

# The Effect of Menopause on the Metabolic Syndrome Among Korean Women

The Korean National Health and Nutrition Examination Survey, 2001

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**OBJECTIVE**— This study examined the effect of menopausal status on the risk of the metabolic syndrome in Korean women.

**RESEARCH DESIGN AND METHODS**— Data were obtained from the Korean National Health and Nutrition Examination Survey of 2001. A total of 2,671 women who did not receive hormone replacement therapy (1,893 premenopausal women and 778 postmenopausal women) were included in the analysis. The metabolic syndrome was defined according to the National Cholesterol Education Program Adult Treatment Panel III.

**RESULTS**— Postmenopausal women had significantly higher mean waist circumference, systolic blood pressure, pulse pressure, total cholesterol, LDL cholesterol, and triglyceride levels than premenopausal women after adjusting for age ( $P = 0.018$ ,  $P = 0.001$ ,  $P < 0.0001$ ,  $P < 0.0001$ ,  $P < 0.0001$ , and  $P = 0.006$ , respectively). Among postmenopausal women, the age-adjusted odds ratio was 1.61 (95% CI 1.15–2.25) for abdominal obesity, 1.11 (0.76–1.61) for elevated blood pressure, 1.24 (0.90–1.72) for low HDL cholesterol, 1.28 (0.89–1.83) for high triglycerides, and 1.07 (0.69–1.65) for high fasting glucose compared with premenopausal women. The multivariate-adjusted odds ratio for the metabolic syndrome was 1.60 (95% CI 1.04–2.46) among postmenopausal women compared with premenopausal women.

**CONCLUSIONS**— Postmenopausal status is associated with an increased risk of the metabolic syndrome independent of normal aging in Korean women.

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Stroke and coronary artery disease were major causes of death among Korean women in 2004, second only to malignant diseases (1). Ischemic heart disease is more common in Korean women aged >50 years than in Korean men of the same age-group (2). Menopause appears to increase the risk of cardiovascular disease (CVD) independently of normal aging, and premenopausal women may be protected against CVD compared with men and postmenopausal women of a similar age (3).

The metabolic syndrome is one of the

major predisposing factors for CVD, and the population-attributable fraction of the metabolic syndrome has been reported to be 12–17% for CVD in the U.S. (4). The prevalence of the metabolic syndrome increases with age in both men and women. From young ( $\geq 20$  years) to middle age (<50 years), Korean men tend to have a higher prevalence of the metabolic syndrome than Korean women. However, Korean women have a higher prevalence than Korean men above the age of 50 years (5,6). It has been suggested that menopause is a contributing factor for

this change in prevalence (6). A study in the U.S. demonstrated an increased risk of the metabolic syndrome among postmenopausal women (7).

To our knowledge, there have been few studies on the effect of menopause on the development of the metabolic syndrome independent of age, and little information is available on an association between the metabolic syndrome and menopausal status in Korean women. This study examined the difference in the prevalence of the cardiovascular risk factors between postmenopausal and premenopausal women and assessed the effect of menopausal status on the metabolic syndrome in Korean women.

## RESEARCH DESIGN AND METHODS

The Korean National Health and Nutrition Examination Survey (KNHANES) was conducted by the Korean Ministry of Health and Welfare in 2001. The participants were noninstitutionalized civilians in the Republic of Korea. The sampling units were households selected through a stratified, multistage, probability-sampling design. The participants completed three parts of a questionnaire, which consisted of a health interview survey, a health behavior survey, and a nutrition survey. A selected sample of participants underwent a health examination survey that included anthropometric measurements, blood pressure measurements, and blood biochemistry tests. Of 12,647 participants aged  $\geq 10$  years, 9,770 (77.3%) attended the health examination survey. Participants aged <20 years were excluded from our analysis, leaving 6,015 participants (2,596 men and 3,419 women). Participants who had one or more missing values of the risk factors necessary for a diagnosis of the metabolic syndrome were also excluded. Ultimately, a total of 5,588 (92.9%) participants (2,369 men and 3,219 women) were included to examine the prevalence of the metabolic syndrome.

