# Level of Psychological and Somatic Symptoms Predict Perimenopausal Syndrome Severity Better Than Obstetric and Psychiatric History Do Among Korean Women

Soyeon Kim<sup>1</sup>, Sun Mi Kim<sup>1</sup>, Da Seul Kim<sup>1</sup>, Seunga Han<sup>2</sup>, Ji Sun Hong<sup>1 ⊠</sup>, and Jeong Seok Seo<sup>1 ⊠</sup>

Department of Psychiatry, College of Medicine, Chung-Ang University, Seoul, Republic of Korea

Objective Menopause symptoms can vary in type, duration, and severity. The purpose of this study was to investigate the key factors predicting severe symptoms among Korean perimenopausal women with various demographic data, obstetric and psychiatric histories, and menopausal symptoms screening scale scores.

Methods Data were collected from 1,060 women, and 4 latent classes were identified using latent profile analysis, with 6 major categories of menopausal complaints. Among the 4 classes, we selectively used data from the "all unimpaired" and "all impaired" groups. Menopause rating scale (MRS), sociodemographic, obstetric, and psychiatric factors were assessed, and hierarchical logistic regression analyses were conducted with the "all impaired" group as a dependent variable.

Results Marital status and scores on the psychological and somatic subscales of the MRS were statistically related to being in the "all impaired" group. Otherwise, family history of menopausal symptoms, menarche age, and history of other psychiatric disorders were not statistically significant predictors of being in the "all impaired" group.

Conclusion The psychological and somatic subscales of the MRS predict the severity of perimenopausal syndrome better than obstetric and psychiatric history do among Korean perimenopausal women. Psychological and somatic symptoms as well as genitourinary symptoms in menopausal patients should be closely evaluated. Psychiatry Investig 2023;20(1):18-26

**Keywords** Perimenopause; Menopause; Somatic symptoms; Psychological factor; Predictor.

# INTRODUCTION

The transition to menopause, perimenopause, is a natural event in every woman's life, led by a progressive decrease in reproductive hormones. By definition, perimenopause is the transitional time around menopause (permanent termination of menstruation) when menstrual periods become irregular before they finally stop. It mostly occurs between 40 and 60 years of age and can last for 2-10 years. 1-5 During peri-

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☑ Correspondence: Ji Sun Hong, MD, PhD

Department of Psychiatry, College of Medicine, Chung-Ang University, 84 Heukseok-ro, Dongjak-gu, Seoul 06974, Republic of Korea

Tel: +82-2-2260-6680, Fax: +82-2-813-5387, E-mail: jisunhong925@cauhs.or.kr

☑ Correspondence: Jeong Seok Seo, MD, PhD

Department of Psychiatry, College of Medicine, Chung-Ang University, 84 Heukseok-ro, Dongjak-gu, Seoul 06974, Republic of Korea

Tel: +82-2-2260-9004, Fax: +82-2-813-5387, E-mail: sjs52632@cauhs.or.kr

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menopause, many women experience physiological and psychological changes, including vasomotor (hot flashes, night sweats), somatic (headaches, joint and muscle aches), cognitive (trouble concentrating, forgetfulness), urogenital (vaginal dryness, frequent voiding, changes in sexual desire), and psychological (insomnia, mood changes, anxiety, irritability) changes.<sup>5-7</sup> Although most symptoms are not fatal, they might affect all aspects of quality of life and have a negative impact on the physical and mental health of perimenopausal women.<sup>8,9</sup>

Perimenopausal symptoms vary in terms of duration, prevalence, and severity. A previous study conducted in the United States found that vasomotor symptoms, one of the primary menopausal complaints for which women seek therapeutic management, 10,111 last for an average of 10 years, 12 with an extended duration in women whose symptoms started earlier.<sup>13</sup> In addition, approximately 75% of women experience varying degrees of menopausal symptoms ranging from mild to very distressing.<sup>14</sup> In general, roughly half of symptomatic women report only mild severity while the other half com-

<sup>&</sup>lt;sup>2</sup>Department of Political Science, Vanderbilt University, Nashville, TN, USA

plain of moderate-to-severe symptoms. 15,16

Previous studies have discovered various risk factors affecting perimenopause symptoms, including ethnicity, socioeconomic features, medical and psychiatric histories, age, obesity, and lifestyles. 13,17-19 Previous multivariable logistic regression analysis revealed that older age, unemployment, irregular menstruation, and constipation were risk factors while a high monthly family income was a protective factor for perimenopausal syndrome.<sup>20</sup> Other studies have also shown that older age, low education level, and history of previous premenstrual syndrome are associated with a high risk of perimenopausal symptoms.21-23

As a screening tool for menopausal women's overall health, the menopause rating scale (MRS) consists of 3 domains of symptoms identified from factorial analysis and statistical methods: psychological, somatic, and urogenital.<sup>24,25</sup> MRS has been used as an efficient screening tool internationally for over 20 years with good validity<sup>26</sup> and was also proven to be useful as a single tool to evaluate the severity of age- or menopause-related complaints among middle-aged women.<sup>27</sup>

Considering the high prevalence, heterogeneity, and negative impact of perimenopause symptoms on women's overall health, there is a growing demand for new evidence regarding the perimenopause period. In this study, we aimed to find the major factors predicting the high-risk group for the severe perimenopausal symptoms among various factors such as sociodemographic, obstetric, and psychiatric factors, and scores on MRS. In addition, we hypothesized that the MRS scale would be the most important predictor among these.

