

Symptoms of anxiety and depression among Chinese women transitioning through menopause: findings from a prospective community-based cohort study

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Objective: To determine the prevalence of symptoms of anxiety and depression in Chinese women during and after menopause, and the associated risk factors.

Design: Prospective community-based cohort study.

Setting: An urban community in Beijing, People's Republic of China.

Patient(s): Four hundred and thirty women who had transitioned through natural menopause.

Intervention(s): None.

Main Outcome Measure(s): Symptoms of anxiety and depression.

Result(s): Symptoms of depression were more common than symptoms of anxiety. The prevalence of symptoms of depression rose from 14.5% during premenopause, to 18.2% during the menopausal transition, and 19.6% in the postmenopause period. The prevalence of symptoms of anxiety rose from 3.1% premenopause, to 7.0% during the menopausal transition, and 7.4% in the postmenopause period. Compared with women in the premenopausal stage, perimenopausal and postmenopausal women were more likely to have symptoms of anxiety and depression, but these differences were not statistically significant. Multivariable analysis showed that poor health status, trouble falling asleep, and early awakening were independently associated with symptoms of anxiety, and that a higher body mass index, poor health, low education status, and night sweats were independently associated with symptoms of depression.

Conclusion(s): Symptoms of depression were more prevalent than symptoms of anxiety. Our findings suggest that symptoms of anxiety and depression are more common during and after menopause than in premenopausal women. These findings highlight the importance of screening and evaluation of women undergoing the menopausal transition for symptoms of anxiety and depression, especially those with risk factors. (*Fertil Steril*® 2019;112:1160–71. ©2019 by American Society for Reproductive Medicine.)

El resumen está disponible en Español al final del artículo.

Key Words: Menopause, postmenopause, symptom of anxiety, symptom of depression, prospective

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Menopause is an inevitable part of aging and marks the end of the female reproductive period. It has been estimated that by 2030 1.2 billion women will be postmenopausal. The growing number of postmenopausal women makes it a major focus for targeted research. The reproductive aging process causes a variety of symptoms. Emotional distress is of particular importance because it increases during the menopausal

transition. Studies have shown that both depression (1, 2) and anxiety (3) are more common among women during their menopausal transition, and that depression (4) and anxiety (5) are both about twice as prevalent in women as in men.

Depression is a prominent public health problem worldwide. Among middle-aged women, depression may impair their quality of life, sleep, sexual function, resilience, and life satisfaction. It is also associated with a greater risk of other health problems, such as poor cognitive function, cardiovascular disease (6), osteoporosis (7), fractures (8), and the metabolic syndrome (9). Early recognition and treatment of depression is important to prevent serious consequences. A substantial number of both longitudinal and cross-sectional studies have focused on depression in women in midlife, and they have shown that depressive symptoms and depression disorders are more common during the menopausal transition than during premenopause, particularly in women with a history of depression (1, 2, 10). However, there is limited information on the prevalence of postmenopausal depression.

There have been few studies of anxiety among women in midlife (11), and those studies have focused mainly on the association between anxiety and vasomotor symptoms (12–16) rather than menopausal status. The results of the Study of Women's Health Across the Nation (SWAN), a large longitudinal, multiethnic, community-based study of the ovarian aging, showed that anxiety is prevalent during the menopausal transition and in early postmenopause (3). However, the association between anxiety and menopausal stage needs further investigation.

Another important issue that requires attention is that the risk of depression (4) and anxiety (3) may vary by ethnicity with some social and demographic factors (including socioeconomic status and level of education). All the longitudinal studies focusing on mood problems are from Western countries and have mainly enrolled women of European descent. Moreover, there has been little discussion of the prevalence of anxiety and depression in the late postmenopausal years.

We analyzed data from the Peking Union Medical College Hospital Aging Longitudinal Cohort of Women in Midlife (PALM), the first longitudinal study of women in midlife in the People's Republic of China (17). Our present study describes the trajectories of anxiety and depressive symptoms in Chinese women and examines the associations between symptoms of anxiety and depression according to the stages of menopause. The study also assessed other risk factors for anxiety and depression.

MATERIALS AND METHODS

Participants

The data for this analysis were part of PALM, a prospective, open-cohort, community-based longitudinal study. A detailed description of the PALM cohort and the study procedures has been already published (17). Briefly, this study was initiated in July 2005. The participants were women living in a community in Beijing. A trained, qualified nurse from the Department of Gynecology of the Peking Union Medical College Hospital (PUMCH) managed the baseline and follow-up interviews and arranged for the participants

to complete the laboratory tests. The participants had annual follow-up visits.

The eligibility criteria for entry into the longitudinal cohort were age 35–64 years, with an intact uterus and at least one ovary, no history of severe systemic diseases, no reproductive endocrinologic disorders, no use of hormone medications in the previous 3 months, and no pregnancy or lactation in the previous 6 months. A total of 954 women were enrolled in the cohort. On enrollment, the participants completed a questionnaire that recorded their sociodemographic characteristics, menopause-related symptoms, and lifestyle behaviors. The women who were still menstruating were given calendars to record their menstrual cycle and related symptoms, and they were instructed on how to record the information. They were asked to continue to complete the menstrual calendar until they had been without bleeding for 1 year. Medical information was collected during the annual follow-up visits. The Hospital Anxiety and Depression Scale (HADS) (18), which introduced during the second year of follow-up evaluation in 2006, was completed at each subsequent annual follow-up visit.

Of the 954 women in the original cohort, a subcohort of 430 women were included in this study. To be eligible for this study, each woman had to have completed at least two HADS assessments during annual follow-up visits and to have completed natural menopause before or during the follow-up period. Women who had a hysterectomy after enrollment were excluded. This study included data from all the annual follow-up visits of the 430 women in the subcohort from 2006 to 2015. The visit at which they had their first HADS assessment was regarded as the baseline visit.

Because hormone therapy use may be associated with symptoms of anxiety and depression, and may hide menopausal status, data from visits at which women reported using hormone therapy during the previous year were excluded from this analysis (17 participants and 42 visits). The data from the subsequent visits of these women were included in the analysis if they had not used hormone therapy for at least 1 year at the time of the visit.

