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BRIEF REPORT
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The association between HIV infection and perimenopausal syndrome: A matched cross-sectional study of women living with HIV/AIDS and their uninfected counterparts in rural areas of Anhui, China

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Abstract: The study compared the level of perimenopausal syndrome (PS) among women age 40 or older living with HIV/AIDS (WLWH) and their HIV-negative counterparts in rural areas of Anhui, China and it analyzed the association between HIV infection and PS. From March 2018 to February 2019, WLWH ≥ the age of 40 and their aged-matched HIV-negative female neighbors in 8 townships in the cities of Fuyang and Bozhou in Anhui Province, China were selected by cluster random sampling to respond to a questionnaire survey. Multivariable logistic regression analysis was performed. Responses from a total of 464 participants were analyzed, including 220 HIV-positive women and 244 HIV-negative female neighbors. The average score for PS was 18.02 and the prevalence of PS was 85.0% in the HIV-positive group, both of which were higher than those in the control group ($p < 0.05$). The most common PS symptoms among WLWH were irritability (83.2%), followed by fatigue (79.5%) and arthralgia myalgia (68.2%). The risk of developing moderate to severe PS in HIV-uninfected women was 0.605 times that in WLWH. Other significant risk factors included being older, a history of chronic diseases, poor sleep quality, and poor appetite. In the future, more attention should be paid to the prevention of PS in WLWH while actively providing antiretroviral therapy and follow-up.

***Keywords*:** HIV/AIDS, women, perimenopausal syndrome, prevalence

Introduction

Perimenopause is the transitional phase in women from reproductive vigor to decline, and its average duration is 3 to 4 years. Perimenopausal syndrome (PS) refers to a series of symptoms in women started by changes in menses and/or development of hypoestrogenic symptoms around the time of the transition to menopause, including vasomotor symptoms (*e.g*. hot flashes and sweating), sleep disturbance, cognitive changes, urogenital symptoms, and sexual dysfunction (*1,2*). Individuals with a previous major depressive disorder have an increased risk of major depressive disorder over the transition to menopause (*3*).

In China, the female population ages 40–60 number about 229 million in 2021 and had a life expectancy of 80.88 years (*4*). Previous studies in China indicated that the incidence of PS is 68.1% (*5*), and insomnia, fatigue, and mood swings might be the three most prevalent menopausal symptoms in middle-aged Chinese women (*6*). From 2007–2018, a total of 272,611 female patients with HIV/AIDS were reported in China (*7*). As the life span of people living with HIV/AIDS increases, the issue of aging among women living with HIV (WLWH) is becoming increasingly serious, as more are entering perimenopause (*8*). A previous study suggested that WLWH undergo menopause at a younger age than women not living with HIV (*9*). The WLWH face the severe impacts of HIV as well as challenges associated with the perimenopausal period upon reaching that age (*10*). WLWH may experience earlier menopause and a higher symptom burden than women without HIV (*11*). However, little attention has been paid to PS among WLWH in China, and data from other countries are also limited.

The aims of the current study were to investigate the prevalence of PS among WLWH age 40 or older and their HIV-negative counterparts in rural areas of Anhui,

China and to examine the association between HIV infection and PS.

Patients and Methods

Study design

This study used a matched cross-sectional design. From March 2018 to February 2019, cluster sampling was used to select eight townships in the cities of Fuyang and Bozhou in Anhui Province, China. Ethical approval for this study was obtained from the Anhui Provincial Center for Disease Control and Prevention. This study was conducted in accordance with the Declaration of Helsinki.

Participant recruitment

WLWH and their neighbors who did not have HIV were included in the study. Inclusion criteria for the patient group were as follows: women ≥ the age of 40, confirmed to be HIV-positive, have intact ovaries and uterus, and no history of chemotherapy or radiotherapy. The inclusion criteria for the control group were as follows: women with an age difference of within 2 years compared to the patients, HIV-negative, have intact ovaries and uterus, and no history of chemotherapy or radiotherapy. The exclusion criteria were cognitive impairments or difficulty communicating, artificial menopause, and unwillingness to participate in the survey.

Data collection

Potential participants provided written informed consent prior to study enrollment. A structured questionnaire was administered by a well-trained research staff member to each participant at a local public health facility. Each interview took approximately 25-30 min to complete. The participation rates of the HIV-positive and HIV-negative groups were 86% (220/255) and 91% (244/267), respectively. The information was dually entered by personnel specifically designated by research team, and checks for logical consistency and duplicate data were conducted.

