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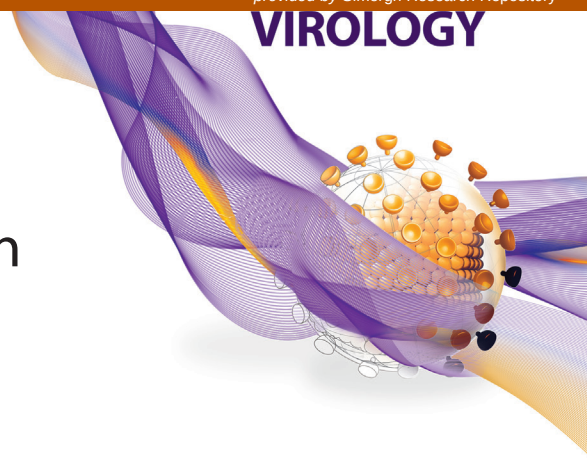

Associated factors of sleep quality in HIV-positive individuals

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ABSTRACT: **Objective:** In the present study, sleep quality and associated factors have been evaluated in HIV-positive individuals. **Methods:** 150 HIV-positive and 50 non-HIV-positive people were included. Pittsburgh Sleep Quality Index, Hospital Anxiety and Depression Scale, somatization subscale of Symptom Checklist-90 were used for evaluation of sleep quality, anxiety, depression and physiological factors respectively. **Results:** Statistically significant differences were found regarding sleep quality ($p < 0.001$) between the HIV-positive and control group. There was significant direct correlation between sleep quality and each of somatization subscale of Symptom Checklist-90, depression and anxiety scores in HIV-positive individuals. **Conclusion:** Depression, anxiety and physical morbidity were detected as main factors that affect sleep quality in the HIV-positive individuals.

KEYWORDS
• associated factors • HIV
• sleep quality

Sleep disturbance is common in HIV-positive individuals [1–3]. Significant increase of slow wave sleep [4], alternations in sleep architecture [5], longer sleep onset latency, earlier morning awakening, more frequent awakenings during the night and reduced sleep efficiency have been reported frequently in these patients [6–9]. The prevalence of sleep disturbance in HIV-positive population was reported as high as 100% [1,10], while in general population the prevalence rate was 10–40% [3]. In addition, insomnia causes chronic fatigue, antiretroviral nonadherence and also affects the quality of life, physical and social functioning of HIV-positive patients [3]. Different factors including environmental, demographic, physiological and psychological factors affect sleep quality in this population [11–13]. There is a strong correlation between sleep disturbance and depression and anxiety. Depressed individuals usually are exposed to high level of sleep disturbance [6,14]. In addition, anxiety disorders can lead to delay sleep onset and reduced total sleep time [14]. During progression of HIV infection, sleep quality is affected by physical symptoms of HIV disease including fever, diarrhea, pain, cough, abdominal cramping, incontinence, itching, burning, night sweats and dyspnea [6]. Also many antiretroviral drugs especially efavirenz can lead to sleep disturbance, depression, anxiety and exacerbation of the physical symptom [3,15–17]. Other medications including benzodiazepines, barbiturates, narcotics and drugs used for treatment of opportunistic infections also can cause sleep disturbance [2]. In the present study, sleep quality and associated factors including demographic characteristics, anxiety–depression and physical morbidity have been evaluated in HIV-positive individuals.

Methods

This cross-sectional study was conducted in HIV clinic of Imam Khomeini Hospital, affiliated to Tehran University of Medical Sciences, Tehran, Iran from March 2013 to April 2014. The