For the analysis of the effect of menopause, 548 of 3,219 women were excluded for the following reasons: missing data on a questionnaire regarding meno-

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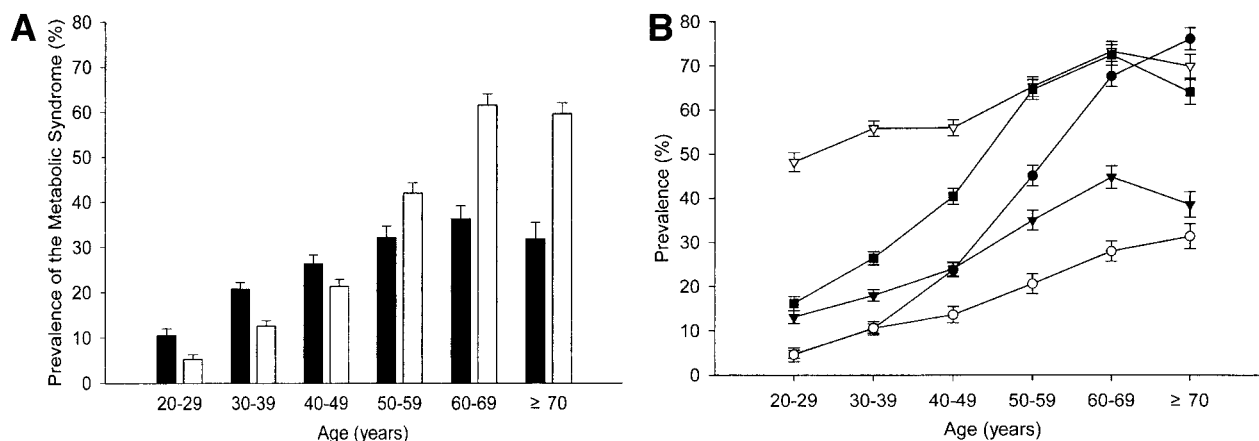
**Abbreviations:** CVD, cardiovascular disease; HRT, hormone replacement therapy; KNHANES, Korean National Health and Nutrition Examination Survey.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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**Figure 1**—Age-specific prevalence of the metabolic syndrome in Korean men and women ( $n = 2,369$  and  $3,219$ , respectively) (A) and age-specific prevalence of the components of the metabolic syndrome among Korean women ( $n = 3,219$ ) from KNHANES 2001 (B). A: ■, men; □, women. B: ○, high fasting glucose; ●, elevated blood pressure; △, low HDL cholesterol; ▲, high triglyceride; ■, abdominal obesity.

pause; menopause duration of <1 year ( $n = 57$ ); premature menopause induced by surgery, chemotherapy, or radiation ( $n = 148$ ); and hormone replacement therapy (HRT) for any cause ( $n = 185$ ). In the end, 2,671 (83.0%) women were considered eligible for the analysis. The sample consisted of 1,893 premenopausal women and 778 postmenopausal women.

Height was measured using a stadiometer in the upright position, and body weight was measured on a balanced scale (2,6). BMI was calculated using the following formula:  $BMI = \text{body weight (kg)} / \text{height}^2 \text{ (m)}$ . Waist circumference was measured at the midpoint between the bottom of the rib cage and the top of the lateral border of the iliac crest during minimal respiration. Blood pressure was measured using a mercury sphygmomanometer in the sitting position after a 10-min rest period. Two measurements were taken from all the subjects at 5-min intervals, and the average of the two measurements was used. Pulse pressure was defined as the difference between systolic and diastolic blood pressure. Blood samples were collected in the morning after an overnight fast, then centrifuged, refrigerated, and transferred to a national central laboratory in Seoul. Total cholesterol, triglycerides, HDL cholesterol, and plasma fasting glucose levels were measured using an autoanalyzer (Hitachi 747 autoanalyzer; Tokyo, Japan). LDL cholesterol level was calculated using the Friedewald equation if the triglyceride level was <400 mg/dl (8).

