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## A menopause survey of women with benign breast disease history in northwest China

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### ABSTRACT

**Objectives:** The present study aimed to determine the prevalence of menopause syndrome (MPS) and the present treatment status for menopause symptoms in women with benign breast disease history, compared with those without breast problems, and to analyze the affecting factors of medical visits and hormone replacement therapy (HRT) application for menopause symptoms.

**Methods:** A questionnaire survey was conducted by face-to-face interview with a general sample of 8500 Chinese women aged 45–55 years from 162 villages and towns of Gansu province, China.

**Results:** The MPS prevalence in the Benign breast disease history group was 76.60%, and was not statistically different from that of the Control group. Few of the participants had medical visits or had undergone treatment. The Benign breast disease history group was more informed of the treatment options available and more likely to start HRT.

**Conclusions:** Most women with benign breast disease history experienced menopausal symptoms when experiencing reproductive senescence, they had more knowledge about menopause syndrome and more positive to the therapeutic than whom without breast problems.

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### Introduction

Both benign breast disease and menopause syndrome (MPS) are very common in a woman's life. It was reported that benign breast disease is diagnosed in nearly half of all American women at some point in their lives. Also, according to a study based on the Chinese population, 36.4% of women have a history of benign breast disease<sup>1,2</sup>. The incidence of benign breast lesions begins to rise in the second decade of one's life, peaks in the fourth and fifth decades, and continues to rise less rapidly after menopause<sup>3</sup>. In contrast, the symptoms of MPS appear early in the premenopause, which significantly reduces the quality of life, and they will persist 5 years beyond the menopause<sup>4</sup>. Undoubtedly, some women with a history of benign breast disease will suffer the symptoms of MPS when they show reproductive senescence.

Based on the degree of cellular proliferation and atypia, benign breast lesions can histologically fall into three types: non-proliferative, proliferative without atypia, and atypical hyperplasia. The proliferative without atypia and atypical hyperplasia types may increase the patient's future risk of developing breast cancer, whereas no increased risk was found in women with no family history and non-proliferative findings<sup>5–7</sup>. Most lesions that occur in the breast are benign. The non-proliferative breast lesion is the most common category and most women suffering benign disease are not at increased risk of cancer<sup>6,7</sup>. However, many studies have been

made on women who have MPS with a breast cancer history, yet those with a history of benign breast disease have been rarely reported in a menopause survey.

Another major question concerns the possible interplay between applying hormone replacement therapy (HRT) for menopause symptoms of benign breast disease history and breast cancer. Exogenous and endogenous estrogens are considered associated with the etiology of breast cancer by stimulating cell growth and proliferation; higher and longer lifetime exposure to estrogens can be a major risk factor for inducing or promoting breast cancer<sup>8</sup>. As a result, the application of HRT for women with a history of benign breast disease has always been accompanied by apprehension and argument. Thus, the present study was conducted to explore the prevalence of MPS in mid-aged women with benign breast disease history compared with those without breast problems, as well as their medical visits and therapeutic conditions about menopause symptoms.

### Materials and methods

#### Participants

This cross-sectional survey was conducted from March 2016 to November 2016 in 162 villages and towns of Gansu, China. To ensure that the sample was representative of the overall population of menopausal women from the whole province, the selection was based on multiorder cluster

random sampling. Participants were interviewed face to face following street interceptions or door-to-door visits. Eligible women were 45–55 years of age and satisfied the following inclusion criteria: lived in the local area for more than 1 year; conscious and able to provide informed consent; no history of mental illness and mental retardation; and no communication problems.

### Interviews

Women were interviewed by trained interviewers. The questionnaire was validated by a panel of researchers.

Ethical approval was gained from local institutes and ethical committees.

The structured questionnaire consisted of multiple-choice questions which are divided as follows:

- (1) Demographics, including information on age, ethnicity, height, weight, education, marital status, menstruation, fertility status, and chronic disease history.
- (2) Breast disease history, which was recorded based on self-report from participants (including benign breast disease, breast cancer, and breast discomfort).
- (3) HRT application and cognition (cognition was classified into three categories based on the questionnaire: understand HRT, know the treatment, and also the benefits and risks of HRT; know about HRT, know the treatment but have no accurate understanding of possible benefits and risks about it; and know nothing about HRT, never heard of the treatment before).

The modified Kupperman Index (KI) was also used<sup>9</sup>. The modified KI consists of 13 items, including the 11 items in the original KI<sup>10</sup>, which are sweating/hot flushes, palpitation, vertigo, headache, paresthesia, formication, arthralgia, myalgia (categorized as somatic symptoms), fatigue, nervousness, and melancholia (categorized as psychological symptoms), and two added urogenital symptoms, which are urinary infection and sexual complaints. The same as the original KI, a scale ranging from 0 to 3 points is used to describe the severity of the complaints. The weighting factors of the 11 items are the same as in the original KI, and also the factors

for both urogenital symptoms. The total score sums all items by their weighting factors. A score above 7 indicates MPS.

