Biopsychosocial risk factors of depression during menopause transition in southeast China

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Research Article

Keywords: Depression, Menopausal symptom, Menopause transition, Risk factors

Posted Date: November 15th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-1069440/v1

Abstract

Objective

More than 2 billion women experiencing menopause transition in China and some of them suffered depression; while the risk factors of depression are still unclearin China. We aimed to investigate the risk factors in mid-life women in Southeast China.

Method

This study included 1748 Chinese women aged 40 to 65 years who visit gynecology outpatient department of Women's hospital School of Medicine, Zhejiang University during 2010 to 2018. Demographic information was collected, and the modified Kupperman Menopausal Index (mKMI) and Hamilton Rating Scale for Depression were assessed. Circulating levels of sex hormones were obtained. Ordinal logistic regression analysis was performed to identify risk factors for depression.

Results

The prevalence of depression symptoms was 47.43%. The majority of women had mild (38.56%) or moderate depression symptoms (8.00%); only 0.86% had severe depression. Compared with perimenopausal women, postmenopausal women had increased risks of depression. The associations between menopausal syndromes and depression were strongly positive (OR 6.69, 95% CI 5.39–8.29). Women with older age, higher follicle stimulating hormone levels, lower estradiol levels, and fewer parity had increased risk of depression. Among postmenopausal women, underweight, mKMI > 14, earlier age at menopause, shorter reproductive period, and longer duration after menopause were risk factors for depression.

Conclusions

The results demonstrated a high proportion of depression in women complaining of menopause. Menopausal symptoms were strongly related to the risk of depression. In postmenopausal women, estrogen related events are associated with depression. Gynecological endocrinologists in China should consider screening for depression in high-risk women.

Introduction

In 2019, more than 95 million Chinese people sufffered from depression, 65% of them are female.[1] Worldwide epidemiological studies consistently showed that women had a two-times increased risk of depressive disorders compared with men. The risk is especially pronounced at life stages with sex hormones fluctuations, such as the postnatal period and the menopause transition.[2] Recent results of the Study of Women's Health across the Nation Mental Health Study (SWAN MHS) showed a three-fold increased risk for the development of major depression during the late perimenopausal or postmenopausal period compared with the pre- or early perimenopausal period.[3] China is an ageing scoiety, according to WHO statistics, there were 160 million postmenopausal women in China in 2010, and the number of postmenopausal women will reach 280 million by 2030. The incidence of depressive symptoms in postmenopausal transitional has increased significantly. Thus, recognizing depressive symptoms and disorders at an early stage is very important for the management of menopause transition in China.

Numerous studies have shown a wide range of risk factor domains for depressive symptoms and disorders during the menopause transition, including demographic factors(age, The body mass index (BMI) unemployment, financial problems,), health factors(history of depressive disorders), psychosocial factors(upsetting life events,anxiety and depressive symptoms,), hormonal levels(higer follicle stimulating hormone (FSH), luteinizing hormone (LH) and estradiol (E2) level) and menopausal symptoms(vasomotor symptoms, night sweats, increased number of bothersome symptoms).[4, 5, 6] Recently, several studies were conducted to determine whether hormone-related events, such as duration of estrogen exposure years, reproductive events, and breast feeding history were related to the risk of depression during menopause transition.[7, 8] However, data on most of these associations are limited and controversial.

In the present study, we aimed to investigate the severity of depression among women experiencing menopause transition and analyze the relationships between demographic characteristics, menopausal symptoms, hormone levels, and depressive symptoms, and further reveal the risk factors for depression. Our findings are expected to help health care providers, especially the gynecological endocrine doctors, to recognize menopausal depressive disorders in the early stage, which, in turn, will be beneficial to improve public health management in China.

Methods

Participants

Subjects were recruited from the gynecology outpatient department of **** between March 2010 and December 2018. Patients who visited the outpatient clinic either because complains about changes in their menstrual cycle or other symptoms related to menopause were asked to provide informed consent for the study. The following inclusion criteria were applied: (1) Aged between 40 and 65; (2) a perimenopausal or postmenopausal status. Women with any of the following conditions were excluded: (1) Patients with a history of mental diseases or the use of antipsychotic drugs; (2) History of sex steroids or oral contraceptives use within the preceding 6 months; (3) History of hysterectomy or oophorectomy; (4) History or evidence of uncontrolled hypertension, diabetes,

cardiovascular disease, untreated thyroid disease, renal insufficiency, liver disease, life threatening disease, history of thrombosis, breast cancer, and inability to participate.

