

# Association Between Depression And Early Menopause In South Korean Women

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## Abstract

**Objectives:** We investigated the association between depression and early menopause in South Korean women using data from Korean National Health and Nutrition Examination Surveys (KNHANES).

**Study design:** Cross-sectional study

**Main outcome measures:** Average sleep time per day, age at diagnosis of depression, depression diagnosis, current depression, depression treatment, restricted activity due to a health, physical, and psychiatric problem, restricted activity, depression/anxiety/emotional problems, anxiety/depression, one-year psychiatric counseling, one-year suicidal thoughts, one-year suicide attempt, and suicidal thought rate were assessed. One hundred ninety five same age-matched women, from 20 to 40 years old, each were included in the menstruation and early menopause groups using the results of KNHANES of over the past 6 years.

**Results:** To determine the differences in characteristics between the groups, we used the analysis of variance. The average patient age was  $32.8 \pm 3.8$  years. Abdominal circumference was  $75.6 \pm 9.8$  cm and  $79.0 \pm 10.9$  cm in the menstruation and early menopause groups, respectively ( $P < .001$ ). Total cholesterol was  $181.0 \pm 30.1$  mg/dL and  $195.2 \pm 41.6$  mg/dL and low density lipids were  $103.8.0 \pm 25.0$  mg/dL and  $113.0 \pm 32.6$  mg/dL for the menstruation group and early menopause group, respectively ( $P < .001$ ).

**Conclusions:** Our result suggests that depression is associated with early menopause. We believe that management of life pattern and depression in early menopause is necessary.

## List of Abbreviations

Korean National Health and Nutrition Examination Surveys (KNHANES)

Body mass index (BMI)

Blood pressure (BP)

## INTRODUCTION

Menopause is the absence of menstruation for at least 12 months that is unrelated to surgical or drug treatment.<sup>1-3</sup> The average age before menopause is between 50 and 51 years.<sup>2,4,5</sup> The cause of menopause is thought to be genetic in about 50 percent of women, but in addition, many other factors including obesity, parity, age at menarche, pattern of menstrual cycles, smoking, socio-economic level, alcohol

intake, educational level, diet, marital status, and use of contraceptives have been investigated.<sup>6-9</sup> However, there are inconsistencies among the studies.<sup>10</sup>

Early menopause refers to the occurrence of menopause in women less than 40 years of age. This heterogeneous disorder affects 1% and 0.1% of women less than 40 and less than 30 years of age, respectively.<sup>11</sup> Early decline in estrogen production has been associated with an overall increase in

body weight and the accumulation of abdominal fat.<sup>12</sup> This unfavorable change in the distribution of body fat explains the increased cardiovascular risk associated with this stage of life.<sup>13</sup> In addition, the risk of many chronic health problems increases including osteoporosis, obesity, and earlier onset of Alzheimer's disease.<sup>14,15</sup> Particularly, in the case of early menopause, it is thought that the problems that arise from the decrease in estrogen secretion before the age of 40 years are more than those at the age of 50 years.

Depression is the leading cause of health disability in women, with a lifetime prevalence of over 20%.<sup>16</sup> It is diagnosed at least twice as often in women compared to men, representing new rather than recurrent episodes; however, the reason for this difference between the sexes is poorly understood.<sup>17</sup> Several prospective cohort studies have reported about two to threefold increase in depressive symptoms over the menopausal transition.<sup>18-20</sup> However, little is known about the trajectories of depressive symptoms across the menopausal transition and the factors that modify the relationship between menopausal stage and symptoms. Depressive symptoms cause less functional impairment than depressive disorders, but are not harmless. Subsyndromal depression increases the risk of major depression<sup>21</sup>, impairs quality of life<sup>22</sup>, and increases health service use.<sup>23</sup> Depressive symptoms may also increase the risk and burden of physical health problems including cardiovascular disease, diabetes, metabolic syndrome, and chronic pain.<sup>24</sup>

The aim of this study was to determine the association between depression and early menopause based on life pattern using the data of Korean same-aged women from Korean National Health and Nutrition Examination Surveys (KNHANES).

