Breastfeeding and Maternal Hypertension

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BACKGROUND
Little is known about the relationship between breastfeeding and hypertension. We performed this study to identify whether breastfeeding itself influenced maternal hypertension and whether degree of obesity or insulin sensitivity would contribute to the relationship between breastfeeding and hypertension in postmenopausal women.

METHODS
Our study population comprised 3,119 nonsmoking postmenopausal women aged 50 years or above in the 2010–2011 Korea National Health and Nutrition Examination Survey. We performed logistic regression analyses to examine the relationship between breastfeeding and hypertension and mediation analyses to examine the contributions of obesity and insulin sensitivity to the breastfeeding-hypertension relationship.

RESULTS
The odds ratios, with 95% confidence intervals, for hypertension among the highest quintile of number of breastfed children (5–11) and the highest quintile of duration of breastfeeding (96–324 months) were 0.49 (0.31–0.75) and 0.55 (0.37–0.82), respectively, compared to each of lowest quintile groups. The population attributable fractions of hypertension caused by breastfeeding 3 or fewer children and breastfeeding for 56 months or less were 10.2% ($P < 0.001$) and 6.5% ($P = 0.017$), respectively. In the mediation analysis, unexpectedly, increased insulin resistance significantly attenuated the protective effect on hypertension of having breastfed more children; additionally, greater obesity and insulin resistance significantly attenuated the protective effects on hypertension of having breastfed for longer.

CONCLUSIONS
More children breastfed and longer duration of breastfeeding were associated with lower risk of hypertension in postmenopausal women, and degree of obesity and insulin resistance moderated the breastfeeding-hypertension association.

Keywords: blood pressure; body mass index; breastfeeding; hypertension; insulin resistance; lactation.

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Elevated blood pressure is the greatest single risk factor for the worldwide burden of disease and mortality.[1,2] High blood pressure explained 9.4 million deaths and 7.0% of global disability-adjusted life years in 2010.[2] In 2000, 26.4% of adults worldwide (972 million) had hypertension, and 29.2% (1.56 billion) are expected to have it by 2025.[3] Global hypertension prevalence increased 4.9% between 2000 and 2010; in 2010, 31.1% of adults worldwide (1.39 billion) had it.[4] With global increases in elderly populations and in cardiovascular diseases, the prevalence of hypertension is consistently expected to increase and to remain a major public health challenge.

The World Health Organization and the American Academy of Pediatrics commonly recommend exclusive breastfeeding for six months, with ongoing partial breastfeeding after complementary foods are introduced.[5] Evidence from epidemiologic data has shown the beneficial effects of breastfeeding on the health of infants and their mothers.[5–14] It has been well documented that long-term breastfeeding is associated with reduced children's allergies, celiac disease, obesity, and diabetes mellitus.[5] However, the effects of breastfeeding on maternal health have been little studied compared with the effects on the children. Several studies consistently found that absent breastfeeding or premature discontinuation was associated with increased risks of diabetes mellitus,[6–9,15] dyslipidemia,[8,10,11,15] metabolic syndrome,[11,15] coronary heart disease,[12] and cardiovascular diseases.[8,15] However, compared with diabetes mellitus, few studies have established a clear relationship between breastfeeding and hypertension.[8,14,15]

Some common mechanisms have been proposed to underlie the relationships between breastfeeding and obesity-related diseases. First, maternal metabolism (e.g., fat accumulation and insulin resistance) may be "reset" by breastfeeding after pregnancy, which decreases the risk of these diseases.[16] Second, oxytocin release stimulated by breastfeeding[17,18] may be associated with the decreased risk of these diseases.[19–21] Third, ghrelin[22–25] and the protein peptide YY,[25–27] a gut-secreted peptide hormone that regulates appetite and is associated with breastfeeding,[28] may also reduce the risk of these diseases.

Because obesity tends to precede hypertension and other metabolic abnormalities, we speculated that it might play a

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role in the relationship between breastfeeding and hypertension.[29,30] Moreover, because obesity could affect hypertension occurrence through insulin sensitivity and other relevant pathways, we assumed that insulin sensitivity could also mediate the breastfeeding-hypertension relationship.[31] Therefore, we hypothesized that more children breastfed and longer breastfeeding duration would be associated with lower risk of hypertension, and that these relationships would be mediated by degree of obesity and insulin sensitivity. Thus, in this study, we examined the hypotheses in parous nonsmoking postmenopausal women aged 50 or above based on data from a nationwide representative population survey.