The ethical committee of the **** approved this study.

Demographic data

Demographic and clinical data including age, residence, academic education, monthly income, parity, times of abortion, age at menarche, age at menopause(for postmenopausal women) and chronic health problem were collected by trained interviewers. The reproductive period was calculated as age at menopause minus the age at menarche; the duration after menopause was calculated as monthes between date at visit and the date at menopause. The body mass index (BMI, kg/m^2) was calculated and classified according to the Chinese World Health Organization criteria: underweight, BMI＜18.5; normal, 18.5≤BMI＜24; overweight, 24≤BMI＜28; obesity, BMI≥28.

Assessment of theHamilton Rating Scale for Depression (24-items) (HAM-D24)

The patients were estimated for depressive symptoms and severity using HAMD-24, which contains 24 items (10 items scored from 0 to 2, and 14 items scored from 0 to 4) A total score in range of 0 to 8, 9 to 19, 20 to 34, and ≥ 35 were considered as an indication of non-depression, mild, moderate, and severe depression, respectively.

Factors as menopausal symptoms and sex steroid concentrations

We made a diagnosis of perimenopausal or postmenopausal status according to the 2012 Stages of Reproductive Aging Workshop (STRAW) criteria.[9]

Menopausal symptoms were assessed using the modified Kupperman Menopausal Index score (mKMI)[10].

For women with no menstruation, blood samples were collected for hormone tests. Women who still had an identifiable menstrual cycle were asked to undergo hormone tests on the second day of the cycle.The sample was collected from each subject the next morning between 8 and 11 am after overnight fast. Levels of E2, progesterone (P), testosterone (TE), LH and FSH were estimated by ELISA with Roche Modular E170 Analyser, Berlin, Germany. To analyze E2, there was a lower limit of detection of 18.35 pmol/L

Statistical analysis

Continuous variables with a normal distribution were presented as the mean ± standard deviation and we used one-way analysis of variance (ANOVA) for comparisons Categorical variables are presented as frequency and proportions and compared using chi-squared tests. Ordinal logistic regression analyses with depression as the outcome were conducted. The estimates of logistic regression are presented as odds ratios (ORs) and 95% confidence intervals (CIs). In the categorical analyses for E2, for which there was a limitation of detection, women with E2≤18.35 pmol/L were categorized separately and the remaining women were divided into two groups by median values with the highest E2 group as the reference category. For categorical analyses of other sex steroids, measurements were divided into four groups according to the quartile distribution of each steroid serum level with the lowest fourth as the reference category.

SPSS 23.0 for Windows (IBM Corp., Armonk, NY, USA) was used for all statistical analyses with $p<0.05$ as statistically significant.

Results

General characteristics of the participants

The general characteristics of participants are summarized in Table 1. A total of 1,748 women were recruited, with a mean age of 48.56 ± 4.60 years. Most of them were perimenopausal (66.36%), living in urban areas (83.52%), employed (73.34%), and highly educated (32.84% with high school and 45.14% with college and above). The mean BMI was 22.19 ± 3.45 kg/m^2, and 69.91% of them were considered as normal. Only 4.17% of the study group had chronic health problems. Age, age at menarche, personal income per month, employment status, and depression status were significantly different among women with different menopausal statuses ($P < 0.05$) (Table 1).