Measures

An on-site questionnaire survey was conducted, which included demographic information, medical history, health status, and PS status. The PS assessment used the Modified Kupperman Index (MKI), consisting of 13 items, to evaluate the severity of various symptoms such as sweating and hot flashes, insomnia, paresthesia, depression, irritability, fatigue, vertigo, arthralgia myalgia, palpitations, headache, a tingling sensation on the skin, sexual problems, and urinary system infections. Each item was rated on a scale from 0 to 3, with higher scores indicating more severe symptoms. The criteria for classification were as follows: a total score of ≤ 6 indicated normal health, 7 to 15 indicated mild symptoms, 16 to 30 indicated moderate symptoms, and a score ≥ 30 indicated severe symptoms (*12*).

Statistical analysis

A database was created using the software EpiData 3.1. Descriptive analyses were performed for all study variables. Categorical variables were expressed as frequencies and proportions, and continuous variables were expressed as means and standard deviations (SD). Univariate logistic analyses were then performed to explore the relationships between independent variables and PS. Multivariable logistic regression was finally used to examine the associations between independent variables and PS. A p-value < 0.05 was considered to indicate a significant difference. All analyses were performed using the software SPSS 23.0.

Results and Discussion

Participant characteristics

A total of 464 individuals were surveyed, including 220 WLWH and 244 controls. The average age of the participants in the WLWH and control group was 52.4 ± 6.0 and 53.4 ± 7.3 years, respectively, with no significant difference in the age distribution between the two groups (t = -1.602, p = 0.110); 41.8% had completed primary school or higher, 86.6% were married, and 62.4%% had a chronic disease. The proportions of participants with good sleep were 51.4% of WLWH and 66.4% of controls. In the WLWH group, 63.2% had a good appetite while 80.7% in the control group had a good appetite (Table 1).

Perimenopausal symptoms in total and by strata

In the WLWH group, the average PS score was 18.02 ± 10.60 points, with a total prevalence of 85.0%, and a higher proportion of moderate to severe PS (44.1% and 13.6%, respectively). In the control group, the average PS score was 14.3 ± 9.18 points, with a total prevalence of 78.7%, and a higher proportion of mild to moderate PS (37.3% and 35.2%, respectively) (Table 2). PS scores differed significantly between the two groups (t = 3.981, $p < 0.001$).

The PS score for and the prevalence of PS in WLWH in this survey were higher than those in studies on the general Chinese population. A study by Du *et al.* (*13*) with a large sample that included 3,147 women ages 40-60 from 16 communities in Shanghai, for example, found that the total prevalence of PS was 73.80%. In 2022, a survey of women ages 40-60 at a hospital health

Table 1. Distribution of participant characteristics

Characteristics	*n* (column%) / mean ± SD			Statistical values*	*p*
	Patient group	Control group	Total		
Age (years)				6.578	0.087
40-44	23 (10.5)	37 (15.2)	60 (12.9)		
45-49	55 (25.0)	43 (17.6)	98 (21.1)		
50-54	59 (26.8)	57 (23.4)	116 (25.0)		
≥ 55	83 (37.7)	107 (43.9)	190 (40.9)		
Mean ± SD	52.4 ± 6.0	53.4 ± 7.3	52.9 ± 6.7	-1.602	0.110
Education				11.489	0.001
no formal education	146 (66.4)	124 (50.8)	270 (58.2)		
primary school or higher	74 (33.6)	120 (49.2)	158 (41.8)		
Marriage				10.072	0.002
married	178 (81.3)	222 (91.4)	400 (86.6)		
divorced/widowed, *etc*.	41 (18.7)	21 (8.6)	62 (13.4)		
Chronic disease				0.003	0.954
no	82 (37.4)	92(37.7)	174 (37.6)		
yes	137 (62.6)	152 (62.3)	289 (62.4)		
Sleep quality				10.825	0.001
good	113 (51.4)	162 (66.4)	275 (59.3)		
poor	107 (48.6)	82 (33.6)	189 (40.7)		
Appetite				17.850	< 0.001
good	139 (63.2)	197 (80.7)	336 (72.4)		
poor	81 (36.8)	47 (19.3)	128 (27.6)		

*A Chi-square test was used for categorical variables, and the Chi-square value and p-value are reported. The Mann-Whitney *U*-test was used for continuous variables that were normally distributed, and the Z score and *p*-value are reported.

