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Association of Poor Sleep With Depressive and Anxiety Symptoms by HIV Disease Status: Women's Interagency HIV Study

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Background: Sleep disturbances are prevalent in women living with HIV (WLWH) and can affect mental health and overall quality of life. We examined the prevalence and predictors of poor sleep quality in a US cohort of WLWH and HIV-uninfected controls and the relationship between sleep quality and mental health symptom burden stratified by HIV disease status (viremic WLWH, aviremic WLWH, and HIV-uninfected women).

Methods: Sleep quality was assessed using the Pittsburgh Sleep Quality Index in 1583 (400 viremic WLWH, 723 aviremic WLWH, and 460 HIV-uninfected women) Women's Interagency HIV Study participants. Depressive and anxiety symptoms were concurrently assessed using the Center for Epidemiological Studies-Depression (CES-D) scale and General Anxiety Disorder (GAD-7) scale. Associations between poor sleep quality (global Pittsburgh Sleep Quality Index >5) and both high depressive (CES-D ≥16) and anxiety (GAD-7 ≥10) symptoms were each assessed by HIV disease status using multivariable logistic regression models.

Results: Prevalence of poor sleep quality in the overall sample was 52%, differed by HIV disease status ($P = 0.045$), and was significantly associated with high depressive and anxiety symptoms in (1) viremic WLWH, (2) aviremic WLWH, and (3) HIV-uninfected women [CES-D: (1) adjusted odds ratio (aOR) = 7.50, 95% confidence interval (CI): 4.10 to 13.7; (2) aOR = 4.54, 95% CI: 3.07 to 6.73; and (3) aOR = 6.03, 95% CI: 3.50 to 10.4; GAD-7: (1) aOR = 5.20; 95% CI: 2.60 to 10.4, (2) aOR = 6.03; 95% CI: 3.67 to 9.91, and (3) aOR = 6.24; 95% CI: 3.11 to 12.6].

Conclusions: Poor sleep quality is highly prevalent, as is mental health symptom burden, among WLWH and HIV-uninfected controls. Future longitudinal studies are necessary to clarify the directionality of the relationship.

Key Words: sleep, minority women, HIV, HIV viremia, mental health

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INTRODUCTION

Systematic reviews suggest that 30%–90% of people living with HIV (PLWH) report disturbed sleep with women and individuals older than 40 years particularly affected.[1,2] In addition to subjective measures of sleep quality, objectively measured shorter total sleep duration, poorer sleep continuity, and substantial night-to-night variability in sleep timing (indicative of circadian disruption) have been reported among PLWH.[3–6] We previously reported that more than 60% of women living with HIV (WLWH) and HIV-uninfected women in the Women's Interagency HIV Study (WIHS) met criteria for insomnia.[7]

Life circumstances including unstable housing, high neighborhood disorder, trauma histories, social isolation, and polypharmacy put aging WLWH at greater risk for sleep disturbances.[8–11] Compared with age-matched women from the general population, WLWH are more likely to have disordered breathing due to high rates of obesity, smoking, and a higher burden of pulmonary disease, all contributors to disrupted sleep.[12,13] In addition, adverse environmental factors are more common among aging WLWH and often include significant co-occurring everyday life stressors, HIV-related stigma and discrimination, low levels of physical activity, inadequate micronutrient intake, too much light or noise at night, and too little daytime light exposure.[14–18] These may disrupt the sleep or wake cycle directly and indirectly through a number of pathways, including neurohormonal dysregulation of melatonin, serotonin, cortisol, and catecholamines[17,18] and vitamin D deficiency.[16] Furthermore, with a decline in estrogen throughout the menopausal transition, vasomotor symptoms and increasing mood or anxiety symptoms interfere with various aspects of sleep.[19]

Sleep disturbances have emerged as a potential cause—and consequence—of higher rates of mental health disorders in samples of men living with HIV; however, relatively little is known about the relationship among WLWH.[20,21] Mood and anxiety disorders are prevalent among WLWH; we reported a 12-month prevalence of 22% mood disorders and 45% anxiety disorders in the WIHS.[22] Understanding the co-occurrence of these mental health problems with poor sleep quality in the context of HIV infection is a first step for mitigating untoward effects.[22,23] Although aging WLWH are heavily affected by mental health disorders and sleep problems, particularly as they transition through menopause, sleep disorders remain infrequently diagnosed, leading to missed opportunities to improve health and quality of life.[1,24–26]

There is relatively limited information on sleep among WLWH and specifically in relation to mental health. Therefore, our primary aim was to determine the prevalence and predictors of poor sleep quality and their relationship with mental health symptom burden in the WIHS. As a secondary aim, we sought to determine whether these sleep or mental health relationships differed when stratified by HIV disease status (viremic WLWH, aviremic WLWH, and HIV-uninfected women).