Ethics approval was granted by the institutional review board of the PUMCH. All participants provided written informed consent.

Measures

Assessment of mood. The primary outcome was symptoms of anxiety or depression measured using the HADS. The HADS is one of the tools most commonly used to detect symptoms of anxiety and depression, based on self-report (18). We used the Chinese version of the HADS, which has been validated and found to have good agreement with the original English version, to measure participants' symptoms of anxiety and depression (19–21). The HADS is a self-administered scale consisting of 14 items, and it focuses on psychological and emotional symptoms of anxiety and depression. The anxiety subscale (HADS-A, 7 items) focuses on worry and restlessness. The depression subscale (HADS-D, 7 items) enquires about depressed mood, hopelessness, and lack of enjoyment. Each of the 14 items is rated on a 4-point scale ranging from

0 to 3. The description indicating “no distress” is scored as 0, followed by descriptions of increasing distress scored as 1 and 2; the description indicating the highest level of distress is scored as 3. The depression score is the sum of seven depression items, the anxiety score is the sum of the seven anxiety items, and the total HADS score is the sum of all 14 items. On each of the subscales, a score of ≥ 8 was taken to indicate the presence of symptoms. The cut-point of 8 was chosen because it was found to give an optimal balance between sensitivity and specificity (22). We also defined participants with either an anxiety score ≥ 8 or a depression score ≥ 8 as having mood problems.

Assessment of menopausal status. The menopausal status of participants was determined according to the 2011 Stages of Reproductive Aging Workshop +10 (STRAW+10) criteria (23) by a clinician who specializes in gynecologic endocrinology. The participants were instructed to keep monthly menstrual diaries, which are used as the principal STRAW+10 criterion for assessing the stage of reproductive aging. Women were classified into four groups: [1] premenopause (Stage -3), comprising regular menstruation in the last 3 months and no change in menstrual frequency in the last 12 months; [2] early menopausal transition (Stage -2), comprising a persistent difference of ≤ 7 days in the length of menstruation (where “persistent” means recurrence within 10 cycles of the first variable length cycle); [3] late menopausal transition (Stage -1), comprising amenorrhea for 60 days or longer; and [4] postmenopause, comprising amenorrhea for 12 consecutive months or longer. Postmenopause was divided into Stage +1a (<1 year after their final menstrual period), Stage +1b (1 to 2 years after their final menstrual period), Stage +1c (2 to 8 years after final menstrual period), and Stage +2 (>8 years after their final menstrual period).

Assessment of time in relation to the final menstrual period. Age at the natural final menstrual period indicated 12 months without menstrual bleeding since the last menstrual period for no other cause (such as hysterectomy or chemotherapy). The age at the final menstrual period was synonymous with the term menopausal age. For women who had not reached menopause before enrolling in this study ($n = 240$), the date of their final menstrual period was determined by reviewing the participants’ menstrual diaries. The menopausal age then was calculated by “Date of final menstrual period” minus “Date of birth.” In women who were postmenopausal on entry into the cohort ($n = 190$), the menopausal age was self-reported. The HADS results were analyzed according to the participants’ age at menopause, ranging from 8 years before to 20 years after the final menstrual period. The year of menopause was designated as time 0 for each participant to allow longitudinal evaluation of within-woman changes in mood problems each year before and after menopause.

Covariates. The selection of covariates was based on their significance in previous studies and the goals of this study. Age, menopausal age, body mass index (BMI), level of education, marital status, income, general health status, presence of vasomotor symptoms and sleeping problems, and serum hormone

levels (estradiol and follicle stimulating hormone [FSH]) were measured at each visit. Body mass index was calculated as weight (kg)/height (m^2). General health status was based on self-report and was classified as poor, good, or excellent.

At each visit, the participants reported the presence and frequency of vasomotor symptoms (including hot flashes and night sweats) and sleeping problems (including trouble falling asleep and early awakening) in the previous 2 weeks. Women were asked, “How often did you experience hot flashes/night sweats in the past 2 weeks?” (never, ≤ 2 times/day, ≥ 3 times/day); and “How often did you experience trouble falling asleep/waking up earlier than planned, without being able to fall asleep again, in the past 2 weeks?” (never, occasionally, often). Sex hormone levels were measured on days 2 to 4 after bleeding stopped in women who were still menstruating, and on any day for postmenopausal women.

Statistical Analysis

Continuous variables with normal distributions were expressed as mean \pm standard deviation (SD). Categorical variables were expressed as percentages. Comparisons of continuous variables between groups were made using Student’s *t*-test for normally distributed data and the Mann-Whitney *U* test if the data were not normally distributed. Categorical data were compared using the chi-square test, and ordered categorical data were compared using the nonparametric Kruskal-Wallis test.

The second set of analyses focused on the longitudinal data on each participant’s measurements repeated over time. We used linear generalized estimating equations (24) to account for within-participant correlations through a working correlation matrix. We estimated the effect of STRAW+10 stage (using the premenopausal stage as the reference group) and time in relation to the final menstrual period (using the year of the final menstrual period as the reference group) on the HADS results. The models included a random intercept only. An exchangeable working correlation matrix that accounts for correlations within subjects was used. Because women who were postmenopausal at enrollment ($n = 190$) may not have recalled their age at menopause accurately due to recall bias (17, 25), we repeated the analysis with these women excluded.

Covariates that were considered clinically relevant or that had previously been reported to be associated with the outcomes were defined a priori and were added to the basic model one at a time. The natural log-transformed values of FSH and estradiol were used in the statistical model instead of the absolute values to reduce the influence of large values. We did three sets of analyses: the association between covariates and symptoms of anxiety, symptoms of depression, and symptoms of anxiety and depression combined. We separately added every variable to investigate the association. Candidate variables with $P \leq .2$ in the univariate analyses were included in the multivariable model to assess the independent effects of these variables on the outcomes. In multivariable models, the FSH and estradiol values and hot flashes and night sweats were evaluated in separate multivariable

TABLE 1

Baseline characteristics of all participants according to the STRAW + 10 stage.