Table 1
General characteristics of participants

Variable	ALL	Menopausal status		P
		Perimenopausal	Postmenopausal	
	n=1748	n=1160	n=588	
Age (n, %)				
40-49	1040(59.50)	863(74.40)	177(30.10)	
50-59	685(39.19)	297(25.60)	388(65.99)	
≥60	23(1.32)	0	23(3.91)	
Age (years, mean, SD)	48.56±4.60	47.89±6.34	51.65±4.52	<0.001
Residence(n, %)				
Urban	1460(83,52)	960(82.76)	500(85.03)	
Rural	288(16.48)	200(17.24)	88(14.97)	
Education level(n, %)				0.264
Under high school	385(22.02)	246(21.21)	139(23.64)	
High school	574(32.84)	362(31.21)	212(36.05)	
College and above	789(45.14)	552(47.58)	237(40.31)	
Employment status(n, %)				<0.001
Employed	1282(73.34)	943(81.29)	339(57.65)	
Unemployed or retired	466(26.66)	217(18.71)	249(42.35)	
Personal income per month(yuan)(n, %)				0.004
<2000	249(14.25)	166(14.31)	83(14.12)	
2000-5000	791(45258)	494(42.59)	297(50.51)	
>5000	708(40.50)	500(43.10)	208(35.37)	
BMI(n, %)				0.38
Underweight (<18.5 kg/m2)	102(5.83)	76(6.55)	31(5.27)	
Normal (18.5~24 kg/m2)	1222(69.91)	809(69.74)	412(70.07)	
Overweight (24~28 kg/m2)	282(16.13)	189(16.29)	94(15.99)	
Obesity (≧ 28 kg/m2)	55(3.15)	32(2.76)	23(3.91)	
Missing	87(4.98)	54(4.66)	28(4.76)	
Past medical history(n, %)				0.752
High blood pressure	35(2.00)	24(2.07)	11(1.87)	
Diabetes Mellitus	10(0.57)	5(0.43)	5(0.85)	
Cancer	28(1.60)	6(0.52)	9(1.53)	
Times of abortion(n, %)				0.221
N=0	427(24.43)	276(23.79)	147(25)	
1≤N≤2	1012(56.75)	667(57.5)	326(55.44)	
N≥3	334(18.82)	217(18.71)	115(19.56)	
Parity(n, %)				0.678
N=0	154(8.81)	102(8.79)	51(8.67)	
N=1	1384(79.18)	924(79.66)	462(78.57)	
N≥2	210(12.01)	134(11.55)	75(12.76)	
Age at menarche(years, mean, SD)	14.54±1.58	14.46±1.54	14.70±1.65	0.003
Age at menopause(years, mean, SD)			48.10±3.82	

Variable	ALL	Menopausal status		P
		Perimenopausal	Postmenopausal	
	n=1748	n=1160	n=588	
Reproductive period(years, mean, SD)			33.38±3.77	
Duration after menopause (years, mean, SD)			3.62±2.86	
Depression status(HAMD scores,n, %)				<0.001
Non-depression (<8)	919(52.57)	653(56.29)	266(45.24)	
Mild depression (8-19)	674(38.56)	428(36.90)	246(41.84)	
Moderate depression (20-34)	140(8.00)	75(6.47)	65(11.05)	
Severe depression (≥35)	15(0.86)	4(0.34)	11(1.87)	

Assessment Of Depression

The mean HAMD score was 9.06 ± 7.44, and only 52.57% of the participants were considered as non-depressed (HAMD-24 less than 8). The majority of women with depression had mild (38.56%) or moderate symptoms (8.00%), only 0.86% had severe depression (Table 1). Age, employment status, menopausal status, personal income per month, and education were significantly different among women with different depression severities (P < 0.05).

Menopausal Syndrome And Depression

The mean mKMI score was 15.10 ± 9.24. The mean mKMI score of 919 patients of Non-depressiion group was 10.81 ± 6.42, the mean mKMI score of patients with mild, moderate and severe depressive symptoms was 18.76 ± 8.11, 24.62 ± 11.17 and 35.53 ± 13.57, respectively. The percentage of mKMI positive (mKMI > 14) individuals was significantly different among depression subgroups (P < 0.001). Significantly difference was obervesed in mKMI score between the depression groups (Table 2).

Table 2
Prevalence of menopausal symptoms according to the modified Kupperman Menopausal Index by HAMD depression degrees