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hospital's ethical committee approved the study protocol and all participants signed the study informed contest form. 200 individuals aged between 21 and 62 years, including 150 HIV-positive patients and 50 non-HIV-positive individuals (as control group), were included. HIV infection of the patients confirmed based on the ELISA and western-blot tests. Demographic data including sex, age, weight, routes of HIV transmission, education level, job, marital status, opportunistic infections and concomitant diseases of the subjects were collected. As it was reported that efavirenz can cause severe sleep disturbance [9], HIV-positive patients divided into three groups; received antiretroviral therapy (ART) including efavirenz, received ART without efavirenz and did not receive ART. Also for further analysis these patients were categorized into two groups; good and poor sleep quality. The validated Persian version of questionnaires including Pittsburgh Sleep Quality Index (PSQI) [18], Hospital Anxiety and Depression Scale (HADS) [19] and somatization subscale of Symptom Checklist-90 (SCL-90) [20,21] were used for evaluation of sleep quality, anxiety symptoms, depression symptoms and physiological factors of the included individuals respectively. PSQI is a self-report instrument based on the sleep quality measuring, in the range of 0–21. A greater amount of this value demonstrates a higher level of sleep disturbance. The patients with PSQI score above five were considered as poor sleepers. The sleep quality was examined by considering seven domains containing subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleeping medication and day time dysfunction during last month [9]. HADS is a well-known self-reported instrument and consists of 14 items for measuring the cognitive symptomatology of both anxiety (seven items) and depression (seven items). Each item is rated from 0 to 3. It has four cutoff points of severity (scores: 0–7 normal; 8–10 mild; 11–14 moderate and 15–21 severe). It should be mentioned that HADS is a psychological screening tool, not a diagnostic measurement [19,22]. SCL-90 is another self-reported questionnaire that was used in this study to evaluate physiological factors. This questionnaire consists of 12 items reported distress in variety of system such as gastrointestinal, cardiovascular and autonomic system and each item scores between 0 (none) to 4 (extreme) [23].

Statistical Package of Social Science version 16 was used for data analysis. Due to non-normal distribution of the data (evaluated by Kolmograph Smirnov test), the nonparametric Mann–Whitney U-test and Kruskal–Wallis one-way analysis of variance were used to compare quantitative data between two and more than two groups, respectively. We used Chi-square test for analysis of qualitative data. The statistical significance level for all tests was considered as $p < 0.05$. Correlations between quantitative variables were assessed based on Spearman rank test. As multiple comparisons for this test, p-value less than 0.01 was considered statistically significant.

Results

Demographic data of included individuals were summarized in **Table 1**. HIV-positive group consisted of 100 males (67%) and 50 (33%) females with mean ± SD age of 35.90 ± 7.75 years old. Control group consisted of 30 males (60%) and 20 females (40%) with mean ± SD age of 34.76 ± 7.36 years old. Sexual contact (51%) followed by injection drug use (43%) were the most common routes of HIV transmission in this cohort. Hepatitis C virus infection was the most common concomitant infection in the HIV-positive individuals and was detected in 53 (35.33%) of them. Sleep disturbances were detected in 88 (55.30%) and 14 (28%) of HIV and non-HIV-positive patients, respectively. Statistically significant differences were found regarding PSQI (median ± IQR: 6.00 ± 7 vs 4.00 ± 4; $p < 0.001$), somatization subscale of SCL-90 (median ± IQR: 11.00 ± 14 vs 26.00 ± 5; $p < 0.001$), depression (median ± IQR: 7.00 ± 7 vs 4.00 ± 4; $p < 0.001$) and anxiety (median ± IQR: 8.50 ± 8 vs 4.50 ± 5; $p < 0.001$) scores between the HIV-positive and control group. Also seven components of PSQI questionnaire (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medications and daytime dysfunction) have been compared between the HIV-positive and control group. Only five components (sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances and daytime dysfunction) showed statistically significant differences between the groups **(Table 2)**.

There was not any significant difference in sleep quality ($p = 0.30$), anxiety ($p = 0.13$) and depression ($p = 0.30$) scores among HIV-positive patients who received ART including efavirenz, ART without efavirenz and no ART. However, there was

Table 1. Demographic data of the HIV and non-HIV-positive individuals.

Characteristic	HIV-infected patients (n = 150); n (%)	Non-HIV-positive individuals (n = 50); n (%)	p-value†
Age (mean ± SD), years	35.90 ± 7.75	34.76 ± 7.36	
Sex:			
– Male	100 (67)	30 (60)	0.39
– Female	50 (33)	20 (30)	
Employment status:			
– Employed	86 (57)	42 (84)	0.001
– Unemployed	64 (43)	8 (16)	
Education level:			
– Primary	16 (11)	0 (0)	p < 0.001
– Intermediate	62 (41)	1 (2)	
– High school	52 (35)	19 (38)	
– Advanced	20 (13)	30 (60)	
Marital status:			
– Single	61 (41)	9 (18)	0.001
– Married	75 (50)	40 (80)	
– Divorced	14 (9)	1 (2)	
HIV transmission routes:			
– Sexual contact	76 (51)	0	
– Intravenous drug injection	64 (43)	0	
– Blood products	8 (5)	0	
– Unknown	2 (1)	0	
Concomitant diseases:			
– Hepatitis B	1 (0.67)	0	
– Hepatitis C	53 (35.33)	0	
– Metabolic diseases	6 (4)		
– Psychiatric diseases	9 (6)	0	
– Gastrointestinal disorders	1 (0.67)	0	
– Renal disorders	2 (1.33)	0	
– Skin problems	1 (0.667)	0	
– Respiratory disorders	2 (1.33)	0	
– Others	9 (6)	0	