Characteristic	All participants (N = 430)	Premenopausal (n = 70)	Menopausal transition (n = 121)	Postmenopausal (n = 239)
Age, mean (SD), y	52.5 (6.4)	45.3 (3.2) ^{a,b}	48.6 (3.4) ^{b,c}	56.6 (4.9) ^{a,c}
Menopausal age, mean (SD), y	50.4 (3.2)	50.8 (2.8) ^a	51.3 (2.9) ^c	49.8 (3.3) ^{a,c}
BMI, mean (SD), kg/m ²	25.3 (3.4)	24.7 (3.6) ^a	25.0 (3.0)	25.7 (3.4) ^a
FSH, mean (SD), IU/L	47.6 (34.1)	12.3 (8.9) ^{a,b}	26.5 (34.1) ^{b,c}	69.4 (26.7) ^{a,c}
Estradiol, mean (SD), pg/mL	53.1 (74.5)	98.9 (86.1) ^a	90.5 (95.8) ^c	19.7 (25.6) ^{a,c}
Marital status, no. (%)	—	— ^a	— ^c	— ^{a,c}
Single	3 (0.7)	0 (0)	0 (0)	3 (1.3)
Married	391 (91.4)	67 (95.7)	112 (93.3)	212 (89.1)
Widowed	15 (3.5)	0 (0)	0 (0)	15 (6.3)
Divorced	19 (4.4)	3 (4.3)	8 (6.7)	8 (3.4)
Educational status, no. (%)	—	— ^a	— ^c	— ^{a,c}
Middle school	131 (30.5)	8 (11.6)	16 (13.2)	107 (44.8)
High school	152 (35.4)	41 (59.4)	65 (53.7)	46 (19.2)
College	113 (26.3)	12 (17.4)	30 (24.8)	71 (29.7)
University or higher	33 (7.7)	8 (11.6)	10 (8.3)	15 (6.3)
Income, no. (%)	—	— ^a	— ^c	— ^{a,c}
<1,000 RMB	200 (46.6)	33 (47.8)	61 (50.4)	106 (44.4)
1,000–2,000 RMB	153 (35.7)	21 (30.4)	40 (33.1)	92 (38.5)
>2,000 RMB	76 (18.4)	15 (21.7)	20 (16.5)	41 (17.2)
General health status, no. (%)	—	— ^a	— ^c	— ^{a,c}
Excellent	85 (19.9)	17 (24.6)	33 (27.5)	35 (14.6)
Good	322 (75.2)	47 (68.1)	82 (68.3)	193 (80.8)
Poor	21 (4.9)	5 (7.2)	5 (4.2)	11 (4.6)

Note: Baseline in this analysis was the date of the first HADS assessment. BMI = body mass index; FSH = follicle-stimulating hormone; HADS = the Hospital Anxiety and Depression Scale; SD = standard deviation; RMB = Renminbi; STRAW+10 = 2011 Stages of Reproductive Aging Workshop +10 criteria.

^a P < .05 premenopause versus postmenopause.

^b P < .05 premenopause vs. menopausal transition.

^c P < .05 menopausal transition versus postmenopause.

Tang. Mood and menopause in Chinese women. *Fertil Steril* 2019.

models because of their strong correlation. Both univariate and multivariable analysis were performed using generalized estimating equations.

Analyses were performed using IBM SPSS software (version 20.0 for the OS X system). All tests were two-sided with a value of ≤ 0.05 considered statistically significant.

RESULTS

Over the 10-year follow-up period, the 430 women had a total of 2,533 HADS assessments, with two to eight visits each (mean: 5.9), and 46.9% were retained in the cohort in 2015 (shown in Supplemental Table 1, available online).

Participants' Baseline Characteristics

The 430 participants had a mean age of 52.47 ± 6.36 years at baseline, and a mean menopausal age of 50.4 ± 3.2 years. Their baseline characteristics are shown in Table 1. The participants' menopausal status at baseline, according to STRAW+10 criteria, was premenopausal: Stage -3, n = 70 (16.3%); menopausal transition: Stage -2 and -1, n = 121 (28.1%); and postmenopausal, Stage +1 and +2, n = 239 (55.6%). The participants' demographic characteristics according to their baseline menopausal status are shown in Table 1. The postmenopausal women had a lower level of education, were more likely to be widowed, and had a poorer health status.

Mood in Relation to STRAW + 10 Stage

The prevalence of symptoms of anxiety, symptoms of depression, and symptoms of anxiety and depression combined (mood problems), according to the menopausal stage are shown in Table 2 and Figure 1A. Depressive symptoms were more common than anxiety symptoms among women in this study. During the premenopausal stage, the prevalence of anxiety and depressive symptoms were 3.1% and 14.5%, respectively. The prevalence of symptoms of anxiety and depression were higher during the menopausal transition (symptoms of anxiety 7.0%; symptoms of depression 18.2%) and the postmenopausal stage (symptoms of anxiety 7.4%; symptoms of depression 19.6%) than in the premenopausal stage. The prevalence of symptoms of anxiety, symptoms of depression, and symptoms of both combined, according to the menopausal stage, was lowest in the premenopausal stage and peaked during the Stage +1c. However, the association between the menopausal stage and symptoms of anxiety or depression, and symptoms of both combined (mood problems) was not statistically significant. The prevalence of symptoms of anxiety and depression of women in the menopausal transition and postmenopausal stage was higher than that of the premenopausal women, but these differences were not statistically significant.

Mood in Relation to the Final Menstrual Period

In each year around menopause, the annual prevalence of symptoms of anxiety ranged from 0 to 12.1%, and the

TABLE 2

Prevalence of symptoms of anxiety and depression by STRAW + 10 category and year in relation to final menstrual period.