	Non-depression (<8)		Mild depression (8-19)		Moderate depression (20-34)		Severe depression (≧35)		P^a	P^b
	n=921		n=672		n=140		n=15			
	Mean(SD)	Positive n(%)	Mean(SD)	Positive n(%)	Mean(SD)	Positive n(%)	Mean(SD)	Positive n(%)		
Hot flashes/sweating	3.35(3.34)	546(59.41)	4.72(3.68)	494(73.29)	5.62(3.95)	111(79.29)	6.67(3.9)	13(86.67)	<0.001	<0.001
Insomnia	1.3(1.36)	504(54.84)	2.38(1.69)	546(81.01)	3.05(1.81)	126(90.00)	4.13(2.2)	13(86.67)	<0.001	<0.001
Mood swings	1.25(1.39)	476(51.80)	2.28(1.62)	538(79.82)	2.97(1.88)	117(83.57)	4.53(2.07)	14(93.33)	<0.001	<0.001
Melancholia	0.25(0.49)	201(21.87)	0.74(0.74)	384(56.97)	1.32(0.92)	111(79.29)	2.07(1.03)	13(86.67)	<0.001	<0.001
Sexual problems	1.46(1.45)	550(59.85)	2.22(1.65)	539(79.97)	2.62(1.89)	117(83.57)	3.6(2.53)	12(80.00)	<0.001	<0.001
Muscle/joint pain	0.58(0.69)	432(47.01)	1.00(0.83)	464(68.84)	1.06(0.93)	97(69.29)	1.27(1.22)	9(60.00)	<0.001	<0.001
Vertigo	0.32(0.52)	273(29.71)	0.67(0.71)	366(54.30)	0.94(0.91)	92(65.71)	1.53(1.25)	11(73.33)	<0.001	<0.001
Fatigue	0.56(0.6)	462(50.27)	1.04(0.68)	552(80.90)	1.28(0.9)	116(82.86)	1.93(1.16)	13(86.67)	<0.001	<0.001
Headaches	0.34(0.54)	285(31.01)	0.62(0.71)	340(50.45)	0.85(0.83)	88(62.86)	1.33(1.23)	10(66.67)	<0.001	<0.001
Formication	0.27(0.78)	112(12.19)	0.59(1.17)	159(23.59)	1.2(1.58)	63(45.00)	1.73(2.12)	8(53.33)	<0.001	<0.001
Urinary tract infection	0.43(1.07)	154(16.57)	0.88(1.41)	230(34.12)	1.08(1.66)	53(37.86)	2(2.39)	8(53.33)	<0.001	<0.001
Palpitations	0.37(0.58)	305(33.19)	0.75(0.74)	402(59.64)	0.97(0.8)	102(72.86)	1.67(0.9)	14(93.33)	<0.001	<0.001
Paresthesia	0.33(0.93)	117(12.73)	0.96(1.45)	231(34.27)	1.66(1.69)	79(56.43)	3.07(1.83)	12(80.00)	<0.001	<0.001
mKMI total score	10.81(6.42)	877(95.43)	18.78(8.11)	667(98.96)	24.62(11.17)	133(95.00)	35.53(13.57)	15(100)	<0.001	<0.001
a P-value for comparison of severity of menopausal syndromes in each depression subgroup										
b P-value for comparison of prevalence of menopausal syndromes in each depression subgroup										

Sex Steroids And Depression

Table 3 shows the E2 and FSH serum levels according to the categorical distribution of depression The mean value of serum E2 was 82.45 ± 137.97 (pmol/L). The population was divided into three groups as T1 (≤18.35), T2(18.35<E2≤62.16), T3 (E2>62.16). A significant decrease in the severity of depression was observed with increasing category of serum estradiol level(Table 3).

Table 3
Estradiol and FSH serum levels according to the categorical distribution and depression cross-tabulation.

	Non-depression (<8)	Mild depression (8-19)	Moderate depression (20-34)	Severe depression (≥35)	P
E2 (pmol/L)(N,%)					<0.001
T1(E2 ≤18.35)	351(40.91)	263(42.15)	69(53.08)	10(83.3)	
T2(18.35<E2≤62.16)	237(27.62)	193(30.93)	38(29.23)	2(16.7)	
T3(E2>62.16)	277(32.28)	168(26.92)	23(17.69)	0(0)	
Total	858	624	130	12	
FSH (IU/L)(N,%)					0.059
Q1(FSH<40)	140(16.28)	70(11.11)	13(10.0)	0(0)	
Q2(40≤FSH<80)	418(48.60)	326(51.75)	62(47.692)	5(41.67)	
Q3(80≤FSH<120)	251(29.19)	188(29.84)	48(36.924)	6(50.00)	
Q4(FSH≥120)	51(5.93)	46(7.30)	7(5.39)	1(8.33)	
Total	860	630	130	12	

The mean value of serum FSH level was 72.53 ± 35.63 (IU/L). The population was divided into four groups according to the FSH serum levels as Q1 (0≤FSH≤40), Q2 (40<FSH≤80), Q3 (80<FSH≤120), Q4 (FSH>120). No significant differences in the severity of depression were found in each FSH category (Table 3).

No significant associations were observed between depression and P(P=0.359), TE（P=0.404）, and LH（P=0.625）levels.