## METHODS

### *Study design and settings*

Our study was designed such that Korean women aged 20 to 40 years were matched with women of the same age and divided into menstrual and menopausal groups using KNHANES data for 6 years from 2010 to 2015. The detailed design of KNHANES has been described in a previously published study.<sup>25</sup> It was conducted by the Korean Ministry of Health and Welfare and was composed of 3 sections: a health survey, health consultations, and a nutrition survey. Health consultations were used to survey blood pressure (BP), age at menarche, abdominal circumference, body mass index (BMI), hemoglobin, total cholesterol, triglycerides, high-density lipoproteins, low-density lipoprotein, and

serum creatinine. The survey data included information regarding one-man households, home ownership status, education level, age allowed to drink alcoholic beverages, frequency of drinking in a year, the amount of alcohol consumed per time, lifetime smoking status, current smoking status, diagnosed depression status, current depression status, history of psychiatric counseling one year previously, having suicidal thoughts within the previous one year, having attempted suicide within the past year, and suicidal thought rate.

The menstruation and early menopause groups had 195 women each; thus, 390 women were included in the study.

All the participants provided written informed consent. The study protocol conformed to the Ethics Guidelines of the 1975 Declaration of Helsinki and was approved by the Institutional Review Board of the Korea Centers for Disease Control and Prevention KCDC (for 2010 to 2012: No. 2010-02CON- 21-C, 2011-02CON-06-C, and 2012-01EXP-01-2C; for 2013 to 2015: No. 2013-07CON- 03-4C, 2013-12EXP- 03-5C, and 2015-01-02-6C).

### *Statistics*

For continuous variables, to determine the subjects' characteristics, a descriptive analysis was performed. Categorical variables were analyzed using chi-square test to determine the correlation between the variables. We divided the subjects into two groups based on the presence of early menopause. To determine the differences in characteristics between the groups, we used the analysis of variance. In the regression analysis of the presence of early menopause, we adjusted for confounding factors, including BP, age at menarche, abdominal circumference, BMI, hemoglobin, total cholesterol, triglycerides, high density lipoprotein, low density lipoprotein, serum creatinine, one-man household, home ownership status, education level, age allowed to consume alcoholic beverages, frequency of drinking in a year, the amount of alcohol consumed per time, lifetime smoking status, current smoking status, diagnosed depression status, current depression status, having received one-year psychiatric counseling, having had suicidal thoughts within the previous one year, having attempted suicide within the past year, and suicidal thought rate. Significance was defined as  $P < .001$ . R version 3.3.1. (R Foundation for Statistical Computing, Vienna, Austria) was used for the statistical analysis.

## **RESULTS**

The average age of the participants was  $32.8 \pm 3.8$  years. Abdominal circumference was  $75.6 \pm 9.8$  cm and  $79.0 \pm 10.9$  cm in the menstruation and early menopause groups, respectively ( $P < .001$ ); total cholesterol was  $181.0 \pm 30.1$  mg/dL and  $195.2 \pm 41.6$  mg/dL, respectively; low density lipids were  $103.8.0 \pm 25.0$  mg/dL and  $113.0 \pm 32.6$  mg/dL, respectively ( $P < .001$ ) (Table 1); no alcohol consumption in a year was found in 33 and 106 women, respectively ( $P < .001$ ); consumption of below 2 cups per time was found in 68 and 52 women, respectively ( $P < .001$ ); average smoking per day was  $12.0 \pm 4.5$  and  $11.0 \pm 7.9$ , respectively ( $P < .001$ ) (Table

2). The number of women diagnosed with depression was 6 and 10, respectively, and those with current depression were 0 and 3 women, respectively ( $P < .001$ ). The number of women who had undergone one year of psychiatric counseling was 5 and 7, respectively; those who had suicidal thoughts within the previous one year was 18 and 19 women, respectively; those who had attempted suicide within the previous one year was 3 and 3 women, respectively; and those had suicidal thought rate was 177 and 176 women, respectively. Among the respondents, responses regarding suicide were higher in the early menopause group (Table 3).