#### **METHODS**

# **Study participants**

This research was part of a cross-sectional study of Korean women aged 40 to 60 years concerning psychosomatic symptoms among Korean perimenopausal women conducted at the Chung-Ang University Hospital, Seoul, Korea. We collected data from 1,060 perimenopausal women through a research company (Macromill Embrain Co., Ltd., Seoul, Korea). To include only perimenopausal women among 40 to 60 years in this study, we recruited those whose last menstrual period was within one year and those whose menstrual cycle had recently become irregular compared to past. Participants' perimenopausal symptoms were evaluated, including overall menopausal symptoms, depression, somatic symptoms, insomnia, memory, sexual dysfunction, and overactive bladder symptoms. Based on this data, we conducted a latent profile analysis as a statistical method, which assumes that the observations are made up of a blend of dissimilar distributions and aims to identify subgroups based on the characteristics of individuals' response patterns and reveal similarities in individuals within groups.<sup>28,29</sup> Using scores of six scales on mood, somatic symptoms, sleep, memory, sexual symptoms, and urinary symptoms, multidimensional psychosomatic symptom profiles were classified according to differences in the level of symptoms and the degree of co-occurrence of symptoms. As a result, 4 latent classes were identified: 1) all unimpaired (class 1, n=530); 2) impaired sexual function, while others are unimpaired (class 2, n=186); 3) unimpaired sexual function, while others are impaired (class 3, n=216); and 4) all impaired (class 4, n=128). That means, class 1 showed lowlevel symptoms on all six scales, with class 4 showed highlevel symptoms on all scales. The statistical analysis method and statistical indices of the latent profile analysis that led to the deduction of the 4 groups were discussed in our previous report.30

In the current study, we selectively used data from the "all unimpaired" group reporting few menopausal symptoms and the "all impaired" group reporting severe menopausal symptoms among the study population. We then investigated the factors predicting the likelihood of being in the "all impaired" group among various factors such as sociodemographic, obstetric, and psychiatric factors, and subscale scores of MRS.

The study protocol was approved by the Chung-Ang University Hospital Institutional Review Board (reference number: 2160-001-464) and written informed consent was provided by all participants.

#### **Measures**

#### **MRS**

The MRS was used to measure health-related quality of life in middle-aged women. 24,31 The MRS consists of 11 questions measured on a 5-point Likert scale, ranging from 0 to 4 points. The scale comprises 3 domains: psychological, somatic, and urogenital. Previously, MRS demonstrated a high level of internal consistency (Cronbach's alpha=0.87).26

# Sociodemographic factors

Sociodemographic factors collected for this study were age, marital status, educational level, job status, and average monthly family income.

# Obstetric factors

Obstetric history collected for this study included premenopausal menstrual cycle regularity, complete menopause status, family history of menopause symptoms, the period from the onset of menopause, menarche age, number of pregnancies, and number of deliveries.

### **Psychiatric factors**

The psychiatric factors investigated for this study included a history of premenstrual syndrome, postpartum depression, postpartum psychosis, and other psychiatric disorders.

# Statistical analysis

The distribution of sociodemographic, obstetric, and psychiatric characteristics across the study population was calculated. For univariate analyses, we used independent t-test and chi-square tests to compare variables between participants in the "all unimpaired" group and "all impaired" group.

To determine the influence of MRS subscales on the severity of perimenopausal symptoms, hierarchical logistic regression analyses were performed. In Model 1, the association between sociodemographic factors and perimenopausal symptoms was tested. Obstetric factors were added to Model 2 to test the associations of obstetric history with sociodemographic factors. Psychiatric factors were added to Model 3 to test the association of psychiatric history beyond the effects of sociodemographic factors and obstetric history. Finally, MRS subscale scores were added to Model 4 to test the association of MRS subscale scores with sociodemographic, obstetric, and psychiatric factors. Statistical significance was set at p=0.05 (two-sided). We used the Complex Samples module of the SPSS Statistics software package, version 19 (IBM Corp., Armonk, NY, USA), to conduct all analyses.

#### **RESULTS**

# The comparison of demographic data, obstetric history, and psychiatric history between the "all unimpaired" group and the "all impaired" group

The distribution of sociodemographic, obstetric, and psychiatric characteristics across the study population is presented in Table 1, and a comparison of these characteristics between the "all unimpaired" group and the "all impaired" group is presented in Table 2. The participants in the "all impaired" group are more likely to live without a partner and have less monthly family income than those in the "all unimpaired" group. In addition, participants in the "all impaired" group are more likely to report a family history of menopause symptoms, older menarche age, and small number of deliveries compared to those in the "all unimpaired" group. Regarding psychiatric history, the participants in the "all impaired" group are more likely to have a history of postpartum psychosis or other psychiatric disorders compared to those in the "all unimpaired" group. The total MRS scores and all 3 subscale scores (psychological, somatic, and urogenital) were higher in the "all impaired" group than in the "all unimpaired" group.

