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Menopausal symptoms and associated factors in women living with HIV in Cambodia

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ABSTRACT


This study investigated the prevalence and severity of menopausal symptoms and associated factors among women living with HIV in Cambodia. Menopause Rating Scale (MRS) assessed the menopausal symptoms, and SPSS Version 20.0 analyzed the data. The three most dominant symptoms, which were also rated the top three “severe” symptoms, were psychological: physical and mental exhaustion (91.5%), irritability (84.1%), and depressive mood (83.6%). The highest incidence was among the perimenopausal women. Severity of symptoms was associated with personal income, abortion, and intake of calcium supplements. Health-care professionals need to provide appropriate individualized interventions to maintain the social, emotional, and overall well-being of menopausal women living with HIV.

KEYWORDS

Cambodia; HIV; menopause; Menopause Rating Scale; severity; symptom

Introduction

Of the 36.7 million people around the world living with HIV in 2016, approximately 48.5% (17.8 million) were females (UNAIDS, 2016). In the current environment, the reported life expectancy of HIV-positive patients receiving antiretroviral therapy is approaching that of the general population (Samji et al., 2013). Nevertheless, the care of women-specific issues such as reproductive and postreproductive health of women living with HIV (WLWH) still poses significant challenges (Loutfy et al., 2013). A high percentage of WLWH are entering menopause transition and are experiencing menopausal symptoms. The World Health Organization (WHO) defined *menopause* as the permanent cessation of menstruation as a consequence of the loss of ovarian follicular activity (WHO, 1996). Although it is a physiological process, menopause is accompanied by a wide range of issues affecting a woman’s quality of life (Utian, 2007). Specific medical conditions may alter the way a woman experiences menopause (Cheung et al., 2015; Katainen, Engblom, Siirtola, Erkkola, & Polo-Kantola, 2016), and HIV is not an exceptional case. Generally, coping with

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ongoing menopausal symptoms is a challenge for women, and this is heightened for WLWH (Nappi et al., 2014). Even though the mechanism behind ovarian dysfunction is not yet understood, the condition has been well described regarding WLWH (Yalamanchi, Dobs, & Greenblatt, 2014). Such data could alter the prevalence and symptomatology of menopause in this group. However, menopause in WLWH is a neglected area of study (Tariq, Delpuch, & Anderson, 2016). So far, the care and treatment of menopausal symptoms in WLWH has also not been focused very much (Cejtin, 2012).

The relationship between menopausal symptoms and HIV infection is inconclusive. Some studies have found the prevalence (Kanapathipillai, Hickey, & Giles, 2013) and severity (Kang & Fantry, 2016) of menopausal symptoms to be higher in seropositive than in seronegative patients. Studies have also found that an HIV-positive status is associated with increased hot flashes (Looby et al., 2014) and other vasomotor symptoms (Ferreira et al., 2007), sexual dysfunction (Boonyanurak et al., 2012), and mood changes (Looby et al., 2014). A bidirectional relationship has also been found between HIV infection and menopause. HIV may alter the natural history, experience, and complications of menopause, and menopause could potentially influence the course of HIV infection (Kojic, Wang, & Cu-Uvin, 2007). In contrast, other studies have not found CD4 count, HIV viral load, or antiretroviral therapy (ART) to be associated with menopause (Fantry, Zhan, Taylor, Sill, & Flaws, 2005; Lui-Filho et al., 2013). The factors responsible for the changes in the prevalence and severity of menopausal symptoms in WLWH include age, retirement, marital status, cigarette smoking, higher parity, self-reported good quality of life, perceptions of life and health, body mass index (BMI), and sexual activity (Agaba et al., 2017; Boonyanurak et al., 2012; Ferreira et al., 2007; Miller et al., 2005). In addition, a review of the literature showed that HIV was not associated with abortion or comorbidities, such as hypertension and diabetes, in WLWH (Lui-Filho et al., 2013).

Women around the world have reported multidimensional biological, psychological, and sociocultural factors related to menopause that require equally multidimensional responses (Huffman, Myers, Tingle, & Bond, 2005). The perception and experience of menopausal symptoms is supposed to be influenced by sociocultural and ethnic factors (Avis et al., 2001). Cambodia is also one of the countries with abundant social and cultural beliefs and traditions. In Cambodia, 35,000 females over the age of 15 live with HIV (prevalence of 0.6%); of those, 7,400 are 50 or older (UNAIDS, 2016). To the authors' knowledge, the prevalence and intensity of menopausal symptoms among this population in Cambodia have not been extensively explored. Therefore, this preliminary study aimed to determine the prevalence, frequency, and severity of menopausal symptoms and the associated factors in WLWH in Cambodia. The appropriate care for this growing sector of Cambodian menopausal women can be provided only when the health issues involving HIV infection and menopause are fully understood.