**Table 1**

Baseline characteristics of women included and excluded from the analysis

Variables		Menstruation group (n=195)	Early menopause group (n=195)	P value
Age		32.8 ± 3.8	32.8 ± 3.8	1.000
Menarche age		13.2 ± 1.6	13.6 ± 1.8	.036
BMI (kg/m <sup>2</sup> )		22.5 ± 3.6	23.2 ± 3.9	.100
AC (cm)		75.6 ± 9.8	79.0 ± 10.9	.001
Hb (g/dL)		12.9 ± 1.1	12.9 ± 1.1	.824
T.chol (mg/dL)		181.0 ± 30.1	195.2 ± 41.6	<.001
Triglycerides (mg/dL)		92.4 ± 51.0	107.6 ± 76.5	.022
HDL (mg/dL)		56.6 ± 12.9	60.6 ± 13.1	.003
LDL (mg/dL)		103.8 ± 25.0	113.0 ± 32.6	<.001
Serum creatinine (mg/dL)		0.72 ± 0.10	0.64 ± 0.12	<.001
GFR (ml/min/1.73m <sup>2</sup> )		102.1 ± 17.4	117.2 ± 26.3	<.001
FBS (mg/dL)		91.0 ± 18.5	86.5 ± 9.7	.003
SBP (mmHg)		104.9 ± 10.7	104.1 ± 9.7	.427
DBP (mmHg)		69.5 ± 8.5	67.8 ± 8.6	.041
HTN Diagnosis, n(%)	Normal	172 (88.2%)	172 (88.2%)	.894
	High BP	20 (10.3%)	21 (10.8%)	
	Hypertension	3 (1.5%)	2 (1.0%)	
DM Diagnosis, n(%)	Normal	177 (90.8%)	186 (95.4%)	.106
	High glucose	14 (7.2%)	5 (2.6%)	
	Diabetes	4 (2.1%)	4 (2.1%)	
DM treatment, n(%)	Yes	1 (0.5%)	1 (0.5%)	.606
	No	1 (0.5%)	0 (0%)	
	Not applicable	193 (99.0%)	194 (99.5%)	
One-man household, n(%)	One	8 (4.1)	1 (0.5)	.016
	Two	20 (10.2)	10 (5.1)	
	Three	59 (30.2)	61 (31.2)	
	Four	79 (40.5)	76 (38.9)	
	Five	22 (11.2)	29 (14.8)	
	Six	7 (3.5)	12 (6.1)	
	Seven	0 (0)	5 (2.5)	
	Not applicable	0 (0)	1 (0.5)	
House ownership status, n(%) (Number of houses)	None	85 (43.6%)	70 (35.9%)	.189
	One	90 (46.2%)	108 (55.4%)	
	Above two	20 (10.3%)	17 (8.7%)	
Education level, n(%)	Middle school	4 (2.1%)	2 (1.0%)	.078
	High school	45 (23.1%)	54 (27.7%)	
	Two-year college	55 (28.2%)	69 (35.4%)	
	University	77 (39.5%)	52 (26.7%)	
	Graduate school	14 (7.2%)	18 (9.2%)	

AC, Abdominal circumference; BMI, Body mass index; Hb, Hemoglobin; T.chol, Total cholesterol; HDL, High-density

lipoprotein; LDL, Low-density lipoprotein; GFR, Glomerular filtration rate; FBS, Fasting blood sugar; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; BP, Blood pressure: Normal: systolic BP<120 mmHg and diastolic BP<80 mmHg, High BP: 120≤systolic BP<140 mmHg or 80 mmHg≤diastolic BP<90 mmHg; hypertension: systolic BP≥140 mmHg or Diastolic BP≥90 mmHg or person taking antihypertensive agent; DM, Diabetes mellitus: Normal: fasting glucose<100 mg/dL, High glucose: 100 mg/dL≤fasting glucose<126 mg/dL, Diabetes: fasting glucose≥126 mg/dL or diagnosis by doctor or taking hypoglycemic agent or insulin injection