Factors Associated With Intensity Perimenopausal Depression

Ordinal logistic regression analyses were performed to investigate independent factors associated with the intensity of depression (Table 4).

Table 4
Multivariable logistic regression analyses for factors associated with depression according to the HAMD

Population	Risk factor	OR	95% CI	P
Total	Age[a]	1.04	1.01-1.06	0.004
	Underweight[a]	1.51	1.01-2.25	0.042
	Postmenopause[a]	1.34	1.07-1.69	0.012
	Parity(0)[a]	1.47	1.01-2.13	0.044
	Parity(≥2)[a]	0.72	0.53-0.97	0.033
	mKMI>14	6.69	5.39-8.29	<0.001
	E2 T1:T3	1.35	1.06-1.73	0.016
	E2 T2:T3	1.36	1.07-1.77	0.012
	FSH Q4:Q1	1.62	1.00-2.62	0.048
	FSH Q3:Q1	1.6	1.15-2.23	0.005
	FSH Q2:Q1	1.44	1.06-1.97	0.022
Postmenopausal	Underweight	2.19	1.04-4.57	0.038
	mKMI>14	6.18	4.25-8.98	<0.001
	Age at menopause	0.93	0.87-0.99	0.027
	Reproductive period	0.93	0.87-1.00	0.04
	Duration after menopause	1.08	1.01-1.16	0.03
Perimenopausal	Age	1.04	1.00-1.07	0.041
	Residence in rural area	1.46	1.03-2.07	0.03
	Parity(0)	2.09	1.33-3.27	0.001
	Parity(≥2)	0.66	0.44-0.98	0.042
	mKMI>14	7.22	5.52-9.45	<0.001

Values are presented as OR (95% CI).Adjusted for Age, place of residence, level of education, employment,income, parity, times of abortion, age at menarche and BMI.

CI=confidence interval, OR=odds ratio.

Age, menopausal status, parity, mKMI score, serum E2, and FSH levels were significantlycorrelated with the intensity of depression. Compared with perimenopausal women, women in the postmenopausal stages had a significantly increased risk of depression (OR 1.34, 95% CI 1.07–1.69). Women who had never given birth to a child had an increased risk of depression (OR 1.47, 95% CI 1.01–2.13), while women with parity of more than two were less likely to suffer from depression than women who had only one parity (OR 0.72, 95% CI 0.53–0.97). A nearly six times increased risk was observed in women with a mKMI score more than 14 (OR 6.69, 95% CI 5.39–8.29).

A significant negative association was found between circulating E2 levels and the intensity of depression. The severity of depression was decreased in participants with higher levels of estradiol (T1:T3 OR 1.35,95%CI 1.06~1.73;T2:T3 1.36，95%CI 1.04~1.78，P=0.016). For FSH analyses, the opposite result was observed, serum FSH level was positive related to the severity of depression (Q4:Q1 OR 1.62，95%CI 1.00~2.62，Q3:Q1 OR 1.60，95%CI 1.15~2.23，Q2:Q1 OR 1.44，95%CI 1.06~1.97，P =0.022).

For postmenopausal women, we also collected the reproductive period, age at menopause, and duration after menopause as hormone-related events. The results supported protective effects of later menopause (OR 0.93, 95% CI 0.87–0.99), longer reproductive period (OR 0.93, 95% CI 0.87–1.00), and a potential harmful effect of duration after menopause (OR 1.08, 95% CI 1.01–1.16) on the risk of depression after menopause. Consistent with the whole population, underweight (OR 2.19, 95% CI 1.04–-4.57) and mKMI > 14 (OR 6.18, 95% CI 4.25–-8.98) were also potential risk factors of depression in postmenopausal women.

In the perimenopausal women, age, residence in a rural area, parity, and mKMI score were significantly associated with depression and an mKMI > 14 (OR 7.22, 95% CI 5.52–-9.45) was strongly associated with depression as well.

The analyses showed storng associations between mKMI score and the severity of depression. Concerning there were some overlaping symptoms between mKMI and HAMD scales, we did the analysis of each menopausal symptoms in the mKMI scale sepreately. All the 13 symptoms were significantly related with the severity of depression. Except the melancholia,the most related symptoms are fatigue (OR 3.09, 95% CI 2.68-3.56), vertigo (OR 2.62, 95% CI 2.27-3.02), palpitations (OR 2.51, 95% CI 2.19-2.88) and headaches(OR 2.19, 95% CI 1.90-4.52) (Supplementary Table 1) .