†Chi-square test.
SD: Standard deviation.

weak but significant direct correlation between the PSQI and each of somatization subscale of SCL-90 (r = 0.508; p < 0.001), depression (r = 0.457; p < 0.001) and anxiety (r = 0.391; p < 0.001) scores in HIV-positive individuals. There was no statistically significant correlation between PSQI scores and age, weight, time from HIV-infection diagnosis (median ± IQR: 27 ± 45 months), duration of ART (median ± IQR: 24 ± 38 months) and CD4 count (r = 0.04; p = 0.63). Effects of different demographic factors including employment status, education level, marital condition, smoking behavior, alcohol addiction and living status on the patient's sleep quality also have been investigated **(Table 3)**. There was not any significant difference in the sleep quality between the patients receiving efavairenz or not (p = 0.56). Among all evaluated factors, only the patient's employment (p = 0.005) and education (p = 0.04) status had significant effect on the sleep quality. Depression score of the HIV-positive patients was categorized as normal (n = 76; 50.67%) or mild (n = 29; 19.33%), moderate (n = 29; 19.33%) and severe (n = 16; 10.66%) depression. Severity of anxiety of the HIV-positive patients also was divided into normal (n = 67; 44.67%), mild (n = 27; 18%), moderate (n = 31; 20.67%) and severe (n = 25; 16.67%).

Discussion

Sleep disturbance was detected in 55.3 and 28% of Iranian HIV-infected and healthy participants respectively. In previous study, incidence of sleep disturbance was reported in 47.5% of Iranian HIV-positive individuals [24]. In other countries, sleep disturbance was reported in 63–100% of these patients [1,9,10]. Significant difference in the sleep quality was detected between the HIV-infected

Table 2. Comparison of seven components of Pittsburgh Sleep Quality Index.

Domain	HIV-positive patients (n = 150); n (%)	Non-HIV-positive individuals (n = 50); n (%)	p-value[†]
Subjective sleep quality:			
– Very good	33 (22.00)	12 (24.00)	0.09
– Fairly good	74 (49.33)	30 (60.00)	
– Fairly bad	27 (18.00)	8 (16.00)	
– Very bad	16 (10.67)	0	
Sleep latency:			
– <15 min, not during the past month	16 (10.67)	18 (36.00)	< 0.001
– 16–30 min, less than once per week	41 (27.33)	28 (56.00)	
– 31–60 min, once or twice per week	40 (26.67)	4 (8.00)	
– >60 min, three- or more times per week	53 (35.33)	0	
Sleep duration:			
– >7 h	91 (60.67)	30 (60.00)	0.03
– 6–7 h	35 (23.33)	19 (38.00)	
– 5–6 h	13 (8.67)	1 (2.00)	
– <5 h	11 (7.33)	0	
Habitual sleep efficiency:			
– >85%	93 (62.00)	46 (92.00)	0.003
– 75–85%	27 (18.00)	3 (6.00)	
– 65–74%	23 (15.33)	1 (2.00)	
– <65%	6 (4.00)	0	
Sleep disturbances:			
– None	14 (9.33)	8 (16.00)	0.04
– 1–9	68 (45.33)	29 (58.00)	
– 10–18	55 (36.67)	13 (26.00)	
– 19–27	13 (8.67)	0	
Use of sleeping medication:			
– Not during the past month	115 (76.67)	44 (88.0)	0.06
– Less than once per week	15 (10.00)	6 (12.0)	
– Once or twice per week	5 (3.33)	0	
– Three or more times per week	15 (10.00)	0	
Daytime dysfunction:			
– Never, no problem at all	53 (35.33)	32 (64.00)	<0.001
– One- or two-times per week, only a very slight problem	44 (29.33)	14 (28.00)	
– One- to two-times per week, somewhat of a problem	34 (22.67)	4 (8.00)	
– Three- or more times per week, a very big problem	19 (12.67)	0	

[†]Chi-square test.