According to the National Cholesterol Education Program Adult Treatment Panel III (9), the metabolic syndrome is

defined as the presence of three or more of the following risk factors: 1) abdominal obesity with a waist circumference  $\geq 90$  cm for Asian men and  $\geq 80$  cm for Asian women according to the World Health Organization (10), 2) high triglyceride level  $\geq 1.69$  mmol/l, 3) low HDL cholesterol level <1.03 mmol/l for men and 1.29 mmol/l for women, 4) elevated systolic blood pressure  $\geq 130$  mmHg or elevated diastolic blood pressure  $\geq 85$  mmHg, and 5) high fasting glucose level  $\geq 6.1$  mmol/l. Subjects who reported taking hypertension or diabetes medications were considered to have elevated blood pressure or high fasting glucose, respectively (11). Menopause is defined as amenorrhea for 12 months following the final menstrual period (12). In our study, a postmenopausal woman was defined as a woman with natural menopause whose current age was  $\geq 1$  year than her age of menopause and who did not receive HRT.

Self-reported questionnaires were administered to determine smoking status, alcohol intake, education level, household income, physical exercise level, and family history of medical disease. Smoking status was categorized into nonsmokers, current smokers, and ex-smokers. Alcohol consumption was categorized according to the amount and frequency of alcohol consumed: none, current drinker, risk drinker, and high-risk drinker (2). A risk drinker was a person who consumed  $\geq 60$  g of alcohol/day and once or twice per week. A high-risk drinker was a person who consumed  $\geq 60$  g of alcohol/day and three or more times per week. A current drinker was a person who drinks less than a risk drinker. Education level was divided into three categories: <9 years,

9–12 years, and >12 years. Household income was divided into quartiles according to the mean household income per month: <1,000,000, 1,000,000–1,499,000, 1,500,000–2,499,000, and  $\geq 2,500,000$  won. The exchange rate on 1 January 2001 was 1,259 won to the U.S. dollar. Physical exercise was categorized into three groups according to the frequency of activity for at least 20 min per week: none, 1–2 times per week, and  $\geq 3$  times per week. Residential area was categorized according to the Korean administrative district as a large city, a medium or small city, and a rural area (12). A family history of CVD was defined as having at least one parent or sibling diagnosed with hypertension, stroke, or coronary heart disease, and a family history of diabetes was defined as having at least one parent or sibling diagnosed with diabetes.

### Statistical analysis

The baseline characteristics of premenopausal and postmenopausal women were compared using an ANCOVA with age as the covariate. Of 2,671 subjects, 195 women (7.3%) on hypertension medications were excluded from the comparison of mean blood pressure, and 60 women (2.2%) on diabetes medications were excluded from the comparison of mean fasting glucose level. The age-adjusted odds ratios (ORs) for risk factors for the metabolic syndrome were calculated by logistic regression with age as a continuous variable. Multivariate logistic regression analysis was used to assess the independent contribution of menopausal status to the presence of the metabolic syndrome with an adjustment for age (a continuous variable), BMI, smoking, alcohol, educa-

**Table 1—Baseline characteristics of premenopausal and postmenopausal women who did not receive hormone replacement therapy**

	Premenopause	Postmenopause	ANCOVA* (P value)
n	1,893	778	
Age (years)	35.4 ± 8.1	65.1 ± 9.3	<0.0001
BMI (kg/m <sup>2</sup> )	22.7 ± 3.3	24.2 ± 3.3	0.191
Waist circumference (cm)	75.4 ± 8.8	83.5 ± 9.0	0.018
Systolic blood pressure (mmHg)†	112.0 ± 13.2	131.2 ± 21.4	0.001
Diastolic blood pressure (mmHg)†	71.6 ± 10.0	79.0 ± 11.4	0.609
Pulse pressure (mmHg)†	40.4 ± 8.4	52.3 ± 15.4	<0.0001
Total cholesterol (mmol/l)	4.60 ± 0.82	5.29 ± 0.87	<0.0001
LDL cholesterol (mmol/l)‡	2.76 ± 0.70	3.35 ± 0.79	<0.0001
HDL cholesterol (mmol/l)	1.28 ± 0.27	1.18 ± 0.25	0.289
Triglyceride (mmol/l)	1.23 ± 0.73	1.70 ± 0.84	0.006
Fasting glucose (mmol/l)§	5.2 ± 0.8	5.5 ± 1.0	0.687