Table 1. The distribution of sociodemographic, obstetric, and psychiatric characteristics of the study population

Variable	Value (N=658)
Age (yr)	46.11±4.05 (40-62)
Marital status	
Living without a partner	109 (16.6)
(single/separated/divorced/widowed)	
Living with a partner	549 (83.4)
(married/in a domestic partnership)	
Education level	
High school graduates or lower	138 (21.0)
College graduates or higher	520 (79.0)
Job status	
Have a job	429 (65.2)
No job	229 (34.8)
Monthly family income	
<4 million won	229 (34.8)
>4 million won	429 (65.2)
Premenopausal menstrual cycle regularity	
Regular	455 (69.1)
Irregular	203 (30.9)
Menopause status	
Completely menopause	56 (8.5)
Irregular but still menstruating	602 (91.5)
FHx of menopause symptoms	
No/Don't know	531 (80.7)
Yes	127 (19.3)
Period from the onset of menopause (mo)	5.53±3.95 (1-12)
Menarche age (yr)	14.22±1.49 (10-20)
Number of pregnancies	1.99±1.26 (0-8)
Number of deliveries	1.64±0.88 (0-4)
Hx of premenstrual syndrome	
Inexperienced	106 (16.1)
Experienced	552 (83.9)
Hx of postpartum depression	
Inexperienced	319 (48.5)
Experienced	339 (51.5)
Hx of postpartum psychosis	
Inexperienced	646 (98.2)
Experienced	12 (1.8)
Hx of other psychiatric disorders	
Inexperienced	642 (97.6)
Experienced	16 (2.4)
MRS_Total	15.94±8.08 (0-40)
MRS_Psychological	6.39±3.64 (0-16)
MRS_Somatic	4.06±2.65 (0-12)
MRS_Urogenital	5.49±3.12 (0-15)

Values are presented as mean±standard deviation (range) or number (%). FHx, family history; Hx, history; MRS, menopause rating scale; MRS\_Psychological, scores of the psychological subscale of MRS; MRS\_Somatic, scores of the somatic subscale of MRS; MRS\_ Urogenital, scores of the urogenital subscale of MRS

Table 2. Comparison of demographic data, obstetric history, and psychiatric history of the "all unimpaired" group and the "all impaired" group

Variable	All unimpaired (N=530)	All impaired (N=128)	$\chi^2/t$
Demographic data			
Age (yr)	46.13±4.03	46.03±4.13	0.254
Marital status			27.502 <sup>‡</sup>
Living without a partner (single/separated/divorced/widowed)	68 (12.8)	41 (32.0)	
Living with a partner (married/in a domestic partnership)	462 (87.2)	87 (68.0)	
Education level			3.892
High school graduates or below	103 (19.4)	35 (27.3)	
College graduates or higher	427 (80.6)	93 (72.7)	
Job status			0.848
With a job	350 (66.0)	79 (61.7)	
Without a job	180 (34.0)	49 (38.3)	
Monthly family income			16.176 <sup>‡</sup>
<4 million won	165 (31.1)	64 (50.0)	
>4 million won	365 (68.9)	64 (50.0)	
Obstetric history			
Premenopausal menstrual cycle regularity			1.927
Regular	373 (70.4)	82 (64.1)	
Irregular	157 (29.6)	46 (35.9)	
Menopause status			0.001
Completely menopause	45 (8.5)	11 (8.6)	
Irregular but still menstruating	485 (91.5)	117 (91.4)	
FHx of menopause symptoms	. ,	` ,	6.600*
Yes	92 (17.4)	35 (27.3)	
No/Don't know	438 (82.6)	93 (72.7)	
Period from the onset of menopause (mo)	5.52±3.94	5.60±4.01	-0.220
Menarche age (yr)	14.16±1.48	14.47±1.52	-2.074*
Number of pregnancies	2.02±1.20	1.88±1.50	1.173
Number of deliveries	1.69±0.85	1.42±0.98	3.071 <sup>†</sup>
Psychiatric history			
Hx of premenstrual syndrome			0.010
Inexperienced	85 (16.0)	21 (16.4)	
Experienced	445 (84.0)	107 (83.6)	
Hx of postpartum depression	(3.13)	(,	0.035
Inexperienced	256 (48.3)	63 (49.2)	
Experienced	274 (51.7)	65 (50.8)	
Hx of postpartum psychosis	2/1(01//)	66 (6010)	11.792 <sup>†</sup>
Inexperienced	525 (99.1)	121 (94.5)	11.772
Experienced	5 (0.9)	7 (5.5)	
Hx of other psychiatric disorders	3 (0.5)	7 (3.3)	19.394 <sup>‡</sup>
Inexperienced	524 (98.9)	118 (92.2)	17.571
Experienced	6 (1.1)	10 (7.8)	
MRS_Total	14.14±7.12	23.38±7.59	-13.005 <sup>‡</sup>
MRS_Psychological	5.60±3.22	9.63±3.50	-13.003* -12.472 <sup>‡</sup>
MRS_Somatic	3.66±2.45	5.71±2.81	-8.241 <sup>‡</sup>
MRS_Urogenital	4.88±2.82	8.04±3.02	-8.241 <sup>+</sup>

Values are presented as mean±standard deviation or number (%). \*p<0.05; †p<0.01; ‡p<0.001. FHx, family history; Hx, history; MRS, menopause rating scale; MRS\_Psychological, scores of the psychological subscale of MRS; MRS\_Somatic, scores of the somatic subscale of MRS; MRS\_Urogenital, scores of the urogenital subscale of MRS

# Results of hierarchical logistic regression analyses of MRS subscale scores with the "all impaired" group as a dependent variable