Methodology

Study population

A cross-sectional study of 201 randomly selected WLWH was conducted from July to August, 2017. The sample size of 153 was calculated using G*Power 3.1.9.2. A maximum of 25 variables associated with the Menopause Rating Scale (MRS) subscales were considered; the significance level was 0.05, and the effect size was 0.25. Considering about a 30% possibility of error and termination of subjects in between, 48 participants were added. Women of age 40–60 years receiving care at the HIV outpatient department of a hospital in Phnom Penh, Cambodia, were invited to participate in the study. Among the inclusion criteria was laboratory verification of the women's seropositive status, as confirmed by either enzyme-linked immunosorbent assay (ELISA) or western blot. Women who were unable to understand the questionnaire were excluded. The data were collected with the help of the research team members, who included a doctor, a social worker, and nurses. All the team members were provided training on the purpose of the study, the contents and administration of the questionnaire, and about how to approach the participants and document their responses accurately by the authors. In a waiting room, all of the eligible women being treated at the hospital were informed about the aim of the study by the research team members, and only those interested in participating in the study were selected. They were assured that there was no any obligation to remain in the study and that they could leave at any point. Informed consent was received from each subject after the study was explained. Any subjects who had difficulties completing the questionnaire could ask a research team member for help. The study was started only after approval had been received from the Human Subjects Committee at the Chonbuk National University and the Cambodia National Ethics Committee of the Ministry of Health.

Interviews and study questionnaire

Face-to-face interviews were conducted using a questionnaire about menopausal symptoms. A room on the hospital premises was used, and the doors and windows were closed to maintain confidentiality. The patients' height and weight were measured. The BMI, defined as the weight divided by the height in meters squared, was calculated. Referred to as "obesity" in this study, BMI was categorized as underweight (<18.5), normal (18.5–22.9), overweight (23.0–24.9), and obese (≥ 25.0), in accordance with the Asia Pacific World Health Organization (WHO) guidelines (WHO, 2000). The HIV infection-related information about the patients came from the hospital records. The participants were

asked to provide general demographics information, e.g., age, residence, and education. They were also asked about their medical histories regarding reproduction (e.g., age at menarche, abortion history, menopausal status, and artificial menopause), diseases or infections (e.g., perceived health and life status and presence of hypertension), and HIV (e.g., duration of HIV, duration of ART, WHO HIV/AIDS clinical stage, and CD4 count).

Menopausal definitions

Menopausal status was classified as premenopausal, early menopausal, late menopausal, and postmenopausal according to the guidelines provided by the Study of Women's Health across the Nation (SWAN) (Avis et al., 2001). Women were considered premenopausal if they had continued to have regular menstrual cycles within the previous three months. They were considered early menopausal if they had had menstrual bleeding within the previous three months but with increasing irregularity in cycle length during the previous year. The late perimenopausal women were those who had not experienced menses in the previous three months but had done so within the previous 12 months. Finally, women who had not experienced menses within the previous 12 months (not because of medication, pregnancy, or severe weight loss) were classified as postmenopausal. Women with a history of hysterectomy or oophorectomy were classified as surgically or artificially menopausal.

MRS

The MRS, a self-administered questionnaire, was used in this study to assess menopausal symptoms. Because there is no Khmer version of the MRS, the English version was translated by an expert, and back translation was applied to ensure accuracy. A pilot study was then performed in Phnom Penh with 30 local women aged 40–60 years and was validated. For increased accuracy, the authors held a roundtable discussion about the Khmer version of the scale with representatives from the hospital used in the study. Attendees included social workers, doctors, nurses, counselors, and research authors. These professionals later collected the data. One of the attendees read out the English version of the scale while the others cross-checked it with the local language version. After a detailed analysis and discussion regarding the translation of each of the symptoms mentioned in the scale, the Khmer version was finalized. The incentive for the subjects was given to the head of the hospital after the meeting.

The MRS is a self-administered tool developed by Heinemann, Potthoff, and Schneider (2003). It contains 11 symptoms on a scoring scale from 0–4: 0 (*no symptoms*), 1 (*mild*), 2 (*moderate*), 3 (*severe*), and 4 (*very severe symptoms*) (Heinemann et al., 2004). Three subscales were developed for the symptoms: (a)

somatic symptoms, addressed in items 1–3 and 11 (hot flushes, heart discomfort, sleeping problems, and muscle and joint problems); (b) psychological symptoms, addressed in items 4–7 (depressive mood, irritability, anxiety, and physical and mental exhaustion); and (c) urogenital symptoms, addressed in items 8–10 (sexual problems, bladder problems, and vaginal dryness). A subscale score was obtained for each of the three categories by adding each item to the relevant category. The total score was obtained by the summation of the subscale score, ranging from minimum 0 (zero) to maximum 44. The Cronbach's alpha (α) coefficient for this Khmer version of the entire scale was determined to be 0.877. The Serbian version of the MRS had a Cronbach's α coefficient of 0.884 for the entire scale (Gazibara et al., 2015). The Chinese version contained Cronbach's α coefficient values of 0.88, 0.68, and 0.59 for the psychological, somatic, and urogenital symptom domains respectively (Wu, Wen, Hwang, & Huang, 2015). The corresponding values for this Khmer version were 0.775, 0.836, and 0.640.