Variable	N	Mood problems ^a			Symptoms of anxiety			Symptoms of depression		
		Proportion (%)	OR (95% CI)	P value	Proportion (%)	OR (95% CI)	P value	Proportion (%)	OR (95% CI)	P value
STRAW+10 stage				.753 ^b			.679 ^b			.579 ^b
Premenopausal, Stage -3	131	16.0	1.00 (Reference)		3.1	1.00 (Reference)		14.5	1.00 (Reference)	
Menopausal transition										
Early, Stage -2	234	20.9	1.13 (0.69-1.84)	.63	6.4	1.13 (0.49-2.65)	.77	17.9	1.17 (0.68-2.02)	.57
Late, Stage -1	353	21.2	0.99 (0.60-1.62)	.96	7.4	1.44 (0.58-3.56)	.43	18.4	0.98 (0.57-1.68)	.94
Postmenopause										
Stage +1a	172	21.5	1.13 (0.65-1.96)	.66	8.1	1.75 (0.71-4.33)	.23	18.0	1.06 (0.58-1.95)	.86
Stage +1b	161	20.5	1.16 (0.68-1.98)	.58	5.6	1.09 (0.39-3.03)	.86	18.6	1.25 (0.69-2.28)	.46
Stage +1c	751	23.3	1.29 (0.79-2.10)	.31	8.8	1.69 (0.72-3.95)	.22	20.6	1.37 (0.80-2.37)	.25
Stage +2	731	21.3	1.29 (0.78-2.16)	.32	6.2	1.66 (0.70-3.95)	.25	19.0	1.34 (0.77-2.34)	.31
Years				.490 ^b			.706 ^b			.122 ^b
< -6 ^c	45	22.2	0.97 (0.53-1.79)	.92	6.7	0.89 (0.36-2.17)	.79	15.6	0.80 (0.36-1.79)	.59
-6	46	17.4	0.61 (0.28-1.33)	.21	6.5	0.97 (0.38-2.49)	.94	13	0.52 (0.20-1.37)	.19
-5	72	19.4	0.79 (0.42-1.51)	.48	2.8	0.50 (0.16-1.56)	.23	18.1	0.87 (0.44-1.73)	.69
-4	108	21.3	0.90 (0.55-1.45)	.66	6.5	1.13 (0.51-2.47)	.77	19.4	0.94 (0.56-1.57)	.81
-3	107	22.4	0.88 (0.54-1.43)	.60	7.5	1.18 (0.51-2.70)	.70	19.6	0.87 (0.52-1.46)	.61
-2	131	16.0	0.51 (0.30-0.90)	.02	7.6	0.95 (0.45-2.02)	.90	13.7	0.51 (0.27-0.95)	.03
-1	147	17.7	0.65 (0.41-1.03)	.07	5.4	0.73 (0.34-1.54)	.40	15.0	0.65 (0.40-1.05)	.08
Final menstrual period	153	26.1	1.00 (Reference)		7.8	1.00 (Reference)		22.9	1.00 (Reference)	
1	168	22.6	0.94 (0.63-1.4)	.75	6.5	0.92 (0.42-1.99)	.83	20.2	1.00 (0.65-1.55)	1.00
2	144	19.4	0.78 (0.49-1.23)	.29	8.3	1.13 (0.57-2.24)	.73	16.0	0.75 (0.46-1.23)	.25
3	140	26.4	1.05 (0.68-1.62)	.83	12.1	1.37 (0.69-2.74)	.37	22.9	1.09 (0.68-1.74)	.73
4	129	27.9	1.23 (0.77-1.95)	.39	10.1	1.39 (0.63-3.05)	.41	25.6	1.37 (0.84-2.22)	.21
5	135	23.0	0.92 (0.58-1.47)	.74	8.1	1.03 (0.46-2.32)	.94	20.7	1.04 (0.64-1.70)	.86
6	125	20.8	0.76 (0.45-1.26)	.28	6.4	0.83 (0.33-2.07)	.69	19.2	0.86 (0.50-1.47)	.57
7	113	18.6	0.79 (0.46-1.36)	.39	5.3	0.81 (0.31-2.13)	.67	17.7	0.92 (0.52-1.62)	.76
8	106	18.9	0.72 (0.41-1.25)	.24	8.5	1.23 (0.53-2.84)	.63	13.2	0.60 (0.33-1.09)	.09
9	94	26.6	1.00 (0.57-1.76)	1.00	9.6	1.52 (0.66-3.51)	.33	23.4	1.04 (0.57-1.91)	.90
10	79	27.8	0.95 (0.50-1.78)	.87	8.9	1.06 (0.40-2.82)	.90	24.1	0.99 (0.50-1.94)	.97
11	65	30.8	1.17 (0.65-2.11)	.59	9.2	1.24 (0.48-3.21)	.65	29.2	1.34 (0.73-2.46)	.35
12	53	28.3	1.20 (0.64-2.25)	.57	3.8	0.64 (0.19-2.12)	.47	28.3	1.50 (0.79-2.85)	.21
13	53	17.0	0.64 (0.30-1.38)	.26	3.8	0.64 (0.19-2.11)	.46	17.0	0.77 (0.35-1.69)	.52
14	55	16.4	0.74 (0.37-1.48)	.40	5.5	1.13 (0.41-3.15)	.82	12.7	0.66 (0.31-1.39)	.28
15	50	14.0	0.50 (0.21-1.22)	.13	2.0	0.34 (0.06-1.91)	.22	14.0	0.62 (0.25-1.52)	.29
16	43	14.0	0.57 (0.25-1.34)	.20	0	NA	NA	14.0	0.71 (0.30-1.66)	.43
17	37	18.9	0.70 (0.32-1.55)	.38	2.7	0.37 (0.06-2.37)	.29	18.9	0.91 (0.41-1.98)	.80
18	34	14.7	0.52 (0.18-1.49)	.22	5.9	0.72 (0.14-3.62)	.69	8.80	0.38 (0.11-1.33)	.13
19	27	11.1	0.49 (0.19-1.27)	.14	3.7	0.41 (0.05-3.60)	.42	11.1	0.61 (0.24-1.57)	.31
20 ^d	24	8.3	0.43 (0.14-1.29)	.13	4.2	0.74 (0.14-4.06)	.73	8.30	0.57 (0.20-1.66)	.31
Total	2,533	21.6			7.1			19.0		

Note: CI = confidence interval; HADS = the Hospital Anxiety and Depression Scale; NA = not available; OR = odds ratio; STRAW+10 = 2011 Stages of Reproductive Aging Workshop +10 criteria.

^a Mood problems: the presence of either symptoms of anxiety or depression.