Table 2. Perimenopausal syndrome scores for and categorization of survey respondents [Number/(Proportion/%)]

PS level	HIV/AIDS patient group	Control group	χ^2	*p*
Normal	33 (15.0)	52 (21.3)	15.071	0.002
Mild	60 (27.3)	91 (37.3)		
Moderate	97 (44.1)	86 (35.2)		
Severe	30 (13.6)	15 (6.1)		

management center in Sichuan Province indicated that 46.44% had mild PS and 24.07% had moderate or severe PS (*3*). This suggests that the prevalence of PS in female HIV/AIDS patients in Anhui Province is concerning, with a higher proportion of moderate and relatively severe disease. In addition to antiretroviral therapy and follow-up, attention should also be paid to the prevention of PS in WLWH.

Types of perimenopausal symptoms reported

Of various perimenopausal symptoms, irritability had the highest prevalence in the WLWH group (83.2%), followed by fatigue (79.5%) and arthralgia myalgia (68.2%); symptoms with a lower prevalence included urinary system infections (23.2%) and a tingling sensation on the skin (26.4%). In the control group, irritability also had the highest prevalence (69.3%), followed by arthralgia myalgia (61.5%) and vertigo (60.2%); symptoms with a lower prevalence were urinary system infections (15.2%) and a tingling sensation on the skin (16.8%). Fatigue, palpitations, irritability, and 8 other symptoms differed significantly between the two groups ($p < 0.05$) (Table 3).

"Irritability" had the highest prevalence among both the WLWH group and the control group, and it was significantly higher in the former compared to the latter. Eight other PS symptoms were more prevalent in Chinese WLWH. However, a survey of Spanish women revealed that 75.1% experienced symptoms, with hot flashes being the most common among those in the perimenopausal group (*14*). This suggests that mood swings are most typical among HIV-positive women with PS in rural China. Health interventions for these populations should focus on education regarding emotional management, and raising awareness of preventing PS among WLWH in particular. In addition, the survey found that "fatigue" had a higher prevalence among WLWH compared to the normal control group, which is likely related to the HIV infection itself. Given the significant effectiveness of current antiretroviral therapy, AIDS has become a long-term chronic infectious disease, with a prolonged course potentially lasting decades. The unavoidable adverse effects of long-term medication may contribute to increased fatigue among HIV-infected individuals. This indicates that female HIV/AIDS patients are prone to fatigue, which is influenced by multiple factors. They should seek to rest and avoid excessive physical labor in their everyday lives.

Risk factor analysis of perimenopausal symptoms

Participants were divided into two groups based on their

PS scores: a normal to mild PS group (score ≤ 15) and a moderate to severe PS group (score > 15). Six factors — HIV infection status, age, marital status, a history of chronic diseases, sleep quality, and appetite — differed significantly between the two groups ($p < 0.05$) (Table 4). Using the forced entry method with PS score as the dependent variable (0 = "score ≤ 15", 1 = "score > 15"), and including criteria while excluding HIV infection status, age, marital status, a history of chronic diseases, sleep quality, and appetite as independent variables, multivariate analysis indicated that the risk of developing moderate to severe PS in women not infected with HIV was 0.605 times that in WLWH, while being older, a history of chronic diseases, poor sleep quality, and a poor appetite were identified as risk factors for developing moderate to severe PS (Table 5).

The adverse effects of HIV infection on an individual include both physiological functions and psychological states, which may increase the severity of PS, but the exact mechanisms are still unclear (*15,16*). Similar domestic studies have also reported that age was a potential influencing factor. Some studies have suggested that the incidence of PS is higher with age among women ages 40-60 in rural areas (*5,17*). Therefore, attention should be paid to PS in postmenopausal women as well as in perimenopausal women.