Discussion

In the present study, we explored the risk factors associated with depression among women who have menopausal symptoms in southeast China. We found that nearly half of the participants who visit the gynecology clinic (47.43%) had depression. The majority of women with depression had mild (38.56%) or moderate symptoms (8.00%), and only 0.86% had severe depression. Compared with perimenopausal women, postmenopausal women had increased risks of depression. The relationships between menopausal syndromes and depression were strong and positive. Women with older age, higher serum FSH levels, lower serum E2 levels, and fewer parity had an increased risk of depression.

In this hospital-based study, a relatively higher prevalence of depression (47.75%) was found in middle-aged women compared with other studies conducted in China (11.4–36.3%).[1, 11, 12] This might be explained by the fact that most of our participants had complaints about menopause, which may have increased the risk of depression in this population.[12] Our findings suggested a positive relationship between age and depression during menopausal transition, which is consistent with previous studies in China. [1] Several studies stated that poor general health status of older women mighty contribute to this relationship.[1] However, in our study, most of the participants had good health status (95.83% did not have disease history), which suggested that the higher prevalence of depression in older women is mainly caused by the physiological and psychological changes during menopause transition.

In our study, we found strong positive correlations between menopausal symptoms (measured by mKMI) and depression. Certain menopausal complaints co-occur and overlap with the presentation of mood disturbances during this stage. The associations between menopausal symptoms and depression had been reported by several studies.[11- 13] However, most studies focused on vasomotor symptoms (VMS), sleeping difficulties or other symptoms separately.[12, 13] Our result showed that not only VMS and sleeping difficulties, but also the other menopausal symptoms are associated with depression in this period, and women with elevated mKMI scores had a nearly six times higher risk of developing depression during the menopause transition and the most related symptoms are fatigue, vertigo, palpitations and headaches.

The association between menopause status and depression has been studied extensively, positive corelations between perimenopause and depression have been observed in both cross-sectional studies and longitudinal studies. For example, a meta-analysis reported that the odds of the presence of depressive symptoms during the perimenopause were doubled when compared with those for premenopausal women; however, the analysis comparing the occurrence of depressive symptoms in the perimenopause versus that in the postmenopause revealed negative results.[14] By contrast, our results showed a 37% increased risk for developing depression in postmenopausal women compared with perimenopausal women. A possible explanation for the inconsistent results is that most of the postmenopausal women in our study were in the early postmenopausal stage and had complained of menopausal symptoms; thus, these women experienced a longer period with unpleasant feelings, which may led to more depression symptoms.

The relationship between body mass index (BMI) and depression during the menopause transition is controversial. Several studies indicated associations between overweight, obesity and depression[15, 16], while others did not[11]. Studies of BMI and depression in general Asian populations had reported a U-shaped pattern of relationship with BMI categories[17]. Our study also indicated a higher risk of depression in underweight women compared with women with a normal BMI. However, we did not find a significant correlation between overweight, obesity and depression, which could be explained by the fact that our population was generally healthy, and chronic diseases were rare, even in the obesity women.

Estrogen exposure may influence women's risk of depression;[18] therefore, we analyzed the effect of hormone-related events on the risk of depression. The majority of our participants were perimenopausal women who still underwent menstruation; therefore, we collected data concerning parity, times of abortion, and age at menarche in the whole population. The results only supported a protective effect of more parity to the risk of depression during the menopause transition, which is consistent with the results from some previous studies.[19, 20]

In postmenopausal women in whom menstrual events reflect endogenous hormone exposure, clinical and epidemiologic data support a protective role for a longer estrogen exposure period in mood disorders.[18, 21] Consistent with these studies we observed a protective effect of longer reproductive period and later age at menopause to the risk of depression after menopause. Interestingly, in our study, longer duration after menopause was found to have a harmful effect after adjusting for demographic variables. Previous studies examining this association in postmenopausal women are scarce, only one American cohort study recruiting 203 women evaluated the depressive symptoms around natural menopause and indicated a decrease of approximately 15% of baseline per year of the CES-D score.[22] As in our study, the negative association of duration after menopause and depression might be an indirect indication of the early use of HRT after menopause to prevent depression, which was proven by a recent clinical trial.[23] However, because of the limited proof, further studies should be conducted to discuss the development of depression after menopause.