**Table 2**  
Alcohol and smoking pattern in early menopausal women

Variables		Menstruation group (n=195)	Early menopause group (n=195)	P value
Age allowed to drink(year)		19.1 ± 2.6	19.1 ± 2.7	.861
Frequency of alcohol consumption in a year n(%)	No drinking in a year	33 (16.1)	106 (54.3)	<.001
	Less than once a month	49 (25.1)	38 (19.4)	
	Once a month	29 (14.8)	16 (8.2)	
	2-4 times a month	52 (26.6)	22 (11.2)	
	2-3 times a week	19 (9.7)	5 (2.5)	
	Above 4 times a week	4 (2.0)	1 (0.5)	
	Not applicable	9 (4.6)	7 (3.5)	
The amount of alcohol consumed per time n(%)	1-2 cups	68 (34.8)	52 (26.6)	<.001
	3-4 cups	34 (17.4)	15(7.6)	
	5-6 cups	21 (10.7)	6 (3.0)	
	7-9 cups	11 (5.6)	6 (3.0)	
	Above 10 cups	19 (9.7)	3 (1.5)	
	Unknown	42 (21.5)	113 (57.9)	
Degree of binge	No	54 (27.6)	49 (25.1)	<.001
	Less than once a month	47 (24.1)	19 (9.7)	
	Once a month	26 (13.3)	9 (4.6)	
	Once a week	20 (10.2)	5 (2.5)	
	Everyday	6 (3.0)	0 (0.0)	
	Not applicable	42 (21.5)	113 (57.9)	
Lifetime smoking status	Less than 5 packs	4 (2.1%)	6 (3.1%)	.512
	More than 5 packs	32 (16.4%)	25 (12.8%)	
	No	159 (81.5%)	164 (84.1%)	
Current smoking status	Yes	11 (5.6%)	3 (1.5%)	.163
	Occasional	5 (2.6%)	4 (2.1%)	
	Past smoker	20 (10.3%)	24 (12.3%)	
	Not applicable	159 (81.5%)	164 (84.1%)	
Average smoking per day (cigarettes)		12.0 ± 4.5	11.0 ± 7.9	<.001

**Table 3**  
Depression in early menopause women

Variables		Menstruation group (n=195)	Early menopause group (n=195)	P value
Average sleep time per day (hours)		7.0 ± 1.3	7.7 ± 6.7	.202
Age at diagnosis of depression (year)		28.3 ± 6.2	29.1 ± 5.8	.309
Depression diagnosis, n(%)	No	108 (94.73%)	70 (87.5%)	.000
	Yes	6 (5.26%)	10 (12.5%)	
	Not applicable	80 (41.0%)	115 (59.0%)	
Current depression, n(%)	No	19 (100%)	24 (85.71%)	<.001
	Yes	0 (0.0%)	4 (14.2%)	
	Not applicable	174 (89.2%)	167 (85.6%)	
Depression treatment, n(%)	No	19 (100%)	25 (89.28%)	<.001
	Yes	0 (0.0%)	3 (10.71%)	
	Not applicable	174 (89.2%)	167 (85.6%)	
Restricted activity due to a health problem, physical, and psychiatric problem, n(%)	Yes	3 (1.5%)	6 (3.1%)	.500
	No	192 (98.5%)	189 (96.9%)	
Restrict activity, n(%) Depression/anxiety/emotional problems	Yes	3 (100%)	5 (83.33%)	.025
	No	0 (0.0%)	1 (16.67%)	
	Not applicable	192 (98.5%)	189 (96.9%)	
Anxiety/depression	No	182 (93.33%)	183 (93.8%)	<.001
	Slight	13 (6.67%)	12 (6.2%)	
	Severe	1 (0.5%)	0 (0.0%)	
One-year psychiatric counseling	Yes	5 (2.6%)	7 (3.6%)	.553
	No	151 (77.4%)	142 (72.8%)	
	Not applicable	39 (20.0%)	46 (23.6%)	
One-year suicidal thoughts	Yes	18 (9.2%)	19 (9.7%)	1.000
	No	177 (90.8%)	176 (90.3%)	
One-year suicide attempt	Yes	3 (1.5%)	3 (1.5%)	.001
	No	107 (54.9%)	69 (35.4%)	
	Not applicable	85 (43.6%)	123 (63.1%)	
Suicidal thought rate	No	177 (90.8%)	176 (90.3%)	1.000
	Yes	18 (9.2%)	19 (9.7%)	