Statistical analysis

The data were analyzed using SPSS version 20.0. The general characteristics of the subjects were analyzed using frequency and percentages. For analysis, the mean values for age (48 years), age at first pregnancy (22 years old), and age at menarche (16 years old) were grouped. The categorical data were compared by performing a chi-square test. For the continuous variables, a *t*-test or Fisher's exact test (when the value of any cell was less than 20%) was used. A *p* value of $<.05$ was considered as the cutoff value for significance. Symptom severity was calculated as a percentage once the scoring of the symptoms had been completed. A parametric analysis of variance (ANOVA) with post hoc tests (only the significant ones are presented in the table) and multiple linear regression analysis were performed to determine the associated factors. The significant factors determined from the ANOVA were entered as confounding variables in a multiple linear regression, and calculations were done for the somatic, psychobiological, urogenital, and total MRS scores, referred to as Models 1, 2, 3, and 4 respectively.

Results

The general characteristics of the participants are shown in [Table 1](#). Although the SWAN guidelines suggest four categories, the early perimenopausal and late perimenopausal participants were placed into one combined perimenopausal group because of the low frequency and the need for the data to be manageable. The final analysis included 72 premenopausal, 51 perimenopausal, and 78 postmenopausal women. Of the total 201 participants, 56.7% were between the ages of 40 and 49, and 43.3% were over 50. Most of the

Table 1. General characteristics of participants by menopausal stage.

Demographic variables	All (N = 201)	Menopausal stage (n, %)		
		Pre (n = 72)	Peri (n = 51)	Post (n = 78)
Socioeconomic history				
Age				
40–49	114 (56.7)	65 (57.0)	31 (27.2)	18 (15.8)
≥50	87 (43.3)	7 (8.0)	20 (23.0)	60 (69.0)
Residence				
Phnom Penh	118 (58.7)	43 (36.4)	31 (26.3)	44 (37.3)
Province	83 (41.3)	29 (34.9)	20 (24.1)	34 (41.0)
Education	132 (65.7)	39 (29.5)	39 (29.5)	54 (40.9)
Primary and below	69 (34.3)	33 (47.8)	12 (17.4)	24 (34.8)
Above primary	131 (65.2)	53 (40.5)	33 (25.2)	45 (34.4)
Employment status	70 (34.8)	19 (27.1)	18 (25.7)	33 (47.1)
Employed	119 (59.2)	34 (28.6)	28 (23.5)	57 (47.9)
Unemployed	82 (40.8)	38 (46.3)	23 (28.0)	21 (25.6)
Monthly personal income	73 (36.3)	32 (43.8)	22 (30.1)	19 (26.0)
≤100\$	12 (6.0)	4 (33.3)	3 (25.0)	5 (41.7)
>100\$	116 (57.7)	36 (31.0)	26 (22.4)	54 (46.6)
Marital status				
Married	31 (15.4)	5 (16.1)	9 (29.0)	17 (54.8)
Unmarried	105 (52.2)	34 (32.4)	35 (33.3)	36 (34.3)
Divorced/widowed/ separately living	32 (15.9)	15 (46.9)	4 (12.5)	13 (40.6)
Obesity	33 (16.4)	18 (54.5)	3 (9.1)	12 (36.4)
Underweight	75 (37.3)	27 (36.0)	17 (22.7)	31 (41.3)
Normal	56 (27.9)	24 (42.9)	19 (33.9)	13 (23.2)
Overweight	70 (34.8)	21 (30.0)	15 (21.4)	34 (48.6)
Obese	2 (1.0)	0 (0.0)	1 (50.0)	1 (50.0)
Physical activity	199 (99.0)	72 (36.2)	50 (25.1)	77 (38.7)
No	26 (12.9)	13 (50.0)	6 (23.1)	7 (26.9)
1–4 days/week	175 (87.1)	59 (33.7)	45 (25.7)	71 (40.6)
5–7 days/week				
Smoking				
Yes				
No				
Drinking				
Yes				
No				

(Continued)

Table 1. (Continued).