Table 3 summarizes the results of the hierarchical logistic regression analyses, which tested the association between being in the "all impaired" group and the sociodemographic, obstetrical, and psychiatric factors, and the MRS subscale scores among postmenopausal women. All 4 models of hierarchical logistic regression showed a significant overall model fit. In Analysis Model 4, both model  $\chi^2$  (186.988, p<0.001) and the Nagelkerke R<sup>2</sup> value (0.395, explaining about 39.5% of the variance in the dependent variable) reflected that the analysis model was adequate to account for being in the "all impaired" group. Looking at the practical effectiveness of the model according to classification accuracy, 19 variables in Analysis Model 4 noticeably improved its explanation accuracy to 85.9% for the group membership of the dependent variable. Wald statistics were used to define whether each indicator had a significant individual relationship with being in the "all impaired" group. Among the independent variables, marital status and scores on the psychological and somatic subscales of the MRS were statistically related to being in the "all impaired" group in Analysis Model 4. The marital status and menarche age score were statistically related to being in the "all impaired" group in Analysis Models 2 and 3. In addition, a history of other psychiatric disorders was statistically related to being in the "all impaired" group in Analysis Model 2. However, marital status, age at menarche, and history of other psychiatric disorders were statistically non-significant in Model 4.

# **DISCUSSION**

This study aimed to determine the association between several sociodemographic, obstetric, and psychiatric predictors and perimenopausal symptom severity during perimenopause. The results of logistic regression analyses revealed that marital status and scores on the psychological and somatic subscales of MRS were statistically related to being in the "all impaired" group. Otherwise, family history of menopausal symptoms, obstetric history, and history of other psychiatric disorders were not statistically significant predictors for being in the "all impaired" group.

Between the two groups, the menarche age of the participants in the "all impaired" group was higher than that of the participants in the "all unimpaired" group. In addition, later menarche age as a dependent variable was identified as a significant risk factor before MRS was added to Model 4 in the regression analysis. The age at menarche has been implicated to be associated with disease risk in women in late life. 32-34 Specifically, early age at menarche is associated with risks of hypertension,35 cardiovascular disease,36 endometriosis,37,38 and metabolic disorders.<sup>39</sup> On the other hand, later age at menarche is associated with risks of depression<sup>40</sup> and lower bone mineral density.41 In relation to depression, it has been suggested that the duration of the reproductive period, rather than the age at menarche itself, is negatively associated with depression prevalence. A meta-analysis of 14 studies revealed that late menopause age and long duration of reproductive years were associated with a decreased depression risk in post-menopause life. 42-44 A longer reproductive period represents longer exposure to endogenous female hormones, including estrogen and progesterone. Estradiol, the main estrogen, moderates the various pathways implicated in the etiologies of depression, anxiety, and various stress reactions, including the regulation of serotonin neurochemistry, 45 activation of the hypothalamic pituitary adrenal axis and immune system, and neuroplasticity.46 Considering the role of estrogen, we might infer that short exposure to estrogen due to late menarche might have contributed to the occurrence of various menopausal symptoms and depression.

Hierarchical logistic regression analysis revealed that living without a partner and high scores on the psychological and somatic subscales of MRS significantly influenced the severity of perimenopausal impairment. Our findings on the relationship between marital status and perimenopausal impairment are consistent with those of previous studies showing that married women's overall perimenopausal health status is better than that of single/divorced/widowed women, probably because of their more positive views about menopause. 47-49 One study revealed that sexually active women reported low total MRS scores and low somatic, psychological, and urogenital subscale scores.<sup>50</sup> In studies conducted on Koreans, it has been repeatedly reported that disease status (hypertriglyceridemia, metabolic syndrome, and depression) and health behaviors (smoking, binge drinking, and inadequate sleep) were significantly poor in middle-aged populations not living with partners, 51-53 and our findings are consistent in this context. Meanwhile, there have been contradictory findings that married women complained more of vasomotor, genitourinary, or sexual symptoms than single/separated/widowed women. 17,54-56 In particular, more sexual problems in women living with partners have been associated with comparatively active sexual lives.<sup>55</sup> Therefore, additional studies are needed to determine the relationship between marital status and the severity of menopausal symptoms.

Results on the association between MRS subscale scores and perimenopausal symptoms severity are more notable. From the results of the hierarchical logistic regression analyses, only psychological and somatic subscales of MRS were

Table 3. Results of the hierarchical logistic regression analyses (N=658)