### Statistical analysis

Categorical data are represented by the number (%), and measurement data are expressed as the mean  $\pm$  standard deviation. Categorical variables were compared by chi-square test; Fisher's exact test was performed when  $>20\%$  of categorical variables had expected numbers  $<5$  for responses. Measurement data were compared by Mann–Whitney *U* test. All statistical assessments were two-sided and assessed at the 0.05 level of statistical significance. Binary logistic regression analysis was conducted to calculate the odds ratios and their associated 95% confidence intervals of factors for medical visits and the use of HRT for menopause symptoms. Statistical analyses were conducted using SPSS statistical software (version 23.0; SPSS, Chicago, IL, USA).

### Results

A total of 8500 samples were distributed, and 8446 questionnaires were collected. The recovery rate of the questionnaire was 99.36%. A total of 2915 questionnaires were excluded (including 379 with incomplete demographic information, 62 incomplete, 28 from women with breast cancer, 1292 from women with breast discomfort but not diagnosed, and 1587 from women with chronic disease histories), and 5531 samples were in the final analysis. The 5531 samples were divided into two groups based on whether there was a history of benign breast disease. One group was the Benign breast disease history group, in which the participants had been diagnosed with a confirmed benign breast disease (the distribution of the confirmed benign breast diseases is shown in Figure 1), and the other was the Control group, in which the participants never had breast discomfort or had been diagnosed with a breast disease.

### Demographics

The demographic characteristics of the participating women are presented in Table 1. Statistical significance for age,

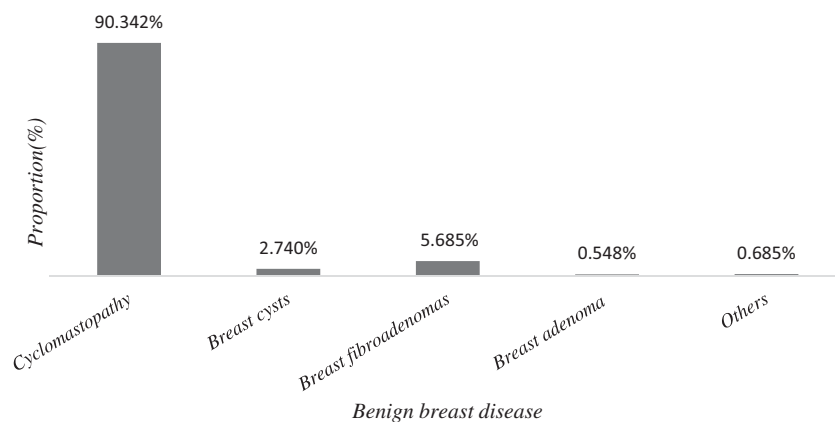


Figure 1. Distribution of benign breast diseases in the participants.

**Table 1.** Demographics of participants stratified with respect to breast disease history.

Characteristic	Benign breast disease history group	Control group	p-value
Sample (number)	1460	4071	
Age (years)	46.05 ± 4.05	46.69 ± 4.41	<0.001
Ethnicity			<0.001
Han people	1385 (94.9%)	3585 (88.1%)	
Minority	75 (5.1%)	486 (11.9%)	
Height (cm)	160.95 ± 4.59	160.35 ± 4.91	<0.001
Weight (kg)	58.92 ± 6.71	58.90 ± 7.30	0.795
Body mass index (kg/m <sup>2</sup> )	22.74 ± 2.35	22.91 ± 2.71	0.121
Education			<0.001
Elementary school and below	324 (22.2%)	2040 (50.1%)	
Secondary	593 (40.6%)	1450 (35.7%)	
College and above	543 (37.2%)	581 (14.3%)	
Marital status			0.586
Married	1412 (96.7%)	3936 (96.7%)	
Unmarried	0 (0.0%)	6 (0.1%)	
Divorced	17 (1.2%)	41 (1.0%)	
Widowed	31 (2.1%)	88 (2.2%)	
Menarche age (years)	14.80 ± 1.72	15.24 ± 1.81	<0.001
Menstrual cycle			<0.001
Regular	245 (16.8%)	900 (22.1%)	
Irregular	749 (51.3%)	2085 (51.2%)	
Menopause	466 (31.9%)	1086 (26.7%)	
Fertility condition			
Number of pregnancies	2.50 ± 1.26	2.47 ± 1.12	0.757
Number of live births	1.59 ± 0.73	2.00 ± 0.85	<0.001
Breastfeeding			0.388
No	76 (5.2%)	189 (4.6%)	
Yes	1384 (94.8%)	3882 (95.4%)	

Data presented as mean ± standard deviation or number (%).