METHODS

Study Population

WIHS, now the Multicenter AIDS Cohort Study/WIHS Combined Cohort Study, is an ongoing, multicenter, longitudinal cohort study that includes WLWH and HIV-uninfected women in the United States. Enrollment occurred in 1994/1995, February 2001/2002, and 2011/2012 at sites in Bronx and Brooklyn, NY, Los Angeles and San Francisco, CA, Washington, DC, and Chicago, IL,[27,28] and during 2013–2015 at Southern sites in Chapel Hill, NC, Miami, FL, Atlanta, GA, Birmingham, AL, and Jackson, MS.[29] In brief, women were seen semiannually for a targeted clinical assessment with specimen collection and a comprehensive structured interview to collect sociodemographic, behavioral, and health history data. All study participants provided written informed consent after review and approval by each site's Institutional Review Board. WIHS study protocols, recruitment procedures, and cohort characteristics have been previously described.[27–29] WIHS interviewers added the Pittsburgh Sleep Quality Index (PSQI) questionnaire for those who agreed (78%) during a single WIHS visit in 2018 when sociodemographic, behavioral, and clinical data for this nested cross-sectional analysis were collected.

Sleep Quality

Global sleep quality during the previous month was measured using the validated PSQI, in which 18 of the 19 items in the self-report questionnaire were scored to generate 7 sleep components: perceived sleep quality, sleep latency (time to fall asleep), sleep duration (hours of sleep per night), sleep efficiency (calculated percentage of time asleep divided by time spent in bed), sleep disturbances (number of reasons for trouble sleeping), use of sleep medications (prescribed or over the counter), and daytime dysfunction (functional impairment due to loss of sleep). The generated components were ordinal variables scored 0–3 per scoring guidelines; higher scores represented worse sleep outcomes.[30] The 7 components were summed to produce a global PSQI score ranging from 0 to 21; higher scores indicated worse sleep quality. The global PSQI score was analyzed continuously and as a binary variable with a score greater than 5 indicating poor sleep quality. A global PSQI >5 demonstrates sensitivity of 89.6% and specificity of 86.5% in distinguishing poor vs. better sleep quality.[30]

Anxiety and Depressive Symptom Burden

The Center for Epidemiological Studies-Depression (CES-D) scale assesses depressive symptom severity in the past week using a 20-item questionnaire in which each response receives a score of 0–3. The items were summed for a CES-D total score ranging from 0 to 60, with higher scores representing higher depressive symptom burden.[31] The WIHS has demonstrated that the CES-D is a reliable assessment of the burden of depressive symptoms among WLWH.[32] Anxiety symptoms were measured using the 7-item self-report General Anxiety Disorder (GAD-7) scale. Users are asked how often anxiety symptoms have bothered them in the past 2 weeks, with each of the 7 items receiving a score from 0 to 3. The 7 items are summed for a total GAD-7 score from 0 to 21. The higher the score, the more frequently they experienced symptoms.[33]

Both questionnaires were scored and analyzed as continuous and as binary variables using cut points indicative of high vs. low symptom burden (CES-D ≥16; GAD-7 ≥10).[31,33] An analysis in the WIHS showed that the CES-D standard cut point of 16, when compared with a higher cut point and with somatic items excluded, produced similar associations with antiretroviral therapy use and demographic characteristics.[34] We examined the CES-D total score with and without the sleep disturbance item (my sleep was restless) due to concerns about collinearity. Inclusion of this item did not change results; therefore, the item was included in the total CES-D score. A GAD-7 score ≥10 demonstrated optimal sensitivity (89%) and specificity (82%) in the general population.[33]

Covariates

Covariates were selected a priori based on published literature and likely confounding; these included features such as: age in years, race/ethnicity (non-Hispanic Black, Hispanic, other, and non-Hispanic White), highest level of education (<high school, high school, and >high school), annual household income (≤$18,000 and >$18,000), employment, housing stability, partner status, cigarette (current and former or never), hazardous alcohol (>7 drinks/wk), noninjection drug use (current and former or never), and injection drug use (ever and never), self-reported menopausal status (menopausal, not menopausal, and n/a due to hysterectomy), body mass index (measured BMI; kg/m2), and WIHS site. Additional variables of interest for WLWH included CD4^{+} T lymphocyte count (CD4 cells/mm³), HIV viral load (copies/mL) and as detectable (>20 copies) vs. undetectable (≤20 copies), and antiretroviral adherence reported (≥95% of the time).