**DISCUSSION**

There was no significant difference in home ownership or educational level, but it was found that postgraduate students had a higher education level in the early menopause group. It is unclear whether the stress of the highly educated women caused the early menopause or whether the women, free from childbearing, could study earlier due to an early menopause.

In the case of smokers who had reached menopause, there was no difference between the menstrual and early menopause groups in our study. On the contrary, the mean smoking amount per day was 12.0 ± 4.5 in the menstrual group and 11.0 ± 7.9 in the early menopausal group and was significantly lower in the early menopausal group.

The prevalence of alcohol consumption and drinking frequency in the early menopausal group were lower than in the menstrual group in our study. In the early menopausal women, it was unclear whether the drinking or smoking habits were pre- or postmenopausal. However, in the early menopause group, there was a difference compared to the general menopause group.

In our study, there was a significantly higher response in the early menopausal group regarding depression diagnosis, current depression, depression treatment, and one-year suicide attempt. This is consistent with the fact that depression is high in menopausal transition women. However, in addition to depression due to menopause, early menopause is thought to cause more depression due to the early onset.

Two different hypotheses link estrogens with depression during and after the menopause: (1) low estrogen is related to a depressed mood and (2) the unstable and irregular hormone production during the menopausal transition increases weakness to mood disorders in susceptible women.<sup>26</sup>

Although there are some studies on menopause and depression, there are not many studies on early menopause. Our study compared the association of depression in early menopausal women with that in same-aged menstruating women. In this study, the number of respondents who answered yes or no, excluding “no responses,” was significantly higher in the early menopausal group than in the menstruation group regarding depression diagnosis, current depression, depression treatment, and suicide attempt within the previous one year.

BMI was 22.5 ± 3.6 kg/m<sup>2</sup> in the menstruation group and 23.2 ± 3.9 kg/m<sup>2</sup> in the early menopausal group. This is consistent with the case of general menopause. Abdominal circumference was also significantly higher in the menopausal group than in the menstruation group (75.6 ± 9.8 cm vs 79.0 ± 10.9 cm, P<.001). Estrogen deprivation causes abdominal and body fat increase, suggesting that BMI is higher in the menopausal group than in the menstrual group. In addition, total cholesterol was 181.0 ± 30.1 mg/dL in the menstrual group and 181.0 ± 30.1 mg/dL in the early menopausal group, and low-density lipids were also significantly higher in the early menopausal group than in the menstrual group. However, our results are inconsistent with the general menopause group. The high high-density lipoprotein level in the early menopause group compared to

the menstrual group was inconsistent with the general menopause group.

However, our study has some limitations. This study was cross-sectional and did not include any research on the premenopausal condition, early menopause, postmenopausal lifestyles, and depression. Furthermore, there have been insufficient analyses of the mechanism by which these factors are associated with depression and life pattern in early menopause.

## CONCLUSIONS

This study suggests that early postmenopausal women have a higher level of depression than menstrual women. This study is a rare study on the association between depression and early menopause in same age-matched early menopausal and menstrual women.

Future studies on the relationship and mechanism between life pattern and depression in early menopausal women are needed.

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