for depression among pregnant women with HIV.[36] Although we did not measure any of these factors in our study, similar risk factors may impact older women with HIV increasing depression risk in Peru that should be evaluated.

Being a current smoker was associated with a higher frequency of depression in our study, as has been reported in other studies. In one study across 7 US sites, depression was common among PLWH who smoke cigarettes (22%).[37] Those with depression were less likely to have ceased smoking after 4 years.[38] Another study in Vietnam found that the prevalence of depression among smokers with HIV was 38.3%, and those who had higher levels of tobacco dependence were more likely to have depression.[39] The results of our study and those of other studies highlight the association between smoking and depression in PLWH and that PLWH who currently smoke may need screening for depression.

Our study found an association between a prior non-CNS opportunistic infection and depression in adjusted regression analyses, including a history of candidiasis, Kaposi's sarcoma, cytomegalovirus, or *pneumocystis* pneumonia, similar to findings of other studies worldwide. For example, one meta-analysis of studies of PLWH in Ethiopia found opportunistic infections increased the risk of depression by an adjusted odds ratio of 3.0 (2.182, 4.151).[40] One of the studies in Ethiopia found that those with a prior history of opportunistic infections, controlling for CD4 count, found a significant association with depressive symptoms.[41] In another study in Somalia, having a current opportunistic infection was associated with depressive symptoms as well.[13] Having a history of or current non-CNS opportunistic infection may be an indicator to clinicians to screen PLWH for depression, in addition to the other factors identified in our study.

Unlike results from many studies on efavirenz, we found that current efavirenz use was associated with lower depression frequency. Neuropsychiatric side effects of efavirenz have been widely reported. A prospective study of PLWH with neuropsychiatric symptoms found that efavirenz was associated with sleep disturbances (75%), anxiety (65%), depression (39%), and attention disturbances (31%).[42] In Tanzania, depression scores were higher for those on efavirenz (Cohen's D: 0.38; $P = .02$).[43] A similar study in Ecuador of PLWH on efavirenz found that 40% had mild depression after 8-12 weeks of treatment initiation with efavirenz-based ART, but on a second depression assessment (median 69 days after ART initiation), depression prevalence had decreased to 22%.[44] which may have attenuated the effect of efavirenz on depression.

Our study has limitations that are difficult to address. First, this is a secondary analysis of cross-sectional data, therefore we can calculate associations but not causality. Also, there were several possible risk factors that were not collected in the parent study and so couldn't be analyzed. Next, this is a single-center study in a large urban city, thus results cannot be generalized across Peru. Next, we used a brief validated depression screening and did not perform a comprehensive psychiatric evaluation of enrolled participants. Despite this, most of the studies regarding depression in PLWH have used the same instrument and the PHQ-9 has been validated for in Peru and has high sensitivity and specificity for depression.[30] Despite these limitations, our study offers valuable insight into risk factors for depression in aging PLWH in Peru.

Conclusions

We identified significant associations between female sex, current smoker and prior opportunistic infection with higher risk of depression in older PLWH. These risk factors may identify PLWH who may be considered for depression screening by primary care providers. Public health strategies should focus on prevention and early intervention of mental health services into HIV care. In Peru, identifying those at highest risk for depression based on the risk factors identified in our study and offering early mental health services is crucial for improving quality of life and adherence to ART.

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Author Contributions

VEF-R was involved in drafting of the manuscript and statistical analyses; DJJ and AL in drafting of the manuscript; MG-Z in data collection and drafting of the manuscript; RC and PJG in conceptualization and critical revision; and MMMD in data collection, drafting of the manuscript, conceptualization, and critical revision.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical Approval

All participants had provided written informed consent prior to being enrolled in the parent study which was approved by the institutional review boards of Universidad Peruana Cayetano Heredia (Lima, Peru) and Via Libre (Lima, Peru). No additional ethical approval was needed for analysis of the de-identified dataset utilized for this study.

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Supplemental Material

Supplemental material for this article is available online.

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