**Table 2.** Kupperman Index and prevalence of menopause syndrome with different breast disease history.

Group	Kupperman Index	Prevalence of menopause syndrome	p-value
Benign breast disease history	14.09 ± 9.44	1119 (76.60%)	0.488
Control	13.83 ± 9.45	3043 (74.70%)	

Data presented as mean ± standard deviation or number (%).

ethnicity, height, education, menarche age, menstrual cycle, and numbers of live births was observed in the two groups ( $p < 0.05$ ).

### Modified Kupperman Index and prevalence of menopause syndrome

The modified KI and prevalence of MPS are presented in Table 2. The two groups showed no statistical significance in the modified KI and prevalence of MPS ( $p > 0.05$ ).

### Medical visits and therapeutic conditions about menopause symptoms

Table 3 shows that the Benign breast disease history group generally had more medical visits for menopause symptoms within half a year than the Control group (16.99% vs. 11.13%). A total of 42.74% in the Benign breast disease history group and 54.54% in the Control group chose other departments than the gynecology and obstetrics department or reproductive center for consulting. Nearly 85% of women in the Control group and 72.19% in the Benign breast disease history group had no knowledge of HRT. In the Benign breast disease history group, 9.86% had applied or were applying HRT for menopause symptoms, whereas only 4.59%

had applied or were applying in the Control group. Statistical significance in all of these items was shown between the two groups ( $p < 0.05$ ). Most women had received information about HRT from physicians (56.22% and 59.31%, respectively), and the two groups showed no statistical significance in the method of obtaining HRT information.

### Factors for medical visits and the use of HRT because of menopause symptoms

According to binary logistic regression analysis, age and benign breast disease history were correlated with medical visits and HRT application because of menopause symptoms. The model also suggested that ethnicity and education were associated with the HRT application but not with medical visits for menopause symptoms. Marital status was proven not correlated with either medical visits or HRT application in the analysis (see Tables 4 and 5).

## Discussion

The 2011 Stages of Reproductive Aging Workshop (STRAW + 10) updated the criteria for the nomenclature and staging system for ovarian aging in 2001 based on the research

**Table 3.** Medical visits and therapeutic conditions about menopause symptoms stratified with respect to breast disease.

	Benign breast disease history group	Control group	$\chi^2$	p-value
Visited for menopause symptoms within half a year	248 (16.99%)	453 (11.13%)	33.328	<0.001
Medical department			7.399	0.025
Reproductive center	2 (0.81%)	7 (1.55%)		
Gynecology and obstetrics	140 (56.45%)	208 (45.92%)		
Others	106 (42.74%)	238 (52.54%)		
HRT cognition			116.960	<0.001
Understand HRT	134 (9.18%)	195 (4.79%)		
Know about HRT	272 (18.63%)	417 (10.24%)		
Know nothing about HRT	1054 (72.19%)	3459 (84.97%)		
HRT application			53.036	<0.001
Applied or in applying	144 (9.86%)	187 (4.59%)		
Unapplied	1316 (90.14%)	3884 (95.41%)		
The way to get HRT information			3.413	0.491
Television or other media	17 (9.19%)	30 (12.99%)		
Internet	17 (9.19%)	20 (8.66%)		
Books	29 (15.68)	27 (11.69%)		
Friends	18 (9.73%)	17 (7.40%)		
Physicians	104 (56.22%)	13 (59.31%)		

Data presented as mean  $\pm$  standard deviation or number (%). HRT, hormone replacement therapy.

**Table 4.** Binary logistic regression analysis of factors for medical visits because of menopause syndrome.

	Odds ratio (95% confidence interval)	p-value
Age (years)	1.05 (1.033–1.073)	<0.001
Ethnicity		
Han people	1	
Minority	1.14 (0.854–1.523)	0.368
Education		0.194
Elementary school and below	1	
Secondary	0.83 (0.662–1.037)	
College and above	0.95 (0.765–1.177)	
Marital status		0.919
Married	1	
Unmarried	1.13 (0.651–1.973)	
Divorced	<0.00 (<0.000)	
Widowed	1.38 (0.561–3.414)	
Benign breast disease history		<0.001
No	1	
Yes	0.63 (0.523–0.746)	