Statistical Methods

Descriptive statistics were generated for demographic, behavioral, and clinical characteristics in the sample overall. The continuous global PSQI score and each of the 7 components as categorical measures were compared by HIV disease status (HIV-uninfected women, aviremic WLWH, and viremic WLWH) using Anova or *t* tests (mean and SD) for continuous variables and the χ^2 tests for categorical variables. Cronbach alpha was run to test the internal reliability of the PSQI (alpha = 0.74).

Participant characteristics by sleep quality (global PSQI score >5 vs. ≤5) were compared with the χ^2 tests for categorical variables and the Wilcoxon rank sum and *t*-tests for continuous variables. Odds ratios and 95% confidence intervals (CIs) were calculated in bivariate analyses to identify predictors of poor sleep quality. Multivariable logistic regression models predicted odds of poor sleep, adjusting for age in years, race, education, income, and study site for the overall sample. The relationship between poor sleep quality and mental health symptom burden (high burden: CES-D ≥16 and GAD-7 ≥10) was also examined in unadjusted and adjusted analyses for the overall sample and stratified by HIV disease status. Additional covariates were included if they

were of a priori interest or significant in unadjusted analyses at $P < 0.05$. Final multivariable models retained all statistically significant variables and those identified from previous literature (including HIV disease status in the overall model, age, race, education, employment, noninjection drug use, injection drug use, BMI, smoking, hazardous alcohol use, menopausal status, and WIHS site). All analyses were performed using SAS software, version 9.4 (SAS Institute, Inc. Cary, NC). A *P* value <0.05 was considered statistically significant.

RESULTS

Sleep and Participant Characteristics

A total of 1583 participants (1123 WLWH/460 HIV-uninfected women) were included in this analysis. Study characteristics are listed in Table 1. The median age was 51 years (interquartile range: 44–57 years). Most of the participants were Black (62%), had a high school education or less (63%), were unemployed (60%), had an income ≤$18,000/yr (62%), and were obese (BMI >30, 56%). Nearly half were menopausal (43%), 38% was current smokers, and 26% was current noninjection drug users. Among WLWH, the median CD4 count was 680 cells/mm³, and although 85% reported ≥95% antiretroviral adherence, 36% had detectable HIV viral loads (>20 copies/mL).

The global PSQI score for our cohort ranged from 0 to 20; the mean was 6.4 and median was 6 (Fig. 1). The PSQI had an overall Cronbach's alpha of 0.74, indicating adequate internal reliability. There were no significant differences in global PSQI score by HIV serostatus (WLWH mean = 6.45 vs. HIV-uninfected mean = 6.43); however, global PSQI score differed significantly when stratified by viremia status (viremic WLWH mean = 6.90 vs. aviremic WLWH mean = 6.20; $P = 0.009$). Among the PSQI components, sleep disturbances significantly differed by HIV disease status ($P = 0.010$); a higher proportion of viremic WLWH (32%) reported more frequent sleep disturbances than aviremic WLWH (25%) and HIV-uninfected women (28%). Aviremic WLWH were more likely to report "very good sleep" (34%) than HIV-uninfected women (26%) and viremic WLWH (28%) ($P = 0.022$). Viremic WLWH (17%) reported more daytime dysfunction than aviremic WLWH (11%) and HIV-uninfected (10%) women. The other PSQI components did not significantly differ by HIV disease status (data not shown).

Predictors of Poor Sleep

Participant characteristics stratified by sleep quality (poor sleep: PSQI >5) are summarized in Table 2; poor sleep quality was found in 821 (52%) participants, which differed significantly by HIV disease status (56.5% viremic WLWH vs. 48.8% aviremic WLWH vs. 52.6% HIV-uninfected; $P = 0.045$). Compared with participants with better sleep quality, those with poor sleep quality were older ($P = 0.0004$), had lower household income (≤$18,000/yr; $P = 0.002$), were unemployed ($P < 0.0001$), and more likely to be unstably housed ($P = 0.015$). Those with poor sleep quality were also more likely to report current smoking,

current noninjection drug use, and history of injection drug use (all $P < 0.0001$). Depressive (CES-D) and anxiety symptoms (GAD-7) were significantly associated with poor sleep quality (both $P < 0.0001$).