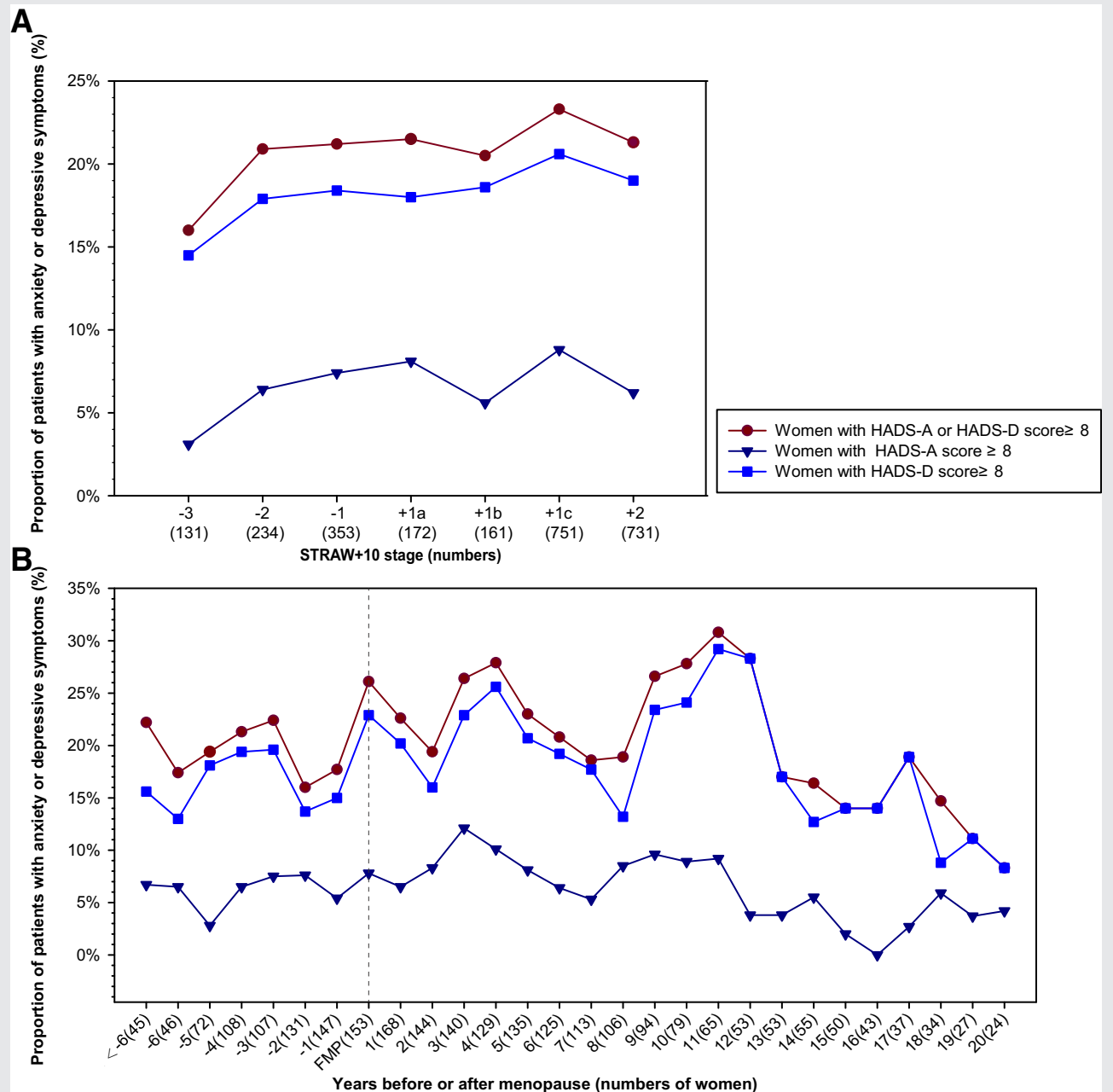
^b Wald statistic for overall test of significance.

^c Participants in years -8 to -7 are combined due to the low numbers (year -8, n = 27; year -7, n = 18).

^d Participants are not presented in 20 years after the final menstrual period due to the low numbers (year 21, n = 16; year 22, n = 11; year 23, n = 9; year 24, n = 4; year 25, n = 3; year 26, n = 2; year 27, n = 2; year 28, n = 2; year 29, n = 1).

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FIGURE 1



Proportion of women with symptoms of anxiety and depression, and mood problems (A) at each stage of STRAW+10 and (B) in each study year before or after menopause. (A) The prevalence was lowest in the premenopausal stage and peaked during +1c stage. (B) Years -8 (n = 27) and -7 (n = 18) before the final menstrual period were combined due to small numbers of observations. Years in the upper end of the postmenopausal range are not included due to the small numbers of observations. Score ≥ 8 on the HADS-A measure of anxiety symptoms; score ≥ 8 on the HADS-D measure of symptoms of depression; score ≥ 8 on HADS-A or HADS-D measure of mood problems; STRAW+10 according to the 2011 Stages of Reproductive Aging Workshop +10 criteria; HADS: Hospital Anxiety and Depression Scale. The gray dotted line shows the results in the year of the final menstrual period.

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prevalence of symptoms of depression ranged from 8.3% to 29.2% (see Table 2 and Fig. 1B). The prevalence of symptoms of anxiety and depression were lower before the final menstrual period than the year of the final menstrual period, whereas their prevalence was relatively high in the early postmenopausal years. However, there were no statistically signif-

icant associations between years relative to the final menstrual period, and the prevalence of symptoms of anxiety or depression. In the analysis of women's symptoms of anxiety and depression by year, in relation to the year of their final menstrual period, those in the 2 years before their final menstrual period had a statistically significantly lower prevalence

TABLE 3

Associations of risk factors with the symptoms of anxiety, symptoms of depression, and mood problems in the whole subcohort (N = 430).