patients and control group. This difference also has been reported in the previous studies [3,9]. In a cross-sectional study by Wibbeler *et al.*, sleep quality has been compared between HIV-positive patients who did not receive efavirenz and non-HIV-positive individuals. They used PSQI and reported significant differences in all seven domains of PSQI between the groups [9]. However, we did not find significant differences in the subjective sleep quality and use of sleeping medication domains between the groups. Furthermore in Gallego *et al.* study, significant difference in the sleep latency was detected between HIV-positive patients receiving efavirenz and non-HIV-positive individuals. Also, HIV-positive patients with insomnia who received efavirenz had significant reduction in sleep efficiency and increase in rapid eye movement episodes and related vivid dreams. These patients regardless of normal or poor sleep quality had reduced deep-sleep duration [15]. In our study, ART regimen containing efavirenz did not significantly affect the HIV-positive patient's

sleep quality, anxiety and depression scores. The neuropsychiatric adverse effects of efavirenz most commonly occur during the first month of ART and thereafter may be detectable in only 13% of patients [25,26]. The majority of our patricians were not in the first month of ART.

HIV infection itself can cause a variety of psychiatric and neurocognitive complications

Table 3. Associated factors of sleep quality in the HIV-positive patients.

Factor	Sleep quality; n (%)		p-value†
	Good sleep	Poor sleep	
Gender:			
– Male	44 (29.33)	56 (37.33)	0.35
– Female	18 (12.00)	32 (21.33)	
Employment status:			
– Employed	44 (29.33)	42 (28.00)	0.005
– Unemployed	18 (12.00)	46 (39.13)	
Education level:			
– Primary	2 (1.33)	14 (9.00)	0.04
– Intermediate	32 (21.33)	30 (20.00)	
– High school	20 (13.00)	32 (21.33)	
– Advanced	8 (5.00)	12 (8.00)	
Marital status:			
– Single	23 (15.33)	38 (25.33)	0.75
– Married	33 (22.00)	42 (28.00)	
– Divorced	6 (4.00)	8 (5.00)	
HIV transmission routes:			
– Sex	28 (18.67)	48 (32.00)	0.27
– Intravenous drug injection	28 (18.67)	36 (24.00)	
– Blood	4 (2.67)	4 (2.67)	
– Unknown	2 (1.33)	0	
Smoking:			
– Yes	36 (24.00)	51 (34.00)	0.99
– No	26 (17.33)	37 (24.67)	
Alcohol use:			
– Yes	7 (4.67)	12 (8.00)	0.67
– No	55 (36.67)	76 (51.00)	
Substance abuse:			
– Yes	31 (20.67)	49 (32.67)	0.49
– No	31 (20.67)	39 (26.00)	
Family support:			
– Yes	54 (36.00)	76 (51.00	0.89
– No	8 (5.00)	12 (8.00)	
Living in own house:			
– Yes	56 (37.33)	81 (54.00)	0.71
– No	6 (4.00)	7 (4.67)	
Imprison history:			
– Yes	27 (18.00)	40 (26.67)	0.82
– No	35 (23.33)	48 (32.00)	
Receiving efavirenz:			
– Yes	34 (22.67)	44 (29.33)	0.56
– No	28 (18.67)	44 (29.33)	
Hepatitis C infection:			
– Yes	24 (16.00)	29 (19.33)	0.47
– No	38 (25.33)	59 (39.33)	

†Chi-square test.

including dizziness, headache, nightmares, abnormal dreams, mild cognitive difficulty, sleep disturbance (somnolence and insomnia), impaired concentration, depression, hallucination, delusion, paranoia, anxiety, agitation, aggressive behavior, mania, emotional lability, catatonia, melancholia, psychosis and fatigue that may overlap significantly with psychiatric adverse effects of ART. The most common neurologic manifestations in HIV/AIDS individuals are minor cognitive and motor disorder and HIV-associated dementia. The most common psychiatric manifestations are depressive spectrum disorders. HIV-associated neurocognitive disorders (HAND) are neurological disorders associated with HIV infection and AIDS. HAND may include neurological disorders of various severity such as AIDS dementia complex also known as HIV dementia and HIV-associated dementia, HIV encephalopathy and mild neurocognitive disorder [25–28].

Sleep disturbance may be an early symptom of CNS involvement in HIV-positive individuals. Fatigue and insomnia in asymptomatic HIV-infected patients may be related to psychological disturbances including major depression. Periodic assessment of HIV-infected patients who complain of fatigue or insomnia is recommended [28,29].

We have not specifically evaluated the included patients regarding to the HANDS based on the diagnostic criteria. Correlation between HANDS and sleep disturbances in HIV-positive Iranian population should be considered in the future studies.