In multivariable models, higher age, lower household income, unemployment, current cigarette smoking, hazardous alcohol use (>7 drinks/wk), current noninjection drug use,

and injection drug use ever were significantly associated with poor sleep quality (all $P < 0.05$). Depressive and anxiety symptoms remained significantly associated with poor sleep quality after adjusting for age, race, education, income, and WIHS site ($P < 0.0001$). (Table 2).

Associations of Poor Sleep and Mental Health Symptom Burden

Prevalence of poor sleep quality by mental health symptom burden (high vs. low burden) is listed in Table 3. In unadjusted analyses, when compared with better sleep, participants with poor sleep quality had increased odds of depressive (OR = 5.92; 95% CI: 4.60 to 7.63, $P \leq 0.0001$) and anxiety symptoms (OR = 6.31; 95% CI: 4.57 to 8.71, $P \leq 0.0001$). In multivariable models, poor sleep remained significantly associated with high depressive (adjusted odds ratio [aOR] = 5.06; 95% CI: 3.87 to 6.63, $P \leq 0.0001$) and anxiety symptoms (aOR = 5.70; 95% CI: 4.05 to 8.02, $P \leq 0.0001$) after adjusting for HIV disease status, age, race, education, employment, BMI, smoking, alcohol use, any drug use, menopausal status, and WIHS site.

When stratified by HIV disease status, those with poor sleep quality had significantly higher mental health symptom burden across all groups (all $P < 0.0001$). This association remained significant for all 3 HIV disease status groups even after adjusting for age, race, education, employment, BMI, smoking, alcohol use, drug use, menopausal status, and WIHS site: (1) viremic WLWH, (2) aviremic WLWH, and (3) HIV-uninfected, respectively [CES-D: (1) aOR = 7.50; 95% CI: 4.10 to 13.7, (2) aOR = 4.54; 95% CI: 3.07 to 6.73, and (3) aOR = 6.03; 95% CI: 3.50 to 10.4; GAD-7: (1) aOR = 5.20; 95% CI: 2.60 to 10.4, (2) aOR = 6.03; 95% CI: 3.67 to 9.91, and (3) aOR = 6.24; 95% CI: 3.11 to 12.6] (Table 4).

DISCUSSION

This study demonstrated that poor sleep quality was common among WLWH and HIV-uninfected women

TABLE 1. Demographic, Behavioral, and Clinical Characteristics Among Women's Interagency HIV Study Participants (n = 1583)

Variables	Overall n (%)
HIV serostatus	
HIV-seropositive	1123 (70.9)
HIV-seronegative	460 (29.1)
Age at visit, mean (SD)	50.8 (9.3)
Race/ethnicity	
Non-Hispanic Black	985 (62.2)
Hispanic	207 (13.1)
Non-Hispanic other	249 (15.7)
Non-Hispanic White	142 (9.0)
Education	
<High school	487 (30.8)
High school	516 (32.6)
>High school	579 (36.6)
Income, ≤$18,000/yr	958 (61.5)
Unemployed	949 (60.0)
Unstable housing	264 (16.7)
Partner status, no partner	1128 (72.0)
Cigarette smoker, current	596 (37.7)
Hazardous alcohol, >7 drink/wk	131 (8.3)
Noninjection drug*, current	418 (26.4)
Injection drug†, ever	251 (15.9)
Menopausal status	
Menopausal	679 (42.9)
Not menopausal	651 (41.1)
N/A due to hysterectomy	253 (16.0)
Body mass index, mean (SD)	32.7 (9.1)
Underweight	26 (1.6)
Normal	263 (16.8)
Overweight	400 (25.5)
Obese	880 (56.1)
Depressive symptoms (CES-D), median (IQR)	8 (3–18)
Anxiety symptoms (GAD-7), median (IQR)	2 (0–7)
HIV-positive participants (n = 1123)	
CD4 count (cells/mm^3), median (IQR)	680 (473–918)
CD4 count below 350	157 (14.0)
Detected viral load	400 (35.7)
Viral load (copies/mL), median (IQR)	98 (36–1115)
cART adherence, ≥95%	902 (85.4)

Owing to missing data, counts may not add up to total n = 1583. Data presented as counts (frequency), unless otherwise noted.