Demographic variables	Menopausal stage (n, %)				
	All (N = 201)	Pre (n = 72)	Peri (n = 51)	Post (n = 78)	
Reproductive history	Age at menarche	116 (57.7)	41 (35.3)	30 (25.9)	45 (38.8)
		85 (42.3)	31 (36.5)	21 (24.7)	33 (38.8)
	Age at first pregnancy	108 (53.7)	39 (36.1)	28 (25.9)	41 (38.0)
		93 (46.3)	33 (35.5)	23 (24.7)	37 (39.8)
	Parity	172 (85.6)	67 (39.0)	46 (26.7)	59 (34.3)
		29 (14.4)	5 (17.2)	5 (17.2)	19 (65.5)
	Abortion	136 (67.7)	49 (36.0)	32 (23.5)	55 (40.4)
		65 (32.3)	23 (35.4)	19 (29.2)	23 (35.4)
	Sexually active	78 (38.8)	35 (44.9)	24 (30.8)	19 (24.4)
		123 (61.2)	37 (30.1)	27 (22.0)	59 (48.0)
Disease/infection related	Calcium	17 (8.5)	5 (29.4)	6 (35.3)	6 (35.3)
		184 (91.5)	67 (36.4)	45 (24.5)	72 (39.1)
	Artificial menopause	12 (6.0)	3 (25.0)	2 (16.7)	7 (58.3)
		189 (94.0)	69 (36.5)	49 (25.9)	71 (37.6)
	Perceived health status	6.98 ± 1.89	7.21 ± 1.81	7.09 ± 1.99	6.68 ± 1.83
	Perceived life status	6.49 ± 2.42	6.59 ± 2.11	6.33 ± 2.63	6.50 ± 2.57
	Hypertension	34 (16.9)	9 (26.5)	10 (29.4)	15 (44.1)
		165 (83.1)	63 (37.7)	41 (24.6)	63 (37.7)
	Diabetes	9 (4.5)	4 (44.4)	2 (22.2)	3 (33.3)
		192 (95.5)	68 (35.4)	49 (25.5)	75 (39.1)
HIV infection related	Duration of HIV	9.60 ± 3.89	9.50 ± 3.95	0.33 ± 3.87	9.27 ± 3.83
	Duration of ART therapy	8.49 ± 3.33	8.24 ± 3.23	9.04 ± 3.21	8.38 ± 3.50
	CD4 cell count	11 (5.5)	3 (27.3)	28 (25.7)	45 (41.3)
		98 (49.0)	33 (33.7)	25 (25.5)	40 (40.8)
		91 (45.5)	36 (39.6)	22 (24.2)	33 (36.3)
		49 (24.5)	19 (38.8)	12 (24.5)	18 (36.7)
		151 (75.5)	53 (35.1)	38 (25.2)	60 (39.7)

Note. Mean age of menopause: 46.65 ± 4.76. Median age of menopause: 47 years.

participants were from Phnom Penh (58.7%), employed (65.7%), and earning \geq US\$100 per month (59.2%). A minority were unmarried (6.0%). More than half (57.7%) had menarche at age 16 or younger, and 53.7% had their first pregnancy at 22 or younger. Only 38.8% indicated that they were sexually active at the time that the questionnaire was administered. Women taking calcium supplements accounted for 8.5% of the sample. In addition, 6% had undergone hysterectomies. Mean values of 6.98 ± 1.89 (*SD*) and 6.49 ± 2.42 (*SD*) for satisfaction regarding the participants' own health and lives were calculated from their ratings on a visual analog scale (0–10). The mean value for the years after the HIV diagnosis for all the participants was 9.60 ± 3.89 , and the mean value for the years of ART was 8.49 ± 3.33 . Only a few women (5.5%) had CD4 counts of less than 200 cells/mm³. A majority of the participants were in either the third or fourth stage of HIV.

The prevalence and frequency of menopausal symptoms are shown in Table 2. Based on the MRS, the three most frequently reported symptoms for all of the women ($N = 201$) were physical and mental exhaustion (91.5%), irritability (84.1%), and depressive mood (83.6%). The two most frequently reported symptoms within each of the subscales were sleep problems (74.1%) and joint and muscle pain (73.6%) (somatic symptoms), physical and mental exhaustion (91.5%) and irritability (84.1%) (psychological symptoms), and sexual problems (67.7%) and vaginal dryness (55.2%) (urogenital symptoms). Regarding menopausal status, physical and mental exhaustion was the most prevalent symptom among the premenopausal (91.7%) and postmenopausal (94.1%) women, and it was the second most common symptom (86.3%) among the perimenopausal women. In the premenopausal group, depressive mood and irritability

Table 2. Frequency and percentage of menopausal symptoms in subjects as per their menopausal status.

Menopausal symptoms (subscale)	All ($N = 201$)	Premenopause ($n = 72$)	Perimenopause ($n = 51$)	Postmenopause ($n = 78$)	χ^2	p
SOMATIC						
Hot flushes, sweating	118 (58.7)	38 (52.8)	32 (62.7)	48 (61.5)	1.64	.453
Heart discomfort	132 (65.7)	40 (55.6)	37 (72.5)	55 (70.5)	5.15	.075
Sleep problems	149 (74.1)	51 (70.8)	41 (80.4)	57 (73.1)	1.49	.489
Joint and muscular discomfort	148 (73.6)	46 (63.9)	40 (78.4)	62 (79.5)	5.50	.069
PSYCHOLOGICAL						
Depressive mood	168 (83.6)	60 (83.3)	46 (90.2)	62 (79.5)	2.58	.290
Irritability	169 (84.1)	60 (83.3)	46 (90.2)	63 (80.8)	2.09	.351
Anxiety	145 (72.1)	48 (66.7)	40 (78.4)	57 (73.1)	2.11	.346
Physical and mental exhaustion	184 (91.5)	66 (91.7)	44 (86.3)	74 (94.1)	2.95	.221
UROGENITAL						
Sexual problems	136 (67.7)	43 (59.7)	38 (74.5)	55 (70.5)	3.46	.181
Bladder problems	96 (47.8)	28 (38.9)	30 (58.8)	38 (48.7)	4.80	.090
Dryness of vagina	111 (55.2)	32 (44.4)	34 (66.7)	45 (57.7)	6.28	.045*