To be a second to the second t		Model 1		7	Model 2			Model 3			Model 4	
mucpenucin variables	В	Wald	OR	В	Wald	OR	В	Wald	OR	В	Wald	OR
Sociodemographic factors												
Marital status (living without a partner)	-1.030	15.846	$0.357^{\ddagger}$	-0.864	8.479	$0.422^{\dagger}$	-0.817	7.197	$0.442^{\dagger}$	-0.800	5.138	2.227*
Education level (High school graduates or below)	-0.255	1.126	0.775	-0.218	0.740	0.804	-0.216	0.686	0.805	-0.306	1.010	1.357
Job status (with a job)	0.260	1.376	1.297	0.199	0.782	1.221	0.215	0.871	1.240	0.172	0.429	0.842
Monthly family income (<4 million won)	-0.411	3.273	0.663	-0.428	3.486	0.652	-0.403	2.992	0.668	-0.371	1.966	1.449
Age	0.000	0.000	1.000	0.009	0.107	1.009	0.012	0.163	1.012	0.030	0.808	1.031
Obstetric factors												
Premenopausal menstrual cycle regularity (regular)				0.173	0.622	1.189	0.121	0.284	1.128	0.115	0.198	0.892
Menopause status (completely menopause)				0.095	0.059	1.100	0.095	0.056	1.099	0.339	0.527	0.712
FHx of menopause symptoms (No/Don't know)				0.707	8.014	2.027	0.598	5.287	1.818	0.415	1.912	0.661
Period from the onset of menopause				0.008	0.077	1.008	0.011	0.157	1.011	-0.017	0.281	0.983
Menarche age				0.149	4.686	1.161*	0.151	4.642	1.163*	0.108	1.798	1.114
Number of pregnancies				0.174	2.267	1.190	0.138	1.288	1.147	0.071	0.239	1.073
Number of deliveries				-0.326	3.084	0.722	-0.322	2.711	0.725	-0.089	0.158	0.915
Psychiatric factors												
Hx of PMS (no)							0.055	0.035	1.057	-0.679	3.838	1.973
Hx of postpartum depression (no)							0.149	0.414	1.161	-0.289	1.149	1.335
Hx of postpartum psychosis (no)							1.055	2.294	2.872	968.0	0.955	0.408
Hx of other psychiatric disorders (no)							1.721	8.146	$5.591^{\dagger}$	0.725	1.026	0.484
MRS												
MRS_Psychological										0.279	31.698	$1.321^{\ddagger}$
MRS_Somatic										0.149	7.932	$1.160^{\dagger}$
MRS_Urogenital										0.050	0.741	1.051
Statistics of the model		Model 1		I	Model 2			Model 3			Model 4	
-2LL		615.987			601.046			588.238			461.436	
Model $\chi^2$	32.	32.437 (df=5) <sup>‡</sup>	++	47.3	47.378 (df=12) <sup>‡</sup>	<del>*</del> (	.09	60.186 (df=16) <sup>‡</sup>	±(°	186.	186.988 (df=19) <sup>‡</sup>	±(0
Step $\chi^2$	32.	32.437 (df=5) <sup>‡</sup>	++	14.9	14.941 (df=7)*	*	12.	12.808 (df=4)*	*(	126	126.802 (df=3) <sup>‡</sup>	#(
Nagelkerke R²		0.077			0.111			0.139			0.395	
Classification accuracy (%)		80.5			81.3			81.9			85.9	
*p_0 05. tp_0 01. tp_0 001 OP odds matic EHv family history. Hv history. DMS	ictory Hy	ictory, Dl		thurs learned	ome. ME	S. Granda	s pating s	Sale: MDS	memenetrial candrome: MPS menonage rating scale: MDS Deachological		scores of the negocial	hological

\*p<0.05; †p<0.01; †p<0.001. OR, odds ratio; FHx, family history; Hx, history; PMS, premenstrual syndrome; MRS, menopause rating scale; MRS\_Psychological, scores of the psychological subscale of MRS; MRS\_Somatic, scores of the somatic subscale of MRS; MRS\_Urogenital, scores of the urogenital subscale of MRS; -2LL, -2 log likelihood

significant predictors of being in the "all impaired" group among various obstetric and psychiatric factors. Family history of menopause symptoms, menarche age, and history of other psychiatric disorders were found to be risk factors only before MRS was added to Model 4. This means that the 2 MRS subscales account for much more weight in evaluating the general health of middle-aged women related to perimenopause symptoms, regardless of obstetric or psychiatric history. Moreover, it is worth noting that the current MRS psychological and somatic subscale scores were more important predictive factors than psychiatric history, including premenstrual syndrome, postpartum depression/psychosis, and other psychiatric disorders, which were previously emphasized as important risk factors for perimenopausal symptoms.<sup>21,23</sup>

Taking a closer look at the characteristics of the MRS scale, the 3 dimensions and 11 questions of MRS are described as follows: 1) psychological: depressive mood, irritability, anxiety, and physical and mental exhaustion; 2) somatic: hot flashes/sweats, heart discomfort, insomnia, and muscle and joint discomfort; and 3) urogenital: sexual problems, bladder problems, and vaginal dryness. Conventionally, interest in menopausal symptom treatment has been limited to gynecological hormonal and non-hormonal treatments targeting urogenital symptoms such as urinary incontinence and vaginal dryness and vasomotor symptoms such as hot flashes and night sweats. 11,57,58 In a study conducted in the USA, only 2% of participants reported having visited a psychiatrist for perimenopausal symptom treatment, while 63% reported visiting gynecologists.<sup>11</sup> Regarding therapeutic targets as reported by the study participants, vasomotor and genitourinary symptoms including hot flashes (21.9%), osteoporosis (7.3%), menstrual cycle regulation (3.6%), and vaginal dryness or irritation (4.4%) were reported frequently, whereas psychological symptoms including anxiety (1.2%) and depression (0.9%) were reported relatively infrequently. 11 Interestingly, however, in the same study, the main symptoms that healthcare professionals discussed with patients were psychological and somatic symptoms such as difficulty sleeping, exhaustion, depression or anxiety, muscle- and joint-ache, and lack of energy as well as vasomotor symptoms such as hot flashes and night sweats.11 In line with our findings, this also suggests that psychological and somatic symptoms that can be treated by psychiatrists are the main impairing symptoms in perimenopausal women, although they are often overlooked as therapeutic targets and it is difficult to sufficiently improve the somatic and psychological symptoms with conventional perimenopause treatment such as hormone therapy.<sup>59</sup>