*Noninjected recreational drugs use since last visit. Includes crack, cocaine, and heroin use, any marijuana use, hallucinogens, club drugs, and methamphetamines.

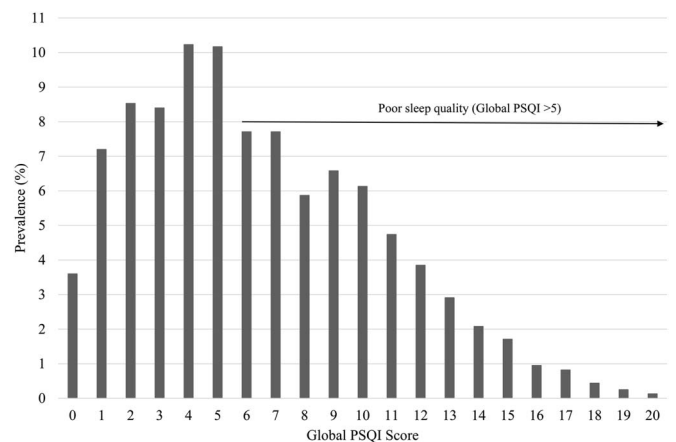†Ever reported use.

IQR, interquartile range.

FIGURE 1. Distribution of global PSQI score among WIHS participants (n = 1583).

TABLE 2. Factors Associated With Poor Sleep in Women's Interagency HIV Study Participants (n = 1583)

Variables	Poor Sleep, PSQI >5 (n = 821) n (%)	Better Sleep, PSQI ≤5 (n = 762) n (%)	Unadjusted OR (95% CI)	P*	Adjusted† OR (95% CI)	P
HIV disease status						
Viremic WLWH	226 (27.5)	174 (22.8)	1.36 (1.07 to 1.74)	0.045	1.26 (0.96 to 1.64)	0.199
Aviremic WLWH	353 (43.0)	370 (48.6)	Ref.		Ref.	
HIV-uninfected women	242 (29.5)	218 (28.6)	1.16 (0.92 to 1.47)		1.18 (0.92 to 1.51)	
Age at visit, mean (SD)	51.6 (9.0)	49.9 (9.5)	1.02 (1.01 to 1.03)	0.0004	1.02 (1.01 to 1.03)	0.003
Race/ethnicity						
Non-Hispanic Black	482 (58.7)	503 (66.0)	0.47 (0.33 to 0.69)	0.0008	0.56 (0.38 to 0.83)	0.036
Hispanic	110 (13.4)	97 (12.7)	0.56 (0.36 to 0.87)		0.61 (0.37 to 0.99)	
Non-Hispanic other	134 (16.3)	115 (15.1)	0.58 (0.38 to 0.89)		0.66 (0.42 to 1.04)	
Non-Hispanic White	95 (11.6)	47 (6.2)	Ref.		Ref.	
Education						
<High school	268 (32.6)	219 (28.8)	1.13 (0.89 to 1.44)	0.146	1.07 (0.82 to 1.40)	0.140
High school	252 (30.7)	264 (34.7)	0.88 (0.70 to 1.12)		0.83 (0.64 to 1.08)	
>High school	301 (36.7)	278 (36.5)	Ref.		Ref.	
Income, ≤$18,000/yr	527 (65.2)	431 (57.5)	1.38 (1.13 to 1.70)	0.002	1.33 (1.06 to 1.67)	0.015
Unemployed	555 (67.6)	394 (51.7)	1.95 (1.59 to 2.39)	<0.0001	1.82 (1.41 to 2.34)	<0.0001
Unstable housing	155 (18.9)	109 (14.3)	1.39 (1.07 to 1.82)	0.015	1.31 (0.98 to 1.76)	0.067
Partner status, no partner	598 (73.6)	530 (70.4)	1.17 (0.94 to 1.46)	0.163	1.14 (0.90 to 1.44)	0.275
Cigarette smoker, current	353 (43.0)	243 (31.9)	1.61 (1.31 to 1.98)	<0.0001	1.49 (1.19 to 1.86)	0.0005
Hazardous alcohol, >7 drink/wk	82 (10.0)	49 (6.4)	1.61 (1.12 to 2.33)	0.010	1.51 (1.03 to 2.23)	0.037
Noninjection drug‡, current	263 (32.0)	155 (20.3)	1.85 (1.47 to 2.32)	<0.0001	1.70 (1.33 to 2.17)	<0.0001
Injection drug§, ever	166 (20.2)	85 (11.2)	2.02 (1.52 to 2.68)	<0.0001	1.47 (1.07 to 2.01)	0.016
Menopausal status						
Menopausal	374 (45.6)	305 (40.0)	1.48 (1.19 to 1.84)	<0.0001	1.30 (0.95 to 1.78)	0.003
Not menopausal	295 (35.9)	356 (46.7)	Ref.		Ref.	
N/A due to hysterectomy	152 (18.5)	101 (13.3)	1.82 (1.35 to 2.44)		1.83 (1.29 to 2.60)	
Body mass index, mean (SD)	32.8 (9.2)	32.5 (9.0)	—	0.580	—	
Underweight	15 (1.9)	11 (1.5)	1.35 (0.60 to 3.06)	0.799	1.22 (0.52 to 2.83)	0.346
Normal	132 (16.2)	131 (17.3)	Ref.		Ref.	
Overweight	213 (26.2)	187 (24.7)	1.13 (0.83 to 1.54)		1.35 (0.97 to 1.88)	
Obese	453 (55.7)	427 (56.5)	1.05 (0.80 to 1.39)		1.26 (0.94 to 1.70)	
CES-D, median (IQR)	14 (6–24)	4 (1–10)	1.10 (1.09 to 1.12)	<0.0001	1.10 (1.09 to 1.11)	<0.0001
GAD-7, median (IQR)	6 (2–11)	0 (0–3)	1.22 (1.19 to 1.25)	<0.0001	1.21 (1.17 to 1.24)	<0.0001