were equally prevalent as (83.3%) the next two most frequently reported symptoms. In the postmenopausal group, irritability (80.8%) and joint and muscular discomfort (79.5%) and depressive mood (79.5%) were the next most frequently reported symptoms. Depressive mood (90.2%) and irritability (90.2%) were the most common symptoms experienced by the women in the perimenopausal stage. Only the occurrence of vaginal dryness ($\chi^2 = 6.28, p = .045$) was statistically significantly different for the women in the premenopausal and postmenopausal stages. In general, an increase in the rate of menopausal symptoms was observed with the progression through the menopause stages. This was particularly noticeable in the progressions from premenopause to perimenopause and premenopause to postmenopause. Overall, the symptoms were experienced most frequently by the women in the perimenopause stage. In addition, somatic and psychological symptoms occurred more frequently than urogenital symptoms in all three stages.

The measurement of symptom severity is shown in Table 3. The three most frequent symptoms reported as “very severe” were sexual problems (15.4%), joint and muscular discomfort (5.5%), and physical and mental exhaustion (4.5%). The three most reported as “severe” were irritability (28.4%), physical and mental exhaustion (23.9%), and depressive mood (22.9%).

Table 4 shows the mean total and subscale MRS scorings based on the participants’ characteristics. The urogenital and total MRS scores were significantly higher among the perimenopausal women. The somatic and total MRS scores were significantly higher for those who had a \leq US\$100 monthly income. Women with a history of abortion and consumption of calcium supplements had significantly higher psychological and total MRS scores. The urogenital scores were also higher for the women taking calcium

Table 3. Severity of menopausal symptoms in subjects.

Menopausal symptoms (subscale)	All (N = 201)	None	Mild	Moderate	Severe	Very severe
SOMATIC						
Hot flushes, sweating	118 (58.7)	83 (41.3)	54 (26.9)	38 (18.9)	22 (10.9)	4 (2.0)
Heart discomfort	132 (65.7)	69 (34.3)	63 (31.3)	44 (21.9)	19 (9.5)	6 (3.0)
Sleep problems	149 (74.1)	52 (34.3)	46 (31.3)	65 (21.9)	28 (9.5)	10 (3.0)
Joint and muscular discomfort	148 (73.6)	53 (26.4)	69 (34.3)	38 (18.9)	30 (14.9)	11 (5.5)
PSYCHOLOGICAL						
Depressive mood	168 (83.6)	33 (16.4)	48 (23.9)	66 (32.8)	46 (22.9)	8 (4.0)
Irritability	169 (84.1)	32 (15.9)	41 (20.4)	63 (31.3)	57 (28.4)	8 (4.0)
Anxiety	145 (72.1)	56 (27.9)	56 (27.9)	49 (24.4)	35 (17.4)	5 (2.5)
Physical and mental exhaustion	184 (91.5)	17 (8.5)	59 (29.4)	68 (33.8)	48 (23.9)	9 (4.5)
UROGENITAL						
Sexual problems	136 (67.7)	65 (32.3)	29 (14.4)	37 (18.4)	39 (19.4)	31 (15.4)
Bladder problems	96 (47.8)	105 (52.2)	37 (18.4)	35 (17.4)	24 (11.9)	0 (0.0)
Dryness of vagina	111 (55.2)	90 (44.8)	42 (20.9)	44 (21.9)	20 (10.0)	5 (2.5)



Table 4. Mean total and subscale MRS scores depending on the subject characteristics.