METHODS

The Korea National Health and Nutrition Examination Survey (KNHANES) is a cross-sectional survey conducted by the Korean Ministry of Health and Welfare to collect health and nutritional status data on a nationally representative population in South Korea; the survey consists of a health interview survey, a nutrition survey, and a health examination. The KNHANES uses stratified, multistage probability cluster sampling to select household units and annually selects 20 households per 192 sampling units for the 2010–2011 survey. A total of 8,473 participants (response rate: 77.5%) in the 2010 survey and 8,055 (response rate: 76.1%) in the 2011 survey completed a health interview survey and a heath health examination; all participants gave signed informed consent for their participation in the survey. The survey followed the Ethical Principles for Medical Research Involving Human Subjects defined by the Declaration of Helsinki, and was approved by the institutional review board of the Korean Centers for Disease Control and Prevention (approval nos. 2010-02CON-21-C and 2011-02CON-06-C). Detailed information is available elsewhere.[32]

The predictor of interest was the number of children breastfed and duration of breastfeeding, which were obtained from self-reported questionnaires, and our outcome of interest was hypertension. The KNHANES followed a stringent quality control protocol for measuring blood pressure. The Korean Centers for Disease Control and Prevention trained the KNHANES staff in spirometry, and staff members used a standard mercury sphygmomanometer (Baumanometer; WA Baum, Copiague, NY) to measure systolic and diastolic blood pressure in the sitting position after 5 minutes of rest. After the staff members measured blood pressure 3 times, they discarded the first measurements and the recorded the averages of the second and third measurements. Participants who had systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg or who used antihypertensive medication were diagnosed as having hypertension.[33]

For this study, we used the following variables, which were collected from the face-to-face interviews or the self-reported questionnaires: age (continuous), alcohol drinking status (drinking at least once a month), regular physical activity (at least 3 times a week for at least 20 minutes each time), income (at least US $2000), and number of pregnancies (continuous). We also used the KNHANES health examination survey data to collect the respondents' obesity and diabetes mellitus status. We based degree of obesity on body mass index (BMI, kg/m^2), which was calculated by dividing weight in kg by height in meters squared; weight and height were measured using a calibrated balance-beam scale (GL-6000–20; G-tech, Seoul, Korea) and a stadiometer (SECA 225; SECA, Hamburg, Germany), respectively. We defined obesity as BMI ≥25 kg/m^2.[34] Participants who had fasting glucose ≥126 mg/dl or used insulin or oral antihyperglycemic agents were diagnosed as having diabetes mellitus.[33] We calculated insulin sensitivity using the homeostasis model assessment of insulin resistance (HOMA-IR) calculated as fasting insulin (μU/ml) × fasting glucose (mg/dl)/22.5;[35] higher HOMA-IR indicates greater insulin resistance. However, HOMA-IR was measured only in KNHANES 2010 (n = 1,384).

We accounted for the sampling weights and complex multistage sampling design in our statistical analyses. Specifically, we compared the characteristics of participants with and without hypertension using the t test and Pearson's χ^2 test for continuous and categorical variables, respectively. We evaluated the risks for hypertension across the quintiles of number of children breastfed and duration of breastfeeding using logistic regression analyses and adjusting for age, alcohol drinking status, regular physical activity, income, number of pregnancies, obesity, and diabetes mellitus. Making the same adjustments, we also evaluated the relationships between hypertension and continuous number of children breastfed and duration of breastfeeding using logistic regression analyses. We calculated the population attributable fractions, with the adjustments for covariates, as measures of hypertension caused by number of children breastfed ≤3 and duration of breastfeeding ≤56 months using the AF package of R version 3.3.1 (R Foundation for Statistical Computing; http://www.r-project.org/).[36] We performed mediation analysis to evaluate whether increased BMI or HOMA-IR mediated the relationship between breastfeeding and hypertension using Mplus 7.3 statistical software (Muthén and Muthén 1998–2014); we used weighted least squares with the mean and variance adjusted estimator in the mediation analysis. We used the Sobel test to evaluate the significance of the indirect effects through BMI or HOMA-IR. With the exceptions of the population attributable fraction calculations and the mediation effects, we conducted all other data analyses using SAS 9.4 software (SAS Institute, Cary, NC) and considered $P < 0.05$ to be statistically significant.