TABLE 2. (*Continued*) Factors Associated With Poor Sleep in Women's Interagency HIV Study Participants (n = 1583)

Variables	Poor Sleep, PSQI >5 (n = 821)	Better Sleep, PSQI ≤5 (n = 762)	Unadjusted		Adjusted†	
	n (%)	n (%)	OR (95% CI)	*P**	OR (95% CI)	*P*
HIV-positive participants (n = 1123)						
CD4 count (cells/mm^3), median (IQR)	681 (460–918)	680 (488–918)	—	0.947	—	
CD4 count below 350	79 (13.6)	78 (14.4)	0.94 (0.67 to 1.31)	0.709	0.93 (0.65 to 1.33)	0.686
Viral load (copies/mL), median (IQR)	108.5 (39–1120)	79 (35–849)	—	0.237	—	
cART adherence, ≥95%	454 (83.9)	448 (87.0)	0.78 (0.55 to 1.10)	0.158	0.72 (0.50 to 1.04)	0.077

Owing to missing data, counts may not add up to total n = 1583. Data presented as counts (frequency), unless otherwise noted.
*P values calculated from the χ^2 tests for categorical variables, Wilcoxon (median), or *t* tests (mean).
†Adjusted for age in years, race, education, income, and WIHS site.
‡Includes crack, cocaine, andr heroin use, any marijuana use, hallucinogens, club drugs, and methamphetamines.
§Ever reported use.
IQR, interquartile range.

enrolled in the WIHS and significantly differed by HIV viremia status. Although the prevalence of poor sleep was similar in aviremic WLWH and HIV-uninfected women, we found worse sleep quality in WLWH who had not achieved viral control. Additional factors significantly associated with poor sleep quality included older age, low income, unemployment, smoking, hazardous alcohol use, noninjection, and past injection drug use. These findings suggest that poor sleep is likely exacerbating the burden of comorbidities in this population.

This study corroborated the high prevalence of poor sleep found in previous studies and expanded these findings by exploring validated measures of mental health symptom burden in a large cohort of women. Significant associations between sleep quality and depressive and anxiety symptoms were found in multivariable models and remained significant when stratified by HIV disease status. In a cohort of French HIV-infected adults (n = 1354), similar proportions of poor sleep quality (global PSQI score >5: 47%) and depressive symptoms (20%) were observed.[35] Although predominantly found in male individuals, they found poor sleep quality more frequently in female individuals. Similar to our study, the

odds of sleep disturbances among participants with depression was 4.6 times that of those without depression.