Demographic variables	Frequency (n)	Somatic M ± SD (0–16)	Psychological M ± SD (0–16)	Urogenital M ± SD (0–12)	Total MRS
Menopausal stage					
Premenopause ^a	72	4.38 ± 3.59	6.36 ± 3.47	2.92 ± 2.94	13.65 ± 8.82
Perimenopause ^b	51	5.55 ± 3.21	7.10 ± 3.44	4.12 ± 2.70	16.76 ± 7.85
Postmenopause ^c	78	5.45 ± 3.57	7.10 ± 3.81	4.01 ± 2.74	16.56 ± 8.38
F (p)		2.37 (.096)	0.98 (.378)	3.82 (.024)	2.93 (.056)
Duncan				b, c > a	b > a
Monthly personal income					
≤ont \$	119	5.66 ± 3.74	7.18 ± 3.63	3.85 ± 2.96	16.70 ± 8.87
>100 \$	82	4.26 ± 2.99	6.33 ± 3.51	3.35 ± 2.65	13.94 ± 7.68
t (p)		2.96 (.003)	1.66 (.098)	1.21 (.226)	2.29 (.023)
Abortion(s)					
Yes	136	5.41 ± 3.47	7.36 ± 3.51	3.79 ± 2.86	16.56 ± 8.56
No	65	4.42 ± 3.54	5.74 ± 3.56	3.35 ± 2.80	13.51 ± 8.03
t (p)		1.89 (.060)	3.05 (.003)	1.01 (.314)	2.41 (.017)
Calcium					
Yes	17	6.47 ± 3.59	8.65 ± 3.69	5.06 ± 2.25	20.18 ± 8.49
No	184	4.96 ± 3.49	6.67 ± 3.55	3.52 ± 2.86	15.15 ± 8.39
t (p)		1.703 (.090)	2.190 (.030)	2.159 (.032)	2.363 (.019)
Diabetes					
Yes	9	7.22 ± 3.49	9.11 ± 3.02	3.78 ± 2.28	20.11 ± 7.61
No	192	4.99 ± 3.49	6.73 ± 3.59	3.64 ± 2.87	15.36 ± 8.49
t (p)		1.88 (.062)	1.96 (.052)	0.14 (.888)	1.65 (.101)

supplements. Women with diabetes were found to have significantly higher psychological symptoms. There were no statistically significant associations with any of the other sociodemographic variables investigated in the study.

The factors responsible for altering the severity of menopausal symptoms are shown in Table 5. After adjustments were made for confounding variables, the multivariate regression analysis showed that the transitions to the perimenopausal stage ($\beta = 0.172, p = .030$) and the postmenopausal stage ($\beta = 0.166, p = .040$) were significantly associated with higher urogenital scorings (Table 4). In addition, the perimenopausal women were likely to have the highest total MRS scores ($\beta = 0.149, p = .052$). The independent factors responsible for the variance in the severity of the menopause symptoms were monthly personal income, abortion history, diabetes, and the consumption of calcium supplements. It was observed that having a \geq US \$100 monthly personal income significantly lowered the somatic scores ($\beta = -0.193, p = .006$) and the total MRS scores ($\beta = -0.155, p = .027$). Women who had had abortions were more likely to have higher somatic ($\beta = 0.151, p = .028$), psychological ($\beta = 0.228, p = .001$), and total MRS ($\beta = 0.187, p = .006$) scores. Those who reported taking calcium supplements had higher somatic ($\beta = 0.133, p = .052$), psychological ($\beta = 0.169, p = .014$), urogenital ($\beta = 0.153, p = .030$), and total MRS ($\beta = 0.178, p = .009$) scores than their counterparts. In addition, the psychological scores ($\beta = 0.134, p = .050$) were higher for women with diabetes.

Discussion

Menopause in HIV individuals appears to be a neglected area of study in Cambodia as there is a paucity of studies on this subject. The appropriate care for women in this status can be provided only if the incidence and mitigating factors are known. This study aimed to evaluate the prevalence, frequency, and severity of menopause symptoms, as well as the associated factors among WLWH Cambodia.

For the participants in this study, the most frequently observed symptom on the MRS was physical and mental exhaustion (91.5%). Similar findings were reported in a study on Indian WLWH (85.4%) (Joseph, Nagaraj, Saralaya, Nelliyanil, & Rao, 2014). Consistent with the results of previous studies (Looby et al., 2014; Miller et al., 2005), the symptoms occurred more frequently and with greater intensity in the perimenopausal period in the present study. However, the possible reasons for these symptoms in WLWH might be the ART or HIV itself; hence, it is difficult to ascertain whether the symptoms were caused by the physiological changes of menopause (Johnson et al., 2008). Nevertheless, the process of menopause is believed to be affected by HIV infection, and the condition is associated with greater symptomatology among WLWH (Fan, Maslow, Santoro, & Schoenbaum, 2008). Because



Table 5. Multiple regression analysis on factors altering the severity of menopausal symptoms.

Variables	Model 1			Model 2			Model 3			Model 4		
	β	t	p	β	t	p	β	t	p	β	t	p
Menopausal stage												
Premenopause	0.135	Reference		0.084	Reference		0.172	Reference		0.149	Reference	
Perimenopause	0.099	1.749	.082	0.067	1.097	.274	0.172	2.192	.030*	0.149	1.952	.052*
Postmenopause		1.264	.208		0.850	.396	0.166	2.067	.040*	0.125	1.601	.111
Monthly personal income												
≤onth		Reference			Reference			Reference			Reference	
>100\$	-0.193	-2.753	.006*	-0.122	-1.751	.082	-0.071	-0.993	.322	-0.155	-2.235	.027*
Abortion												
No	0.151	Reference		0.228	Reference		0.085	Reference		0.187	Reference	
Yes		2.219	.028*		3.354	.001*		1.222	.223		2.773	.006*
Calcium												
No	0.133	Reference		0.169	Reference		0.153	Reference		0.178	Reference	
Yes		1.952	.052*		2.476	.014*		2.192	.030*		2.623	.009*
Diabetes												
No	0.128	Reference		0.134	Reference		0.012	Reference		0.113	Reference	
Yes		1.885	.061		1.976	.050*		0.168	.867		1.684	.094
Constant		4.094	<.001*		5.364	<.001*		2.665	<.001*		12.122	<.001*
Adj R ²		0.082			0.087			0.040			0.096	
F		3.972			4.170			2.404			4.528	
p		.001			.001			.029			<.001	