Numerous studies on animals and cells demonstrated a beneficial effect of estrogen on mood. Epidemiological studies found heterogeneous results, lower serum levels of E2[25, 26] and higher levels of FSH[5, 24] have been associated with depressive symptoms in perimenopausal and postmenopausal women. However, other studies found no relation between estrogen or FSH levels and mood or depression.[26, 27] Meanwhile, some investigators identified that fluctuations in estrogen levels over time were more closely linked to depression than absolute hormone levels.[28, 29] Our results suggested women with a higher level of serum E2 and lower serum FSH had lower risk of depression. Together with our findings of the associations between depression and hormone-related events, our results support the view that more estrogen exposure decreased the risk of depression in midlife women in China.

This study has several strengths. First, our study is one of the few studies to show the risks of the depression during the menopausal transition in southeast China. Second, this was the first study to comprehensively measure the demographic, symptomatic, and hormonal risk factors of the depression, as well as historical events in Chinese population. Third, some important new findings were revealed, including the association between the mKMI score, duration after menopause, and the risk of depression. Further, our study showed a relatively high prevalence of depression in women who have complaints about menopause; therefore, gynecologists as the first health care providers for these women in China should not only focus on the treatment of menopausal

symptoms, but also be concerned about the mental state of the patients. Thus screening for depression during consultations with mid-life women with menopausal symptoms should be considered for the early detection and prevention of depressive disorders.

While, there are several limitations of the present study. First, our findings were based on a cross-sectional study; therefore, we can only report the potential risk factors of depression and causal inferences could not be made. Second, some the data were collected by self-reporting. This could lead to inaccurate information such as childbearing history and menstrual history, which occurred many decades before. However, a high degree of accuracy has been reported for women recalling their reproductive events.[30] Third, our population was hospital based, which may have caused selection bias. Further population-based studies and meta-analyses are expected to minimize bias and systematic error.

Conclusions

The present study showed increased age, lower monthly income, underweight, postmenopause, menopausal by surgery, lower serum level of E2, and higher serum level of FSH were associated with an increased risk of depression, and an increased mKMI score was strongly related with the intensity of depression. An increased number of parities was associated with a reduced risk of depression in Chinese women during menopausal transition.

China is currently an ageing society, with more than 2 billion women experiencing the menopausal transition and this number is expected to increase to 2.8 billion by 2030. Screening for depression in this population is a huge, but necessary, task. The results of the present study might be helpful to improve clinical management and public health programs to prevent and detect depression in the very early phase in high-risk women.

Abbreviations

mKMI: Kupperman Menopausal Index ; HAMD-24: 24-item Hamilton Rating Scale for Depression; SWAN MHS: Study of Women's Health across the Nation Mental Health Study; E2:estradiol; P: progesterone; TE:testosterone; LH: luteinizing hormone; FSH: follicle stimulating hormone; STRAW:2012 Stages of Reproductive Aging Workshop; ANOVA: one-way analysis of variance; OR: odds ratio; CI: confidence interval.

Declarations

Ethics approval and consent to participate

Ethical approval was obtained from the Ethics Committee of Women's Hospital,Zhejiang University School of Medicine. All participating women provided written informed consent for this study. All methods were performed in accordance with the the Declaration of Helsinki.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

This work was supported by the National Natural Science Foundation [grant number: 82003469]; the Zhejiang Provincial Natural Science Foundation of China [grant number: LY18H040003]; and Zhejiang Provincial Natural Science Foundation of China [grant number: LGF20H040009].

Authors' contributions

Dr. Jianhong Zhou and Dr. Fei Ruan designed the project and contributed to the paper writing, Dr. Ketan Chu and Dr. Jing Shui performed data analysis and write the paper, Dr. Linjuan Ma, Dr. Yizhou Huang and Dr. Fan Wu conducted the scale and the interviews, Dr Xingjun Meng and Dr. Jie luo collected the data, Ms. Fang Wei contributed to data processing.

Acknowledgments

We would like to show our great appreciation to Dr Mengling Tang from Department of Epidemiology and Biostatistics, Zhejiang University School of Medicine for her help within the statistics, Chief officer Wenjun Zhu from the Medical-record Department and Shumin Xu from the Zhejiang University Health Care Fund for women for their help with the data management.

Authors' contributions

JHZ and FR designed the project and contributed to the paper writing, KTC and JS performed data analysis and write the paper, LJM, YZH and FW conducted the scale and the interviews, XJM and JL collected the data, FW contributed to data processing.

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