This study has some limitations that should be considered when interpreting the results. First, the cross-sectional design enabled the identification of associations, but not necessarily causal relationships. Second, because we collected data using a self-reported online survey, a reporting bias should be considered. It has been shown that women often fail to provide reliable reports, particularly regarding the history of menstrual cycle-related mood disorders and peripartum psychiatric disorders such as premenstrual syndrome (PMS), peripartum depression, or peripartum psychosis. 60 This might be due to the characteristics of retrospective descriptions and the tendency of a long time elapsed since labor. Therefore, it is important to remember that information about PMS and peripartum psychiatric history could be over- or under-reported. Third, laboratory data on biological hormone levels, including estrogen and follicle-stimulating hormone, were not available in this study. If sex hormone levels could be measured, it would have been possible to accurately determine participants' menopausal stage and understand the precise biological role of hormonal factors on perimenopausal symptoms. Fourth, the two latent class groups included in this study may not sufficiently represent the characteristics of the entire population. Therefore, further longitudinal studies using a more diverse and representative population would be helpful to confirm the validity and generalizability of the current results.

In summary this study aimed to identify the determinant factors of menopausal symptom severity among perimenopausal Korean women using multivariate regression analysis. Consequently, psychological symptoms including depressive mood, irritability, anxiety, and physical/mental exhaustion and somatic symptoms including hot flashes/sweats, heart discomfort, insomnia, and muscle/joint discomfort assessed with the MRS scale predicted the severity of perimenopausal syndrome better than a family history of menopausal symptoms and the obstetric or psychiatric history of perimenopausal Korean women did. In conclusion, MRS (more precisely, the psychological and somatic subscales of MRS) is an excellent screening tool, which is important to offset the effects of other risk factors in regression analysis. In addition, more careful evaluation and treatment should be performed on individuals reporting high scores on the psychological and somatic subscales of the MRS. Thus, psychological and somatic symptoms, as well as genitourinary symptoms in menopausal patients, should always be closely evaluated. Further research on various treatment methods that focus on the treatment of psychological and somatic symptoms is needed.

#### Availability of Data and Material

The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

# Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

#### **Author Contributions**

Conceptualization: Ji Sun Hong, Jeong Seok Seo. Data curation: Da Seul Kim, Seunga Han. Formal analysis: Da Seul Kim, Sun Mi Kim. Investigation: Soyeon Kim, Seunga Han. Writing-original draft: Soyeon Kim, Ji Sun Hong. Writing—review and editing: Sun Mi Kim, Jeong Seok Seo.

#### **ORCID iDs**

Soyeon Kim	http://orcid.org/0000-0002-2753-0875
Sun Mi Kim	http://orcid.org/0000-0003-4131-0542
Da Seul Kim	http://orcid.org/0000-0001-5374-1636
Seunga Han	http://orcid.org/0000-0003-3210-1570
Ji Sun Hong	http://orcid.org/0000-0002-3898-8427
Jeong Seok Seo	http://orcid.org/0000-0002-4880-3684

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#### **REFERENCES**

- 1. Grigoriou V, Augoulea A, Armeni E, Rizos D, Alexandrou A, Dendrinos S, et al. Prevalence of vasomotor, psychological, psychosomatic and sexual symptoms in perimenopausal and recently postmenopausal Greek women: association with demographic, life-style and hormonal factors. Gynecol Endocrinol 2013;29:125-128.
- 2. Hulka BS, Meirik O. Research on the menopause. Maturitas 1996;23: 109-112.
- 3. Treloar AE, Boynton RE, Behn BG, Brown BW. Variation of the human menstrual cycle through reproductive life. Int J Fertil 1967;12(1 Pt 2):
- 4. Yang D, Haines CJ, Pan P, Zhang Q, Sun Y, Hong S, et al. Menopausal symptoms in mid-life women in southern China. Climacteric 2008;11: 329-336.
- 5. Yim G, Ahn Y, Chang Y, Ryu S, Lim JY, Kang D, et al. Prevalence and severity of menopause symptoms and associated factors across menopause status in Korean women. Menopause 2015;22:1108-1116.
- 6. Moilanen J, Aalto AM, Hemminki E, Aro AR, Raitanen J, Luoto R. Prevalence of menopause symptoms and their association with lifestyle among Finnish middle-aged women. Maturitas 2010;67:368-374.
- 7. Pérez JA, Garcia FC, Palacios S, Pérez M. Epidemiology of risk factors and symptoms associated with menopause in Spanish women. Maturitas 2009;62:30-36.
- 8. Greenblum CA, Rowe MA, Neff DF, Greenblum JS. Midlife women: symptoms associated with menopausal transition and early postmenopause and quality of life. Menopause 2013;20:22-27.
- 9. Nisar N, Sohoo NA. Severity of menopausal symptoms and the quality of life at different status of menopause: a community based survey from rural Sindh, Pakistan. Int J Collab Res Intern Med Public Health 2010; 2:118-130.
- 10. Nicholson WK, Ellison SA, Grason H, Powe NR. Patterns of ambulatory care use for gynecologic conditions: a national study. Am J Obstet Gynecol 2001;184:523-530.
- 11. Williams RE, Kalilani L, DiBenedetti DB, Zhou X, Fehnel SE, Clark RV. Healthcare seeking and treatment for menopausal symptoms in the United States. Maturitas 2007;58:348-358.
- 12. Freeman EW, Sammel MD, Lin H, Liu Z, Gracia CR. Duration of menopausal hot flushes and associated risk factors. Obstet Gynecol 2011; 117:1095-1104.
- 13. Avis NE, Crawford SL, Greendale G, Bromberger JT, Everson-Rose SA, Gold EB, et al. Duration of menopausal vasomotor symptoms over the menopause transition. JAMA Intern Med 2015;175:531-539.