Qiu et al[36] evaluated sleep quality in a cohort of HIV-uninfected pregnant US women (n = 1488). Similar to our study, they found that poor sleep measured by the PSQI was associated with 6.5 and 3.6 increased odds of depression and anxiety. Qiu et al[36] used a different scale to measure anxiety, which could explain the differences in the magnitude of the odds of association.

In our previous study among 1682 WIHS participants, Jean-Louis et al assessed prevalence and predictors of insomnia symptoms and found that WLWH were more likely to report insomnia symptoms than HIV-uninfected women, and depression was a significant predictor of insomnia symptoms. Unlike this study, insomnia symptoms were used as a measure of sleep disturbances and defined as a report of difficulty in initiating or maintaining sleep or early morning waking 3 or more times per week in the past 2 weeks. This study, although using the same cohort, included measures collected 12 years before this study, and therefore, sociodemographic changes due to increasing age and time are expected and were observed. The cohort also expanded during the past 12 years. Two additional enrollment

TABLE 3. Prevalence and Association of Sleep Quality as Measured by the Pittsburgh Sleep Quality Index by Mental Health Symptom Burden (n = 1583)

Measures	Poor Sleep, PSQI >5 (n = 821) n (%)	Better Sleep, PSQI ≤5 (n = 762) n (%)	*P*	Unadjusted OR (95% CI)	Adjusted† OR (95% CI)
High depressive symptoms					
Yes, CES-D ≥16	383 (46.7)	98 (12.9)	<0.0001	5.92 (4.60 to 7.63)*	5.06 (3.87 to 6.63)*
No, CES-D <16	438 (53.3)	664 (87.1)		Ref.	Ref.
High anxiety symptoms					
Yes, GAD-7 ≥10	252 (30.7)	50 (6.6)	<0.0001	6.31 (4.57 to 8.71)*	5.70 (4.05 to 8.02)*
No, GAD-7 <10	569 (69.3)	712 (93.4)		Ref.	Ref.

*Significant at $P < 0.0001$.
†Adjusted for HIV disease status, age in years, race, education, employment, body mass index, smoking, drinking, noninjection and injection drug use, menopausal status, and WIHS site.

TABLE 4. Association of Sleep Quality as Measured by the Pittsburgh Sleep Quality Index by Mental Health Symptom Burden, Stratified by HIV Disease Status

Measures	Viremic WLWH (n = 400)		Aviremic WLWH (n = 723)		HIV-Uninfected Women (n = 460)	
	Unadjusted OR (95% CI)	Adjusted* OR (95% CI)	Unadjusted OR (95% CI)	Adjusted* OR (95% CI)	Unadjusted OR (95% CI)	Adjusted† OR (95% CI)
High depressive symptoms						
Yes, CES-D ≥16	7.29 (4.34 to 12.2)†	7.50 (4.10 to 13.7)†	4.90 (3.43 to 7.02)†	4.54 (3.07 to 6.73)†	6.83 (4.14 to 11.3)†	6.03 (3.50 to 10.4)†
No, CES-D <16	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
High anxiety symptoms						
Yes, GAD-7 ≥10	6.03 (3.21 to 11.3)†	5.20 (2.60 to 10.4)†	5.91 (3.74 to 9.35)†	6.03 (3.67 to 9.91)†	7.51 (3.85 to 14.6)†	6.24 (3.11 to 12.6)†
No, GAD-7 <10	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.

*Adjusted for age in years, race, education, employment, body mass index, smoking, drinking, noninjection and injection drug use, menopausal status, and WIHS site.
†Significant at $P < 0.0001$.

waves occurred, one in 2011/2012 and another targeting women at new Southern sites in 2013–2015, resulting in increased representativeness of the cohort.[7]

Given the high co-occurrence of poor sleep and mental health symptoms found in this study, both should be assessed and effectively treated to prevent or mitigate effects of the other. We found the PSQI components had adequate internal reliability (Cronbach $\alpha = 0.74$); therefore, in the context of clinical assessment, sleep can reliably be evaluated using the PSQI. The opportunity for patient–provider discussion about problematic sleep during the clinical encounter could enhance not only understanding of and treatment for sleep but also co-occurring mental health problems in this population. Most importantly, given the high co-occurrence of poor sleep and poor mental health, it is possible that effective treatment of either condition may help resolve or prevent the other and lead to higher quality of life. We also acknowledge that research suggests that neighborhood environment and life stressors beyond one's control could negatively influence sleep and mental health, and these are not easily modifiable at the individual level. Finding ways to promote and support policy level changes and empower community members could prove useful in the context of neighborhood disorder from an ecological perspective.