Note. Confounding variables (only the significant ones from ANOVA) monthly personal income, abortion, diabetes, rheumatoid arthritis, and depression were controlled.

of the high severity, the symptoms can have a significant effect on the quality of life of WLWH. Thus, enhancing the knowledge of health-care professionals and improving the comprehensive care and education for WLWH is crucial.

The three most dominant symptoms that were also indicated as “severe” for all the participants in the present study were from the psychological domain, and the highest incidence was among the perimenopausal women. Living with HIV is one of the causes of depression in almost one-half of those who are infected (Eller et al., 2005). Studies have shown that menopausal WLWH (Ferreira et al., 2007), especially those who are perimenopausal (Looby et al., 2018; Maki et al., 2012), have a higher incidence of depressive symptoms than non-HIV-infected women. The SWAN also indicated that the rates of psychological distress are highest in perimenopausal women (Bromberger et al., 2001). A possible reason is that the perimenopausal stage, more than the other stages, is associated with a decrement in cognitive performance, which contributes to psychological problems (Greendale et al., 2009). Furthermore, in Cambodia, the society does not foster the acceptance of HIV/AIDS as a typical chronic disease, so those who are HIV-infected are stigmatized (Yi et al., 2015).

A previous study found that Cambodian WLWH (51%) were more likely than males living with HIV (41%) to experience low self-esteem (Cambodian People Living with HIV Network, 2010). Even though the participants in the present study were recruited from a hospital in an urban area that is renowned for treating HIV, including providing multidisciplinary care for patients, there was still a high prevalence of psychological symptoms. The situation is perhaps worse for rural HIV-infected women who do not have frequent and easy access to hospital-provided HIV care. It is important to note that these women experienced two different conditions that could have influenced their psychological symptoms: menopause and HIV infection. Thus, specific interventions that can contribute toward minimizing the psychological effects of an individual’s serological status need to be developed as part of the multidisciplinary care that is provided to all WLWH, including those in rural Cambodia. Hormone initiation prior to the final menstrual period has been suggested for women in general to improve their psychological performance (Greendale et al., 2009). However, prospective studies are needed to determine the effects of hormonal or alternative therapies for the relief of menopause symptoms in WLWH (Ferreira et al., 2007).

In the present study, vaginal dryness was the only symptom significantly associated with the menopausal transition ($p = .045$). Normal vaginal microbiota are a defense against urogenital infections in non-HIV-infected women (Mendling, 2016). A decrease in their number can result in the increased growth of potential pathogenic bacteria (Gupta, Kumar, Singhal, Kaur, & Manektala, 2006). The composition of the vaginal microbiota changes

dramatically in the menopausal phase because of reduced estrogen levels (Cribby, Taylor, & Reid, 2008), resulting in signs of increased vaginal atrophy, such as vaginal dryness in non-HIV-infected menopausal women (Mac Bride, Rhodes, & Shuster, 2010). For WLWH, the vaginal microbiota are even more disturbed (Petrova, van den Broek, Balzarini, Vanderleyden, & Lebeer, 2013), and ovarian dysfunction starts earlier than in women without HIV infection (Fan et al., 2008). Hence, the vaginal symptoms might be more complicated for menopausal WLWH and thus require timely management. Nonhormonal vaginal lubricants and moisturizers are recommended for such women as first-line treatment, and vaginal estrogen therapy is further recommended if the symptoms persist beyond the first-line treatment (North American Menopause Society, 2007).

The results of previous studies have indicated that WLWH, especially those classified as menopausal, experience greater sexual problems and lower sexual satisfaction (Wilson et al., 2010). Sexual problems were the most frequently reported “very severe” symptoms by the participants in the present study. It is possible that menopausal women might attribute their misconceptions of HIV, their fears of transmitting it to their HIV-negative partners, and their concerns about the consequences of sexual activity for their health to menopausal symptoms (Lee, Li, Iamsirithaworn, & Khumtong, 2013). Sexual health in menopausal WLWH is an important topic that warrants in-depth study. Even though communication about sexual problems is difficult in Cambodia (United Nations Fund for Population Activities & National Institute of Statistics, 2015), the questions, concerns, and issues of WLWH must be addressed appropriately by the health-care personnel. Educational programs on sex and sexual health need to target this population.