- 14. Utian WH. Psychosocial and socioeconomic burden of vasomotor symptoms in menopause: a comprehensive review. Health Qual Life Outcomes 2005;3:47.
- 15. Freeman EW, Grisso JA, Berlin J, Sammel M, Garcia-Espana B, Hollander L. Symptom reports from a cohort of African American and white women in the late reproductive years. Menopause 2001;8:33-42.
- 16. Kuh DL, Hardy R, Wadsworth M. Women's health in midlife: the influence of the menopause, social factors and health in earlier life. Br J Obstet Gynaecol 1997;104:1419.
- 17. Lee MS, Kim JH, Park MS, Yang J, Ko YH, Ko SD, et al. Factors influencing the severity of menopause symptoms in Korean post-menopausal women. J Korean Med Sci 2010;25:758-765.
- 18. Ryu KJ, Park H, Kim YJ, Yi KW, Shin JH, Hur JY, et al. Comparison of various menopausal symptoms and risk factor analysis in Korean women according to stage of menopause. Maturitas 2020;140:41-48.
- 19. Tepper PG, Brooks MM, Randolph JF Jr, Crawford SL, El Khoudary SR, Gold EB, et al. Characterizing the trajectories of vasomotor symptoms across the menopausal transition. Menopause 2016;23:1067-1074.
- 20. Li RX, Ma M, Xiao XR, Xu Y, Chen XY, Li B. Perimenopausal syndrome and mood disorders in perimenopause: prevalence, severity, relationships, and risk factors. Medicine 2016;95:e4466.
- 21. Avis NE, Crawford SL, McKinlay SM. Psychosocial, behavioral, and health factors related to menopause symptomatology. Womens Health 1997-3-103-120
- 22. Gold EB, Colvin A, Avis N, Bromberger J, Greendale GA, Powell L, et al. Longitudinal analysis of the association between vasomotor symptoms and race/ethnicity across the menopausal transition: study of women's health across the nation. Am J Public Health 2006;96:1226-
- 23. Schwingl PJ, Hulka BS, Harlow SD. Risk factors for menopausal hot flashes. Obstet Gynecol 1994;84:29-34.
- 24. Hauser GA, Huber IC, Keller PJ, Lauritzen C, Schneider HP. [Evaluation of climacteric symptoms (Menopause Rating Scale)]. Zentralbl Gynakol 1994;116:16-23. German
- 25. Potthoff P, Heinemann LA, Schneider HP, Rosemeier HP, Hauser GA. [The Menopause Rating Scale (MRS II): methodological standardization in the German population]. Zentralbl Gynakol 2000;122:280-286. German
- 26. Heinemann LA, Potthoff P, Schneider HP. International versions of the Menopause Rating Scale (MRS). Health Qual Life Outcome 2003;1:28.
- 27. Chedraui P, Blümel JE, Baron G, Belzares E, Bencosme A, Calle A, et al. Impaired quality of life among middle aged women: a multicentre Latin American study. Maturitas 2008;61:323-329.
- 28. Lanza ST, Bray BC, Collins LM. An introduction to latent class and latent transition analysis. In: Schinka JA, Velicer WF, Weiner IB, editors. Handbook of psychology (2nd ed). Hoboken, NJ: John Wiley & Sons, 2013, p. 691-716.
- 29. Lo Y, Mendell NR, Rubin DB. Testing the number of components in a normal mixture. Biometrika 2001;88:767-778.
- 30. Kim NY, Yoo SK, Jin JC, Yoon YJ, Han DH, Kim SM. Latent profile analysis for classification of psychosomatic symptoms in perimenopausal women. J Acad Consult Liaison Psychiatry 2022 Aug 27. [Epub]. Available at: https://doi.org/10.1016/j.jaclp.2022.08.005.
- 31. Heinemann LA, DoMinh T, Strelow F, Gerbsch S, Schnitker J, Schneider HP. The Menopause Rating Scale (MRS) as outcome measure for hormone treatment? A validation study. Health Qual Life Outcomes 2004;2:67.
- 32. Forman EJ, Hong KH, Ferry KM, Tao X, Taylor D, Levy B, et al. In vitro fertilization with single euploid blastocyst transfer: a randomized controlled trial. Fertil Steril 2013;100:100-107.
- 33. Boynton-Jarrett R, Wright RJ, Putnam FW, Lividoti Hibert E, Michels KB, Forman MR, et al. Childhood abuse and age at menarche. J Adolesc Health 2013;52:241-247.
- 34. Li J, Eriksson M, Czene K, Hall P, Rodriguez-Wallberg KA. Common diseases as determinants of menopausal age. Hum Reprod 2016;31:

- 2856-2864.
- 35. Bubach S, De Mola CL, Hardy R, Drevfus J, Santos AC, Horta BL, Early menarche and blood pressure in adulthood: systematic review and meta-analysis. J Public Health (Oxf) 2018;40:476-484.
- 36. Peters SA, Woodward M. Women's reproductive factors and incident cardiovascular disease in the UK Biobank, Heart 2018;104:1069-1075.
- 37. Matalliotakis M, Goulielmos GN, Matalliotaki C, Trivli A, Matalliotakis I, Arici A. Endometriosis in adolescent and young girls: report on a series of 55 cases. J Pediatr Adolesc Gynecol 2017;30:568-570.
- 38. Ottolina J, Bartiromo L, Viganò P, Makieva S, Schimberni M, Candiani M. Does endometriosis influence the age of menopause? Minerva Ginecol 2018;70:171-177.
- 39. Kim Y, Je Y. Early menarche and risk of metabolic syndrome: a systematic review and meta-analysis. J Womens Health (Larchmt) 2019;28:
- 40. Graber JA, Seeley JR, Brooks-Gunn J, Lewinsohn PM. Is pubertal timing associated with psychopathology in young adulthood. J Am Acad Child Adolesc Psychiatry 2004;43:718-726.
- 41. Eastell R. Role of oestrogen in the regulation of bone turnover at the menarche. J Endocrinol 2005;185:223-234.
- 42. Georgakis MK, Thomopoulos TP, Diamantaras AA, Kalogirou EI, Skalkidou A, Daskalopoulou SS, et al. Association of age at menopause and duration of reproductive period with depression after menopause: a systematic review and meta-analysis. JAMA Psychiatry 2016;73:139-
- 43. Ryan J, Carrière I, Scali J, Ritchie K, Ancelin ML. Lifetime hormonal factors may predict late-life depression in women. Int Psychogeriatr 2008:20:1203-1218.
- 44. Jung SJ, Shin A, Kang D. Menarche age, menopause age and other reproductive factors in association with post-menopausal onset depression: results from Health Examinees Study (HEXA). J Affect Disord 2015;187:127-135.
- 45. Lokuge S, Frey BN, Foster JA, Soares CN, Steiner M. Depression in women: windows of vulnerability and new insights into the link between estrogen and serotonin. J Clin Psychiatry 2011;72:e1563-e1569.
- 46. Rubinow DR, Schmidt PJ, Craft CD. Gonadal steroids and mood disorders. In: Charney D, Buxbaum J, Sklar P, Nestler E, editors. Neurobiology of mental illness (4th ed). New York: Oxford University Press, 2013, p. 483-495.
- 47. Alakananda DN, Das BP. Age of menopause and menopausal symptoms among women attending Gauhati Medical College and Hospital, Guwahati, Assam: a cross-sectional study. Sch J App Med Sci 2015;3:

- 48. Dennerstein L, Lehert P, Dudley E, Guthrie J. Factors contributing to positive mood during the menopausal transition. J Nerv Ment Dis 2001;189:84-89.
- 49. Koirala S, Manandhar N. Quality of life of peri and postmenopausal women attending outpatient department of obstretics and gynecology of a tertiary care hospital. J Nepal Health Res Counc 2018;16:32-35.
- 50. Chedraui P, Aguirre W, Hidalgo L, Fayad L. Assessing menopausal symptoms among healthy middle aged women with the Menopause Rating Scale. Maturitas 2007;57:271-278.
- 51. Jung YA, Kang LL, Kim HN, Park HK, Hwang HS, Park KY. Relationship between marital status and metabolic syndrome in Korean middle-aged women: the Sixth Korea National Health and Nutrition Examination Survey (2013-2014). Korean J Fam Med 2018;39:307-312.
- 52. Kim A, Lee JA, Park HS. Health behaviors and illness according to marital status in middle-aged Koreans. J Public Health (Oxf) 2018;40:
- 53. Yim HJ, Park HA, Kang JH, Kim KW, Cho YG, Hur YI, et al. Marital status and health behavior in middle-aged Korean adults. Korean J Fam Med 2012;33:390-397.
- 54. Brzyski RG, Medrano MA, Hyatt-Santos JM, Ross JS. Quality of life in low-income menopausal women attending primary care clinics. Fertil Steril 2001;76:44-50.
- 55. Taşkıran G, Özgül S. Individual characteristics associated with menopausal symptom severity and menopause-specific quality of life: a rural perspective. Reprod Sci 2021;28:2661-2671.
- 56. Żołnierczuk-Kieliszek D, Kulik TB, Jarosz MJ, Stefanowicz A, Pacian A, Pacian J, et al. Quality of life in peri- and post-menopausal Polish women living in Lublin Province--differences between urban and rural dwellers. Ann Agric Environ Med 2012;19:129-133.
- 57. Kagan R, Kellogg-Spadt S, Parish SJ. Practical treatment considerations in the management of genitourinary syndrome of menopause. Drugs Aging 2019;36:897-908.
- 58. Palacios S, Stevenson JC, Schaudig K, Lukasiewicz M, Graziottin A. Hormone therapy for first-line management of menopausal symptoms: practical recommendations. Womens Health (Lond) 2019; 15:1745506519864009.
- 59. Pearce J, Hawton K, Blake F. Psychological and sexual symptoms associated with the menopause and the effects of hormone replacement therapy. Br J Psychiatry 1995;167:163-173.
- 60. Richards M, Rubinow DR, Daly RC, Schmidt PJ. Premenstrual symptoms and perimenopausal depression. Am J Psychiatry 2006;163:133-