Data are means ± SD. \*ANCOVA with age as a covariate. †Of 2,671 women, 195 on hypertension medications were excluded from comparison of mean blood pressure. ‡Of 2,671 women, 28 with which LDL cholesterol could not be calculated were excluded. §Of 2,671 women, 60 on diabetes medications were excluded from comparison of mean fasting glucose.

tion level, household income, physical exercise level, residential area, and family history of CVD and diabetes. Data analysis was carried out using SPSS software (version 11; SPSS, Chicago, IL). A *P* value <0.05 was considered significant.

**RESULTS**— The prevalence of the metabolic syndrome and its risk factors increased with age in both Korean men and women (Fig. 1). Above the age of 50 years, the prevalence of the metabolic syndrome was significantly higher in women than in men (*P* < 0.05). Table 1 shows the baseline characteristics in relation to menopausal status. Postmenopausal women had significantly higher mean waist circumference, systolic blood pressure, pulse pressure, total cholesterol, LDL cholesterol, and triglyceride levels than premenopausal women, ad-

justed for age (*P* = 0.018, *P* = 0.001, *P* < 0.0001, *P* < 0.0001, *P* < 0.0001, and *P* = 0.006, respectively).

Table 2 displays the prevalence and ORs of the risk factors for the metabolic syndrome in relation to menopausal status. Abdominal obesity, elevated blood pressure, low HDL cholesterol, high triglycerides, and high fasting glucose were significantly associated with postmenopausal status (*P* < 0.0001 for all). However, when these factors were adjusted for age, only abdominal obesity was significantly associated with postmenopausal status (OR 1.61 [95% CI 1.15–2.25]; *P* = 0.005).

Table 3 presents the ORs for the metabolic syndrome after adjusting for menopausal status, BMI, smoking, alcohol consumption, education level, household income, exercise, residential area, and

family history of CVD and diabetes. The unadjusted and multivariate-adjusted ORs for the metabolic syndrome in postmenopausal women were 7.50 and 1.60, respectively (95% CI 6.18–9.08 and 1.04–2.46, respectively) compared with premenopausal women. Multivariate analysis revealed that a high BMI and a family history of CVD and diabetes were significantly associated with an increased risk of the metabolic syndrome (OR 1.73 and 1.55, respectively). However, the multivariate model showed that smoking, alcohol intake, education level, household income, physical exercise level, and residential area were not significantly associated with the risk for the metabolic syndrome.

**CONCLUSIONS**— A higher prevalence of the metabolic syndrome among

**Table 2—Prevalence and age-adjusted ORs of risk factors of the metabolic syndrome among premenopausal and postmenopausal women who did not receive hormone replacement therapy**

Risk factors	Premenopause (n = 1,893)	Postmenopause (n = 778)	P value*	Postmenopause (n = 778)	
				Age-adjusted OR (95% CI)†	P value
Abdominal obesity (≥80 cm)	28.1	67.1	<0.0001	1.61 (1.15–2.25)	0.005
Elevated blood pressure (≥130/85 mmHg)	13.7	63.6	<0.0001	1.11 (0.76–1.61)	0.599
Low HDL cholesterol (<1.29 mmol/l)	54.2	69.8	<0.0001	1.24 (0.90–1.72)	0.190
High triglyceride (≥1.69 mmol/l)	18.9	39.3	<0.0001	1.28 (0.89–1.83)	0.184
High fasting glucose (≥6.1 mmol/l)	9.8	26.0	<0.0001	1.07 (0.69–1.65)	0.775
Number of risk factors					
One or more	70.4	96.3	<0.0001	2.79 (1.67–4.64)	<0.0001
Two or more	35.1	81.0	<0.0001	1.35 (0.96–1.91)	0.087
Three or more	13.8	54.6	<0.0001	1.51 (1.04–2.19)	0.030
Four or more	4.4	27.4	<0.0001	2.20 (1.33–3.65)	0.002