Variable	Univariable analysis		Multivariable analysis	
	P value	OR (95% CI)	P value	OR (95% CI)
Symptoms of anxiety				
BMI, kg/m ²	.03	1.09 (1.01–1.17)	.44	0.97 (0.91–1.04)
Log FSH ^a	.06	1.63 (0.99–2.71)	.76	1.10 (0.62–1.95)
Log estradiol ^a	.18	0.88 (0.72–1.76)	.69	0.96 (0.76–1.19)
Income	.15		.25	
<1,000RMB		1.39 (0.96–2.00)		0.87 (0.55–1.38)
1,000–2,000 RMB		0.98 (0.72–1.33)		1.26 (0.83–1.89)
>2,000 RMB		1.00 (Reference)		1.00 (Reference)
General health status	<.001		<.001	
Excellent		1.00 (Reference)		1.00 (Reference)
Good		2.01 (1.25–3.24) ^b		2.20 (1.26–3.83) ^b
Poor		5.29 (2.62–10.72) ^c		5.41 (2.46–11.67) ^c
Hot flashes ^a	.003		.34	
None		1.00 (Reference)		1.00 (Reference)
Occasionally		1.65 (1.17–2.34) ^b		1.38 (0.90–2.20)
Often		1.81 (1.23–2.67) ^b		1.18 (0.74–1.86)
Night sweats ^a	.007		.26	
None		1.00 (Reference)		1.00 (Reference)
≤2/days		1.60 (1.15–2.23) ^b		1.38 (0.92–2.09)
>3/days		1.65 (1.12–2.43) ^d		1.08 (0.68–1.72)
Trouble falling asleep	<.001		.001	
None		1.00 (Reference)		1.00 (Reference)
Occasionally		1.60 (1.10–2.33) ^d		0.91 (0.56–1.46)
Often		4.99 (2.15–7.91) ^c		2.22 (1.23–3.98) ^b
Early awakening	<.001		<.001	
None		1.00 (Reference)		1.00 (Reference)
Occasionally		2.30 (1.61–3.30) ^c		2.24 (1.39–3.59) ^b
Often		4.81 (3.15–7.35) ^c		3.16 (1.82–5.50) ^c
Symptoms of depression				
BMI, kg/m ²	.09	1.04 (0.99–1.08)	.04	1.05 (1.002–1.091) ^d
Log FSH	.20	1.24 (0.89–1.73)	.87	1.03 (0.70–1.52)
Educational status	.04		.04	
Middle school		2.12 (1.11–4.05) ^d		2.42 (1.17–5.00) ^d
High school		1.53 (0.80–2.93)		1.70 (0.83–3.48)
College		1.31 (0.66–2.60)		1.52 (0.72–3.22)
University or higher		1.00 (Reference)		1.00 (Reference)
General health status	.01		.04	
Excellent		1.00 (Reference)		1.00 (Reference)
Good		1.42 (1.05–1.92) ^d		1.29 (0.94–1.77)
Poor		2.06 (1.22–3.49) ^b		2.00 (1.15–3.48) ^d
Hot flashes ^a	.002		.07	
None		1.00 (Reference)		1.00 (Reference)
≤2/d		1.38 (1.11–1.73) ^b		1.31 (1.02–1.69) ^d
>3/d		1.54 (1.14–2.06) ^b		1.33 (0.95–1.86)
Night sweats ^a	<.001		.02	
None		1.00 (Reference)		1.00 (Reference)
≤2/days		1.38 (1.12–1.71) ^b		1.31 (1.02–1.68) ^d
>3/days		1.82 (1.34–2.47) ^c		1.59 (1.13–2.24) ^b
Trouble falling asleep	<.001		.09	
None		1.00 (Reference)		1.00 (Reference)
Occasionally		1.34 (1.09–1.66) ^b		1.16 (0.89–1.51)
Often		2.07 (1.48–2.90) ^c		1.62 (1.06–2.49) ^d
Early awakening	.003		.58	
None		1.00 (Reference)		1.00 (Reference)
Occasionally		1.18 (0.97–1.44)		1.05 (0.81–1.35)
Often		1.67 (1.25–2.25) ^b		1.23 (0.83–1.82)
Mood problems				
Log FSH	.19	1.23 (0.90–1.68)	.70	0.93 (0.65–1.34)
Educational status	.19		.07	
Middle school		1.32 (0.72–2.39)		1.65 (0.87–3.12)
High school		1.00 (0.55–1.82)		1.14 (0.61–2.13)
College		0.87 (0.46–1.65)		1.03 (0.54–1.98)
University or higher		1.00 (Reference)		1.00 (Reference)
General health status	<.001		.006	

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TABLE 3

Continued.				
Variable	Univariable analysis		Multivariable analysis	
	P value	OR (95% CI)	P value	OR (95% CI)
Excellent		1.00 (Reference)		1.00 (Reference)
Good		1.44 (1.08–1.92) ^d		1.37 (1.01–1.85) ^d
Poor		2.34 (1.45–3.76) ^c		2.19 (1.34–3.59) ^b
Income	.10		.24	
<1,000RMB		0.77 (0.59–0.99) ^d		0.84 (0.63–1.11)
1,000–2,000 RMB		0.96 (0.76–1.21)		1.06 (0.82–1.37)
>2,000 RMB		1.00 (Reference)		1.00 (Reference)
Hot flashes ^a	.002		.06	
None		1.00 (Reference)		1.00 (Reference)
≤2/d		1.42 (1.15–1.75) ^b		1.35 (1.06–1.72) ^d
>3/d		1.40 (1.06–1.85) ^d		1.16 (0.85–1.58)
Night sweats ^a	<.001		.03	
None		1.00 (Reference)		1.00 (Reference)
≤2/days		1.42 (1.16–1.74) ^b		1.34 (1.06–1.70) ^d
>3/days		1.62 (1.22–2.16) ^b		1.38 (1.01–1.89) ^d
Trouble falling asleep	<.001		.10	
None		1.00 (Reference)		1.00 (Reference)
Occasionally		1.36 (1.11–1.66) ^b		1.11 (0.86–1.43)
Often		2.38 (1.73–3.27) ^c		1.54 (1.03–2.29) ^d
Early awakening	<.001		.02	
None		1.00 (Reference)		1.00 (Reference)
Occasionally		1.25 (1.04–1.51) ^d		1.15 (0.91–1.46)
Often		2.10 (1.60–2.77) ^c		1.64 (1.15–2.33) ^b

Note: BMI = body mass index; CI = confidence interval; FSH = follicle-stimulating hormone; OR = odds ratio; RMB = Renminbi; STRAW+10 = 2011 Stages of Reproductive Aging Workshop +10 criteria; HADS = the Hospital Anxiety and Depression Scale.