We also found that the association between sleep quality and mental health symptom burden was significant for all HIV disease status groups. Although WIHS studies a decade earlier found that depression was associated with reduced ART adherence and greater viral load,[37] it is possible that in the current era, poor sleep quality and mental health symptom burden are attributable to additional factors beyond ART nonadherence and lack of viral control.

We found that sleep quality was worse among viremic WLWH, a similar finding to the study conducted by Balthazar et al,[38] who found that higher sleep efficiency was associated with lower HIV-RNA levels. Similar to our study, they did not find an association with lower CD4 count and greater sleep disturbances despite previous evidence,[39] suggesting that HIV viral control may play a more important role in sleep quality than CD4 count. Viremic and aviremic WLWH in our

study did differ significantly by smoking, drinking, and substance use (current and previous), which were adjusted for in analyses. Possibly, there is residual confounding that includes risk behaviors that contribute to HIV viremia independent of ART adherence, and these behaviors may negatively influence sleep quality.

Markers of inflammation or immune activation have been found to be associated with both depressive symptoms[40,41] and sleep disturbance[42,43] in the general population and in PLWH. It is possible that disturbed sleep and poor viral control have a bidirectional association through other pathways including activation of the kynurenine pathway by indoleamine 2,3 dioxygenase enzyme responsible for tryptophan catabolism. Tryptophan is both a precursor of melatonin, a sleep and circadian regulator, and important in depression.[44] In a study conducted by Cho et al[45] among currently, previously, and never depressed participants, they found an association between sleep disturbances (PSQI) and kynurenine metabolism in depressed participants only. Inflammation or immune activation may be an additional pathway by which poor sleep and depressive symptoms interact. In PLWH, evidence suggests that the HIV Tat protein can trigger indoleamine 2,3 dioxygenase activity and, subsequently, the kynurenine pathway.[46] This may be a mechanism linking poor sleep and high depressive symptom burden and the stronger association among viremic WLWH. Our cross-sectional study is unable to determine the complex relationships between inflammation or immune activation, sleep quality, and depressive symptoms, so future studies are needed.

Although this cross-sectional study highlighted a significant association between sleep quality and mental health symptoms, we could not determine the directionality of this relationship. In a prospective study of men who have sex with men, self-reported sleep disturbance was associated with a significant increase in depression 6 months later in men with HIV, but not in men without HIV, suggesting that sleep disturbances may lead to depressive symptoms, particularly among people living with HIV.[20] Future steps for this cohort include repeat administrations of the PSQI for longitudinal analyses to delineate the directionality of the relationship

between sleep and mental health symptom burden, including stratification by HIV disease status.

Strengths and Limitations

Other studies have looked at the association between sleep quality and mental health burden in PLWH, but our study is unique because of its size, the presence of an HIV-uninfected control group, the use of a large number of relevant covariates, and the wide geographic and racial/ethnic representation of WLWH in the United States. Nesting this study within a large longitudinal cohort lays the foundation for future longitudinal quality of sleep studies to assess causality in the association of sleep quality and mental health symptom burden.

This study had several limitations. We assessed the associations between the PSQI and mental health symptom burden cross-sectionally, and therefore, directionality cannot be established. Using self-reported sleep quality with the well-validated PSQI allowed us to assess sleep quality in a large number of women; however, self-reported data have limitations compared with objective measures of sleep quality, including social desirability and recall biases or the participant's perception of sleep need. Other disordered sleep may also be missed or underrepresented by the PSQI. Our mental health instruments were also subjective measures; however, they are widely accepted in the literature. It is also plausible that the PSQI differentially captures psychological aspects of sleep. Similarly, some of the emotional symptoms identified by the CES-D and GAD-7 could be manifestations of daytime dysfunction due to sleep disturbances.

CONCLUSIONS

Poor sleep is highly prevalent, associated with mental health symptom burden, and likely underappreciated in the context of care in aging WLWH. Sleep quality and mental health should be priority components of the clinical management of chronic HIV. Providers should be aware of the high frequencies of these symptoms, particularly as PLWH age and risk of aging-related comorbidities increases. Routine and concurrent assessment and effective treatment of mental health and sleep disorders and maintained viral suppression have the potential to profoundly affect the overall quality of life in WLWH.

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