Data are prevalence (%). \* $\chi^2$  test. †Logistic regression adjusted for age (continuous variable).

Table 3—Unadjusted and adjusted ORs for the metabolic syndrome in Korean women

	n (%)	Metabolic syndrome			
		Unadjusted OR (95% CI)	P value	Adjusted OR* (95% CI)	P value
Menopause					
Premenopause	1,893 (13.8)	1		1	
Postmenopause on no HRT	778 (54.6)	7.50 (6.18–9.08)	<0.0001	1.60 (1.04–2.46)	0.032
BMI (kg/m <sup>2</sup> )					
<18.5	168 (3.6)	0.21 (0.09–0.47)	<0.0001	0.19 (0.08–0.47)	<0.0001
≥18.5 and <25	1,798 (15.2)	1		1	
≥25 and <30	625 (55.7)	6.99 (5.70–8.57)	<0.0001	6.26 (4.90–7.99)	<0.0001
>30	80 (73.8)	15.63 (9.34–26.14)	<0.0001	19.08 (10.57–34.45)	<0.0001
Smoking					
Nonsmoker	2,510 (24.9)	1		1	
Current smoker	128 (37.5)	1.81 (1.25–2.61)	0.002	0.99 (0.61–1.62)	0.966
Ex-smoker	33 (39.4)	1.96 (0.97–3.96)	0.062	1.51 (0.55–4.08)	0.423
Alcohol					
None	1,873 (28.7)	1.84 (1.48–2.29)	<0.0001	0.99 (0.75–1.32)	0.966
Current drinker	702 (17.9)	1		1	
Risk drinker	62 (22.6)	1.33 (0.71–2.49)	0.368	1.64 (0.76–3.52)	0.207
High-risk drinker	30 (26.7)	1.66 (0.72–3.82)	0.231	0.68 (0.24–1.96)	0.480
Education level (year)					
<9	1,034 (47.7)	12.26 (8.82–17.05)	<0.0001	1.51 (0.97–2.37)	0.071
9–12	999 (14.9)	2.36 (1.66–3.35)	<0.0001	1.21 (0.81–1.81)	0.362
≥13	636 (6.9)	1		1	
Household income†					
<1,000	329 (49.8)	5.14 (3.70–7.15)	<0.0001	0.94 (0.61–1.47)	0.943
1,000–1,499	638 (31.3)	2.36 (1.75–3.19)	<0.0001	1.19 (0.81–1.74)	0.386
1,500–2,499	1,103 (19.8)	1.28 (0.95–1.70)	0.101	1.03 (0.72–1.48)	0.873
≥2,500	457 (16.2)	1		1	
Exercise (times/week)					
No	2,050 (27.0)	1.27 (0.97–1.66)	0.083	1.21 (0.87–1.68)	0.248
1–2	234 (17.5)	1.33 (0.87–2.04)	0.185	1.00 (0.60–1.66)	0.993
≥3	382 (23.6)	1		1	
Residential area					
Large city	1,246 (23.8)	1		1	
Medium/small city	876 (20.2)	0.82 (0.66–1.02)	0.075	0.77 (0.58–1.02)	0.067
Rural area	647 (39.9)	2.22 (1.80–2.73)	<0.0001	1.22 (0.92–1.61)	0.161
Family history of CVD	384 (27.9)	1.14 (0.89–1.44)	0.299	1.73 (1.26–2.38)	0.001
Family history of diabetes	267 (25.5)	0.99 (0.74–1.32)	0.921	1.55 (1.07–2.27)	0.022