^a FSH and estradiol were considered to have high intercorrelation clinically, and log FSH and log estradiol were evaluated in separate multivariable models. Hot flashes and night sweats were considered to have high intercorrelation clinically and were evaluated in separate multivariable models.

^b $P \leq .01$.

^c $P \leq .0001$.

^d $P \leq .05$.

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of symptoms of depression, but none of the other differences in depression and anxiety was statistically significantly different from those of women in the year of their final menstrual period.

We repeated the analysis on the 240 women who were in the premenopausal stage or menopausal transition at baseline and found that the results were not changed. The prevalence of anxiety and depressive symptoms was still not statistically associated with menopausal status or time in relation to the final menstrual period.

Mood in Relation to Other Risk Factors

The results of comparisons of selected variables and symptoms of depression and anxiety in univariate analysis and multivariable analysis of the whole subcohort are shown in Table 3. In the multivariable model, poor health status, difficulty falling asleep, and early awakening were independently associated with symptoms of anxiety. Women who reported poor health were more than five times as likely to have anxiety symptoms compared with women reporting excellent health. Women who often had sleeping problems were about three times as likely to have symptoms of anxiety compared with women without sleeping problems. Similarly, women with a high BMI, poor health, low education status, and night sweats were statistically significantly more likely to have symptoms of depression, independent of the other covariates. With regard to the presence of symptoms of anxiety and

depression combined, women with poor health status, night sweats, and early awakening were statistically significantly more likely to have mood problems.

DISCUSSION

This is the first prospective study of mood problems in Chinese women in midlife in relation to their menopausal status, and it included a large proportion of women in their late postmenopausal years. Our study showed that depressive symptoms were more common than anxiety symptoms, despite menopausal women often being portrayed as restless and worried. Both anxiety and depressive symptoms were more frequent in the early years after menopause. The analysis revealed that poor health status and sleep problems were independently associated with symptoms of anxiety, whereas higher BMI, poor health, a low level of education, and night sweats were independently associated with symptoms of depression.

The People's Republic of China has an aging population, with an increasing number of aged people whose physical and mental health status affects the stability of their families and society. The physiological and psychological changes in the postmenopausal period are important fields for targeted research. The occurrence of emotional problems, especially depression, has long been a focus. However, most studies have compared the problems of depression in women in the menopausal transition with those in the premenopausal period, and few studies have included women in their late

postmenopausal period. Studies that have assessed a postmenopausal cohort often have failed to distinguish between early and late postmenopause, which are distinct stages of reproductive aging. Moreover, symptoms of anxiety among women in midlife have received relatively little attention.

Our study provides information on the symptoms of anxiety and depression in a prospective cohort of women in midlife, and the results improve our understanding of women's moods as they transition from midlife to late life. We assessed the prevalence of mood problems according to the menopausal stage using the STRAW+10 staging system and from 8 years before to 20 years after the women's final menstrual period. Some cross-sectional studies have been performed in the People's Republic of China previously (26, 27). In a cross-sectional survey (27), 12.6% of participants experienced symptoms of anxiety, and 26.0% experienced symptoms of depression. The prevalence of symptoms of anxiety and depression among women in our study was 7.0% and 18.2% during the menopausal transition and 7.4% and 19.6% after menopause, which is slightly lower than the findings of the cross-sectional surveys.

The final menstrual period is pivotal in the overall pattern of mood problems. The time in relation to the final menstrual period is commonly used in clinical practice when evaluating postmenopausal women. In this study, we found that the prevalence of symptoms of anxiety and depression were lower in the year before the final menstrual period than in the year of the final menstrual period, but that the prevalence in the early postmenopausal years was higher. Our study, the first study to describe the risk of anxiety in each year relative to the final menstrual period in a cohort of women transitioning through menopause, could serve as a model for future studies.

Freeman et al. (2) have reported on the patterns of depression among women in the Penn Ovarian Aging Study (POAS), a population-based cohort study of naturally menopausal women. However, in contrast to the findings of our study, they found that the risk of symptoms of depression was higher in each year before the final menstrual period, and lower in each year after the final menstrual period. This difference in the findings of the two studies may be attributable to the socioeconomic and cultural differences between the study populations. Previous studies conducted in United States, a multiethnic country, have shown that socioeconomic and health factors have an influence on racial disparities in the course of depressive symptoms (28, 29). Chinese women may experience other life changes during their menopausal transition and the early postmenopausal period, including financial pressure, health problems related to aging, and the empty nest syndrome. Cultural factors may also play a role in causing mood problems. Chinese parents often buy new houses for their children, and Chinese women often help take care of their grandchildren. These specific life stresses occur mostly among women in their 50s and 60s, and might contribute to mood problems in this age group.

The association between menopausal stage and mood has long been a major concern. We found that symptoms of anxiety and depression were not statistically significantly associated with the menopausal stage and that, although mood problems increased around the time of menopause, this

change was not marked. These findings suggest that menopause has an influence on mood problems, but that the effect is not as great as has been thought previously. However, it cannot be ruled out that there were important changes in mood associated with menopause but we did not find statistically-significant associations because of the sample size.

Our results are consistent with some, but not all, findings from previous studies (16, 30–33). There has been limited research on the relationship between menopause and anxiety, and a meta-analysis of nine studies on anxiety and the menopausal transition did not find a clear association (11). More recently, other studies have found an increase in symptoms of anxiety during perimenopause (3) and postmenopause (34) relative to premenopause whereas other studies, including the POAS cohort study (14, 16), found that anxiety was not related to menopausal stage (35, 36). Our results provide evidence that anxiety is not related to menopausal stage.

Our study found that depressive symptoms increased during the menopausal transition and postmenopausal years, especially in the early postmenopausal stage. Previous studies of depressive symptoms in postmenopausal women have shown conflicting results: some studies showed an increase (1, 37, 38), some studies showed a decrease (2, 39, 40), and other studies showed no change (33).