Reduction of viral load and regulation of HIV-induced immune and endocrine activation following ART may lead to improve sleep quality in these patients. Adjusting administrating times of antiretroviral medications can also decrease their sleep disturbances [2]. We did not detect any significant correlation between the patient's CD4 cell count and sleep quality. Some studies suggested inverse correlation between immune system activity and sleep quality in HIV-positive patients [29] but others did not show this relationship. However, boosting immune system following antiretroviral therapy may improve HANDS and consequently improve sleep quality in this population [11]. Further future studies are needed to clarify correlation between immune system function, HANDS and sleep quality in HIV-positive individuals.

Significant direct correlations were observed between PSQI and each of anxiety, depression and physical morbidity among Iranian HIV-infected patients. These findings also have been reported in the previous studies [3,6,9]. In Wibbeler *et al.* study, depression is defined as the most important factor that affects sleep quality in HIV-positive individuals [9]. Pain as a physiologic factor and depression and anxiety as two psychological factors showed strong correlation with sleep quality of HIV-positive individuals in Robbins *et al.* study [6]. HIV-positive patients are vulnerable to depression and anxiety as psychological disorders. Due to depression, HIV-infected patients experience high levels of anxiety and more sleep difficulties including more problems in falling asleep, decreased slow-wave and more nonrapid-eye-movement sleep. *Vice versa*, anxiety and sleep disturbances may promote or affect depression severity [3,6].

Among the demographic factors, only employment status and education level had significant effect on sleep quality in the HIV-positive individuals. In Saberi *et al.* cross-sectional study, depression, unemployment, use of illicit substances, history of incarceration were associated with poor sleep quality in HIV-positive individuals [13]. Also emotional stress and pain can affect sleep quality in HIV-positive patients [12]. Substance dependency is a main cause of insomnia in HIV-positive people [2]. Significant correlations between sleep quality of HIV-positive individuals and each of the times of living with HIV infection, substance abuse including cigarettes, receiving ART, anxiety, depressive symptoms and sleeping alone have been reported by Nokes *et al.* They did not find any relation between the patient's age, employment status and route of HIV transmission [11]. However, we did not detect any correlation between sleep quality and social support, substance abuse and imprisonment in the included patients.

Sleep disturbances have negative effects on mood, cognition, physical and social functioning, quality of life and life expectancy. Recognition of these conditions and applying appropriate interventions to improve them are essential [2]. In the future studies, different nonpharmacological and pharmacological interventions to improve neuropsychiatric complications in HIV-positive individuals may be compared.

The main limitation of present study is the relative small sample size in both patient and control

groups which should be considered in future studies. We also did not have access to the patient's laboratory data including viral load. Evaluation of correlation between these parameters and sleep quality may show interesting results.

Conclusion

Sleep disturbance was significantly more common in Iranian HIV-positive individuals compared with non-HIV-positive people. Depression, anxiety and physical morbidity were detected as main factors that affect sleep quality in the HIV-positive individuals.

Future perspective

Evaluation of correlation between sleep quality and each of the following items may show interesting results; viral load, CD4 cells count, duration and types of ART regimens, adherence to ART, concomitant diseases and opportunistic infections, and neurocognitive problems. Appropriate approach and managing of predisposing factors of sleep disturbance can improve quality of life and life expectancy in these patients. As neurocognitive problems are common in HIV/AIDS patients that can affect sleep quality, defining appropriate and practical tools for assessment of these problems should be considered in the future studies.

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The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

EXECUTIVE SUMMARY

Introduction

- The prevalence of sleep disturbance in HIV-positive population was reported as high as 100%, while in general population the prevalence rate was 10–40%.

Methods

- Sleep quality and associated factors have been evaluated in 200 individuals aged between 21 and 62 years, including 150 HIV-positive patients and 50 non-HIV-positive individuals (as a control group).

Results

- Sleep disturbances were detected in 88 (55.3%) and 14 (28%) of HIV and non-HIV-positive patients respectively. Statistically significant differences were found regarding sleep quality, somatization subscale of somatization subscale of Symptom Checklist-90, depression and anxiety scores between the HIV-positive and control group.
- There was significant direct correlation between the Pittsburgh Sleep Quality Index and each of somatization subscale of Symptom Checklist-90, depression and anxiety scores in HIV-positive individuals.

Conclusion

- Depression, anxiety and physical morbidity were detected as main factors that affect sleep quality in the HIV-positive individuals.

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