**Table 5.** Binary logistic regression analysis of factors for hormone replacement therapy application.

	Odds ratio (95% confidence interval)	p-value
Age (years)	1.04 (1.014–1.070)	0.003
Ethnicity		0.007
Han people	1	
Minority	0.60 (0.409–0.869)	
Education		<0.001
Elementary school and below	1	
Secondary	0.14 (0.093–0.196)	
College and above	0.60 (0.467–0.772)	
Marital status		0.992
Married	1	
Unmarried	1.12(0.477–2.622)	
Divorced	<0.00 (<0.000)	
Widowed	1.22 (0.348–4.287)	
Benign breast disease history		<0.001
No	1	
Yes	0.64 (0.502–0.809)	

progress of 10 years, and refined the reproductive aging stage (divided into  $-5$ ,  $-4$ ,  $-3b$ ,  $-3a$ ,  $-2$ ,  $-1$ ,  $+1a$ ,  $+b$ ,  $+1c$ ,  $+2$ ), in which stage 2 to stage 1a correspond to perimenopause, suggesting that these stages are the most likely to be related to menopause symptoms<sup>11</sup>. As women approach reproductive senescence, they must face problems

caused by physiologic changes of the menopausal transition, and women who have a history of benign breast disease are in the same situation. Unlike breast cancer, little concern is given to menopause symptoms occurring in women with a history of benign breast disease. This study analyzed the prevalence of MPS, medical visits, and therapeutic conditions about menopause symptoms, and knowledge regarding HRT in midlife women with a benign breast disease history.

Findings from previously published studies revealed that a very high percentage (>90%) of women experienced some form of menopause symptoms<sup>12,13</sup>. This study indicates that the prevalence of MPS in women with a history of benign breast disease was 76.6% and had no statistical significance with the Control group. Shea<sup>14</sup> reported significantly lower prevalence rates for menopause symptoms in a population of Chinese women aged between 40 and 60 years, suggesting that the statistical significance is associated with their positive, neutral, or ambivalent attitudes toward menopause. A study of southern Chinese women also pointed out that the prevalence of menopausal symptoms is lower, at 77.2%<sup>15</sup>. We observed a relatively lower prevalence in this study too; besides the reason mentioned by Shea's report of attitudes<sup>14</sup>, the study population and the inclusion criteria may cause the difference, because the prevalence of MPS can be affected by socioeconomic and educational factors of the population surveyed<sup>15</sup>. Also, the range of age differs in many of the presented studies, which may also lead to the difference.

For medical visits and therapeutic conditions about menopausal symptoms, it was found that only 16.99% in the Benign breast disease history group and 11.13% in the Control group attended for menopausal symptoms within half a year, and only 9.86% in the Benign breast disease history group and 4.59% in the Control group had applied or were applying HRT. This is sharply lower than the percentage reported in previous studies<sup>16–18</sup>. Although the percentages of the two groups were both at low levels, it seems that the women with a history of benign breast disease were more likely to have medical visits, more informed of the treatment options available, and more likely to start HRT.

The Asian Menopause Survey has argued that the low prevalence of the application of HRT in China can be attributed to a general lack of knowledge regarding treatment<sup>17</sup>. It seems this is true from the present study. This survey showed that 72.19% in the Benign breast disease history group and 84.97% in the Control group had known nothing about HRT. Regarding the method of obtaining HRT information, the result of this study is not consistent with the previously published results, in which obtaining HRT information was primarily by way of magazines/newspapers or the other mass-media communication<sup>16,19</sup>. Here, most women either in the Benign breast disease history group (56.22%) or the Control group (59.31%) primarily obtained HRT information from physicians. Nevertheless, it is noteworthy that the education level of the participants here had an effect on their use of HRT (the higher educated were more inclined to accept HRT treatment) but did not affect their medical visits for menopausal symptoms.

Also, the binary logistic regression analysis also suggested that a benign breast disease history is an independent factor affecting medical visits and the application of HRT. This is probably because women in the Benign breast disease history group are more likely to have medical counsel than those in the Control group. Some studies have reported that breast cancer was considered a major risk for HRT by the interviewees<sup>16,20</sup>. However, in 2011, the International Menopause Society updated its recommendations for postmenopausal hormone therapy and middle-aged health prevention strategies, upholding a rational attitude to the relationship between HRT and breast cancer<sup>21</sup>. In 2013, the International Menopause Society also highlighted that the risk of breast cancer associated with menopausal hormone therapy is small, lower than the risk associated with common lifestyle factors<sup>22</sup>. However, arguments remain on the standards for application of HRT.

## Conclusions

This study revealed that, just as in the general population, most women with a history of benign breast disease experience menopausal symptoms when they show reproductive senescence, and only a few of them made medical visits or were treated. However, compared with the general population, those with a history of benign breast disease seem to be more informed of the treatment options available, and more likely to start HRT.

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