We tried to account for the differences between the findings of our study and some of the previous studies. First, this might be partly attributable to differences in the study populations, such as ethnicity and culture. The SWAN study found that Chinese women had half the risk of depressive symptoms (41) and lower anxiety symptoms (3) than people of European descent. Different settings (community versus clinical) may also have contributed to differences in the study results. Our study participants were recruited in a community setting, so they are more representative of women in the general population than the women in studies done in a clinical setting. Moreover, previous research studies on menopausal status and mood have used different questionnaires and different staging classifications, and some studies have used single-item measures or nonvalidated measures, bringing into question the validity of the results.

Numerous other studies have also identified risk factors for mood problems around menopause. Depression in women at midlife has been reported to be more strongly associated with menopausal symptoms, such as vasomotor symptoms and poor sleep, than with menopausal status per se (26, 30, 31). Other studies have found that symptoms of anxiety are also strongly related to menopausal symptoms (3, 16), and that poor sleep was more strongly associated with anxiety than with depression (42). Our study demonstrated that poor sleep was independently associated with symptoms of anxiety but not with symptoms of depression. Women who had sleep problems were about three times more likely to report symptoms of anxiety than women without sleep problems. Night sweats, a troubling menopausal symptom, were independently associated with symptoms of depression. In addition to the discomfort of menopausal symptoms, previous studies have found that other factors

such as educational level, health status, life stresses, and obesity are associated with depression (10, 43, 44). In this study, a lower level of education, poor health, and obesity were independently associated with symptoms of depression.

This study has several strengths. It was a prospective cohort study with a long follow-up period in a large community-based sample of women. Mood symptoms were measured annually using HADS, which has been validated and is a widely used instrument for measuring mood problems. Our classification of menopausal status was based on the STRAW+10 staging system, which relies on women's menstrual diary and hormone profile at each assessment. Most of the previous studies have not drawn a distinction between early and late perimenopause, but our study distinguished substages of the early and late menopausal transition as well as early and late postmenopause, and we determined how the prevalence of mood problems changed during these periods. Another major strength of the study is that it included a long post-final menstrual period of 20 years. We believe that our findings contribute to a greater understanding of the symptoms of depression and anxiety in relation to menopausal status.

Our study's limitations also need to be considered. First, we did not have data on the participants' history of depression and anxiety before enrollment, which is associated with an increased risk of subsequent clinical episodes (2). The participants had annual follow-up visits, so short-term symptoms may not have been fully identified. Second, because this study relied on reported symptoms alone, which are highly correlated with clinical diagnosis of diseases but are not equivalent, caution should be taken in extrapolating the results to depression or anxiety disorders. Nonetheless, we consider that mood problems that do not meet clinical criteria for a psychiatric diagnosis still warrant public health attention; the presence of symptoms is also associated with functional impairment such as disability and lost work days (45). Third, recent studies have shown that the HADS does not provide good separation between symptoms of anxiety and depression due to the presence of a strong general factor (46), whereas the scores are a reliable and valid unidimensional measure of mood problems (47). In addition, we only included women who transitioned through menopause naturally without hormone treatment. Studies have shown that women who undergo surgical menopause and hormone users have a different experience of the psychological symptoms associated with menopause (10). Therefore, our results may not apply to women in these groups.

Finally, there were some differences in BMI, marital status, education, and general health status between the premenopausal women and postmenopausal women at baseline, mainly due to increasing ages. The postmenopausal women at baseline had an earlier menopausal age because they recalled their menopausal age, which could be approximately 1 to 2 years earlier than the real menopausal age, as has been shown by other studies (17, 25). However, a repeat analysis excluding women who were postmenopausal at baseline found that the results were not altered, suggesting that any inaccuracies in women's recollection of their menopausal age did not bias the results.

In conclusion, this study provides a better understanding of the prevalence of mood problems in relation to menopause in a large prospective cohort of Chinese women. These findings suggest that symptoms of depression are more prevalent than symptoms of anxiety. It is important that clinicians screen women for mood problems, especially women with risk factors, to increase the likelihood of them receiving effective and timely interventions.

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Síntomas de ansiedad y depresión entre mujeres chinas en transición hacia la menopausia: hallazgos de un estudio comunitario prospectivo de cohortes

Objetivo: Determinar la prevalencia de síntomas de ansiedad y depresión en mujeres chinas durante y después de la menopausia y los factores de riesgo asociados.

Diseño: Estudio comunitario prospectivo de cohortes.

Entorno: Comunidad urbana en Beijing, República Popular de China.

Paciente(s): Cuatrocientas treinta mujeres que habían alcanzado la menopausia de forma natural.

Intervención(es): Ninguna.

Medida del resultado principal: Síntomas de ansiedad y depresión.

Resultado(s): Los síntomas de depresión fueron más frecuentes que los de ansiedad. La prevalencia de síntomas de depresión aumentó desde 14.5% durante la premenopausia hasta 18.2 % durante la transición menopáusica y llegaron al 19.6% en el periodo postmenopáusico. La prevalencia de síntomas de ansiedad aumentó desde el 3.1% en la premenopausia hasta el 7.0% durante la transición menopáusica y llegó al 7.4% en el periodo postmenopáusico. Cuando se compararon con mujeres premenopáusicas, las mujeres peri y postmenopáusicas era más probable que tuvieran síntomas de ansiedad y depresión, pero estas diferencias no fueron estadísticamente significativas. El análisis multivariable demostró que el estado de salud deficiente, la dificultad para conciliar el sueño y el despertar pronto se asociaban de manera independiente a los síntomas de ansiedad y que un índice de masa corporal elevado, salud deficiente, bajo nivel de educación y sofocos nocturnos se asociaban de manera independiente con síntomas de depresión.

Conclusión(es): Los síntomas de depresión fueron más prevalentes que los síntomas de ansiedad. Nuestros hallazgos sugieren que los síntomas de ansiedad y depresión son más frecuentes durante y después de la menopausia que en la premenopausia. Estos hallazgos subrayan la importancia de realizar screening y evaluación de síntomas de ansiedad y depresión en las mujeres en transición menopáusica, especialmente en aquellas con factores de riesgo.