\*Multivariate-adjusted odds ratio. Age was inserted as a continuous variable. †Unit is thousands won (₩)/month.

women aged >50 years compared with men of the same age has been reported in several Korean studies (6,13–16) with various age-groups of peak prevalence. One Korean study reported an unusual peak prevalence in men of age 40–49 years (13). This study was performed in a medium-sized city in Korea. The subjects were aged ≥40 years and were adjusted to the standard world population of Segi.

To the best of our knowledge, our study is the first to demonstrate the effect of menopause on the metabolic syndrome in Korean women. This finding is consistent with a U.S. study (7) based on the National Health and Nutrition Examination Survey III. However, two small stud-

ies have reported no association between the risk of the metabolic syndrome and postmenopausal women. One study of 124 Argentine women reported that postmenopausal women had a 22% higher prevalence of the metabolic syndrome than premenopausal women, but this difference disappeared after an age adjustment (17). A study of 300 Swedish women reported that postmenopausal women not on HRT did not have an increased risk of the metabolic syndrome (18). These two studies appear to be less reliable due to their small sample size, which is in contrast to our study and the U.S. study (6).

Natural menopause is associated with

increased central adiposity (19). Abdominal obesity is a cardiovascular risk factor that is independent of overall adiposity (20,21). Middle-aged women gain ~0.55 kg per year, but most studies have not found that BMI increases independent of normal aging (22,23). In our study, the mean BMI of premenopausal and postmenopausal women was similar, but a large waist circumference was significantly associated with postmenopausal status after adjusting for age.

The influence of menopause on blood pressure is difficult to evaluate because menopause coincides with aging (24). Some studies have reported a strong association between blood pressure and

menopause, but other studies have not (24–26). In Korea, middle-aged women ( $\geq 50$  years) have a higher prevalence of hypertension than age-matched men (2). We found that mean systolic blood pressure and pulse pressure were higher in postmenopausal women than premenopausal women after adjusting for age.

Menopause is associated with an increase in total and LDL cholesterol and triglyceride levels (21,27), while HDL cholesterol level decreases with menopause (28,29). However, not all studies (28,30) agree with this conclusion. In our study, mean HDL cholesterol levels were similar in premenopausal and postmenopausal women.

Oral postmenopausal hormone therapy decreases LDL cholesterol level and increases HDL cholesterol and triglyceride levels (31). A number of studies have shown that women on HRT have a reduced incidence of coronary heart disease and stroke. However, controversy still exists regarding the effect of HRT in preventing CVD in postmenopausal women (32). The Women's Health Initiative study group reported that the overall health benefits did not exceed the risks of using combined estrogen plus progestin in healthy postmenopausal women and conjugated equine estrogen in postmenopausal women (mean age was 63.2 years) who had undergone a hysterectomy (33,34). However, the recent Women's Health Initiative report suggests that conjugated equine estrogen in postmenopausal women aged 50–59 years is associated with a lower risk of coronary heart disease (35). In our study, the small sample of women receiving HRT was excluded on account of its controversial effects. Further research will be needed to determine the effect of HRT on the metabolic syndrome in postmenopausal women.

There were major limitations in our study. Selection bias might have occurred during the exclusion of ineligible women. In addition, our study was cross-sectional. This design limits generalization of our findings to all Korean women. In our study, modifiable health behaviors such as smoking and alcohol intake were not associated with an increased risk of the metabolic syndrome. A Korean study using the data from KNHANES 1998 found a significant association between alcohol and smoking and the risk of the metabolic syndrome in women (6). An association with smoking and alcohol intake might not have been observed due to the im-

proper stratification, the limitations of a self-reported questionnaire, and other confounding factors.

In conclusion, there is an association between postmenopausal status and an increased risk of the metabolic syndrome independent of normal aging in Korean women.

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