Joint and muscular discomfort was the second most common “very severe” symptom reported by the participants. Though the finding was insignificant, the prevalence of the symptom increased with the progression through the stages of menopause. In the general population, menopause, with its associated estrogen deficiency, is a well-known risk factor for osteoporotic fractures, bone turnover, and bone loss (Akhter, Lappe, Davies, & Recker, 2007). In addition, menopausal WLWH experience comparatively more bone loss and fragility fractures than noninfected women (Yin et al., 2010). A meta-analysis concluded that people infected with HIV have a 6.4-fold increased risk of osteopenia or low bone mineral density and a threefold increased risk of osteoporosis (Brown & Qaqish, 2006). The contributing multifactorial mechanisms are likely the chronic inflammation caused by HIV, which stimulates osteoclast differentiation and resorption (Gibellini et al., 2008), and the effects of ART, irrespective of the regimen (Brown et al., 2009). Thus, the specific guidelines for managing bone disease in HIV-positive patients suggest that all HIV-infected patients be assessed for fracture risk through the clinical tools suggested in the applicable regional guidelines (Brown et al., 2015). The guidelines further recommend that

postmenopausal WLWH be screened, starting at age 50, with dual-energy X-ray absorptiometry scans. The development and implementation of national guidelines may control the risk of bone disease among WLWH in Cambodia. In addition, bone-related discomfort can also be controlled through the cessation of smoking, the avoidance of excessive alcohol intake, adequate nutrition, adequate physical exercise, and sufficient consumption of calcium and Vitamin D (Brown et al., 2015; Cosman et al., 2014).

While a study conducted in the United States concluded that menopause symptoms were more prevalent in HIV-infected women with higher CD4 counts (Clark et al., 2000), studies on women in Thailand and Brazil found no association (Boonyanurak et al., 2012; Ferreira et al., 2007). Studies also did not find the converse for the United States: The symptoms were more prevalent in American women with lower CD4 counts (Miller et al., 2005). No correlation was found in this study. CD4 counts of less than 200 cells/KL were found to be associated with the early onset of menopause (de Pommerol et al., 2011; Schoenbaum et al., 2005); however, the relation between the CD4 counts and the symptomology is unclear. Further rigorous research is suggested for determining the relationship (Andany, Kennedy, Aden, & Loutfy, 2016).

In the bivariate and multivariate analyses, when all of the control variables were included, menopausal status was found to be significantly associated with the urogenital and total MRS symptoms. In the present study, the factors responsible for the increased severity of the menopausal symptoms in WLWH in Cambodia were lower personal income, a history of abortion, the presence of diabetes, and the consumption of calcium supplements. These results are consistent with those obtained for non-HIV-infected (Castelo-Branco et al., 2006; Chuni & Sreeramareddy, 2011; Li et al., 2012) and HIV-infected women (Li, Lee, Thammawijaya, Jiraphongsa, & Rotheram-Borus, 2009) in previous studies. A possible reason could be that women with low incomes and a history of abortion(s) may experience the stigma of disease more intensely, increasing the stress of living with HIV (Li et al., 2009). Negative events in the lives of WLWH were correlated with the high prevalence of menopausal symptoms (Miller et al., 2005). However, previous studies have not explained the physiological mechanisms behind the relationship between abortion history and menopausal symptoms in WLWH. Also, the results of this study do not support the findings of previous studies that calcium supplements could be a prophylactic against menopausal symptoms in HIV-infected women (Brown, 2015; Li Vecchi et al., 2012). The review of the literature suggests that the efficacy of calcium supplements is controversial (Prentice et al., 2013). The reason for this controversy is worthy of further examination.

The study has limitations. First, the accuracy and generalizability of the results may be affected by the cross-sectional study design. Second, the menopausal status was self-reported by the participants. The biochemical confirmation of menopause would have presented this study more rationally (Andany et al., 2016).

Conclusion

The present study showed a high prevalence of menopausal symptoms among women living with HIV in Cambodia and suggests that they tend to suffer from psychological problems more than somatic and urogenital problems. This study alerts health-care providers about their health status. A comprehensive evaluation of WLWH is essential for addressing the features of menopause specific to them. Health-care professionals need to identify and to provide appropriate and individualized interventions to maintain the social, emotional, and overall well-being of menopausal WLWH. The current policies have often failed to address the more vulnerable members of this population, such as women in rural areas and women with limited access to health-care facilities. Because of lack of information, women might attribute the symptoms to HIV itself or to the side-effects of ART because menopause would be new and unexpected for them. Thus, health-care providers need to discuss aging, menopause, and menopause symptoms with WLWH to help them to be better prepared for the changes and symptoms that can accompany aging. The government should develop programs to create awareness and to provide counseling for this population. Such initiatives would be beneficial as they would enhance the ability of WLWH to cope with the infection and to manage their menopausal symptoms. Future research should focus on the long-term relationships among HIV infection, hormone therapy, CD4 count, and calcium supplements in Cambodian women in menopausal transition.

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