A previous study (*18*) has found that chronic diseases are positively correlated with various syndromes of perimenopause. Individuals with physical illnesses are more likely to experience sexual problems, depression,

Table 3. Prevalence of symptoms related to perimenopausal syndrome among survey respondents [number/(proportion/%)]

Syndrome	Patient group		Control group		χ^2	p
	Yes	No	Yes	No		
Sweating and hot flashes	89 (40.5)	131 (59.5)	91 (37.3)	153 (62.7)	0.486	0.486
Paresthesia	97 (44.1)	123 (55.9)	76 (31.1)	168 (68.9)	8.289	0.004
Insomnia	147 (66.8)	73 (33.2)	132 (54.1)	112 (45.9)	7.808	0.005
Palpitations	148 (67.3)	72 (32.7)	122 (50.0)	122 (50.0)	14.187	< 0.001
Irritability	183 (83.2)	37 (16.8)	169 (69.3)	75 (30.7)	12.241	< 0.001
Depression	111 (50.5)	109 (49.5)	92 (37.7)	152 (62.3)	7.642	0.006
Arthralgia myalgia	150 (68.2)	70 (31.8)	150 (61.5)	94 (38.5)	2.277	0.131
Vertigo	144 (65.5)	76 (34.5)	147 (60.2)	97 (39.8)	1.342	0.247
Fatigue	175 (79.5)	45 (20.5)	141 (57.8)	103 (42.2)	25.214	< 0.001
Headache	140 (63.6)	80 (36.4)	144 (59.0)	100 (41.0)	1.040	0.308
Tingling sensation on the skin	58 (26.4)	162 (73.6)	41 (16.8)	203 (83.2)	6.300	0.012
Urinary system infections	51 (23.2)	169 (76.8)	37 (15.2)	207 (84.8)	4.839	0.028
Sexual problems	149 (67.7)	71 (32.3)	145 (59.4)	99 (40.6)	3.434	0.064

Table 4. Univariate analysis of perimenopausal syndrome

Variables	Normal to mild perimenopausal syndrome group		Moderate to severe perimenopausal syndrome group		χ^2	p
	n	%	*n*	%		
HIV infection status					12.350	< 0.001
yes	93	39.4	127	55.7		
no	143	60.6	101	44.3		
Age					31.493	< 0.001
40-49	109	46.2	49	21.5		
≥ 50	127	53.8	179	78.5		
Education					1.006	0.316
no formal education	132	55.9	138	60.5		
primary school or higher	104	44.1	90	39.5		
Marriage					8.065	0.005
married	213	91.0	187	82.0		
divorced/widowed, *etc.*	21	9.0	41	18.0		
History of chronic diseases					22.446	< 0.001
no	113	48.1	61	26.8		
yes	122	51.9	167	73.2		
Sleep quality					46.626	< 0.001
good	176	74.6	99	43.4		
poor	60	25.4	129	56.6		
Appetite					47.305	< 0.001
good	204	86.4	132	57.9		
poor	32	13.6	96	42.1		

Table 5. Multivariable logistic regression analysis of perimenopausal symptoms

Factors	β	S.E.	*p*	OR	95% CI
HIV infection status					
yes				1	
no	-0.503	0.219	0.022	0.605	(0.394-0.929)
Age					
40-49				1	
≥ 50	0.959	0.232	< 0.001	2.609	(1.656-4.110)
Marriage					
married				1	
divorced/widowed, *etc*.	0.313	0.323	0.333	1.367	(0.726-2.576)
Chronic disease					
no					
yes	0.685	0.222	0.002	1.984	(1.284-3.063)
Sleep quality					
good				1	
poor	0.937	0.220	< 0.001	2.553	(1.659-3.928)
Appetite					
good				1	
poor	1.061	0.256	< 0.001	2.889	(1.750-4.770)

anxiety, and vasomotor symptoms than those without physical illnesses. Sleep problems, including insomnia, not only reduce physical immunity but may also affect the psychological state of menopausal women. This can exacerbate endocrine disorders and potentially lead to a nervous breakdown and an increased risk of cardiovascular diseases (*19*). Psychological guidance should be enhanced for WLWH to improve their sleep quality or treat sleep problems through medical intervention (*20,21*). For WLWH, maintaining a good appetite can promote normal eating, help them obtain sufficient nutrition, and provide a sense of satisfaction and pleasure during meals, thereby alleviating mood swings. To prevent and treat PS in WLWH, special attention should be paid to women who are older, have a history of chronic diseases, poor sleep quality, and a poor appetite. Targeted health education and behavioral interventions should be provided for these individuals (*22*).

In conclusion, this study found that the prevalence and severity of PS in WLWH were higher than those in the control group, and mood swings were most evident in PS. While actively providing antiviral therapy and following up with WLWH, attention must be paid to female reproductive health, and relevant education, emotional management, and health education must be provided.

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