RESULTS

From the postmenopausal women ≥50 years (n = 3,320), we excluded participants who had not given birth (n = 80), who were current smokers (n = 20), or who were not measured for blood pressure (n = 1); ultimately, we used the data from 3,119 menopausal women. The mean age of the study population was 64.1 years (Table 1), and mean number of children breastfed and duration of breastfeeding were 3.2 and 56.5 months, respectively. Prevalence of hypertension was 53.3%. Participants with hypertension had breastfed

significantly more children (3.4 vs. 2.8) and for longer (65.4 vs. 46.4 months) than had the women without hypertension.

We divided our study population into quintiles according to the number of children breastfed (0 to 1, 2, 3, 5 to 11) and duration of breastfeeding (0 to 17, 18 to 35, 36 to 52, 54 to 92, and 96 to 324 months), and we found no significant trends of hypertension prevalence across the quintiles for number of children breastfed (Table 2) or for duration of breastfeeding (Table 3) in age-adjusted models. After further adjustments for the other covariates, trends of hypertension prevalence became significant. In particular, the highest quintile of number of children breastfed (5–11) showed a 51% lower risk of hypertension (odds ratio [OR] = 0.49, 95% confidence interval [CI] = 0.31–0.75) compared with the lowest quintile (Table 2). The highest quintile of duration of breastfeeding (96–324 months) showed a 45% lower risk of hypertension (OR = 0.55, 95% CI = 0.37–0.82; Table 3).

We found significant linear relationships of number of children breastfed (OR = 0.90, 95% CI = 0.83–0.97, $P = 0.006$) and duration of breastfeeding (OR = 0.96, 95% CI = 0.93–0.99, $P = 0.016$) with odds of hypertension (Figure 1); the risk of hypertension lowered by 10% for every one-child increase in the number of children breastfed and by 4% for every 1-year increase in duration of breastfeeding. With adjustments for all covariates, the population attributable fractions of number of children breastfed ≤3 and duration of breastfeeding ≤56 months were 10.2% (95% CI = 4.6–15.7%, $P < 0.001$) and 6.5% (95% CI = 1.2–11.8%, $P = 0.017$), respectively.

In the mediation analysis, we found significant relationships between the number of children breastfed and duration of breastfeeding and hypertension when we considered the role of mediators such as BMI and HOMA-IR. However, unexpectedly, increased HOMA-IR attenuated the protective effect of more children breastfed on hypertension; increased BMI and HOMA-IR attenuated the protective effects of both more children breastfed and greater duration of breastfeeding on hypertension (Figure 2).

DISCUSSION

In this study, we found that both more children breastfed and longer duration of breastfeeding were significantly associated with lower risk of hypertension in postmenopausal women, and these associations remained significant in the relationships between the linear breastfeeding variables and hypertension. The estimated attributable fractions of hypertension resulting from number of children breastfed ≤3 and duration of breastfeeding ≤56 months were also significant. Interestingly, we also found moderation effects of BMI and HOMA-IR in the relationship between breastfeeding and hypertension.

Table 1. Characteristics of study participants

	No hypertension	Hypertension	*P* value
No. of participants (%)	1,443 (46.3%)	3,119 (53.7%)	
Age, year	60.9 ± 0.3	66.8 ± 0.3	<0.001
Lifestyle variable			
Alcohol consumption (≥once a month), %	27.4 ± 1.4	23.9 ± 1.3	0.07
Regular physical activity (≥20 minutes in each time and ≥3 times/week), %	11.2 ± 1.1	7.4 ± 0.9	<0.001
Socioeconomic status variable			
Education level, %			
≤Elementary school	52.3 ± 2.0	74.0 ± 1.4	<0.001
Middle school	20.9 ± 1.5	12.1 ± 1.0	
≥High school	26.8 ± 1.6	13.8 ± 1.1	
Income (≥2,000 US $/month), %	58.6 ± 1.7	44.6 ± 1.6	<0.001
Metabolic or disease variable			
BMI, kg/m^2	23.6 ± 0.1	24.9 ± 0.1	<0.001
Obesity (BMI ≥25 kg/m^2), %	29.4 ± 1.5	45.1 ± 1.4	<0.001
HOMA-IR, unit	2.4 ± 0.1	3.1 ± 0.1	<0.001
Diabetes mellitus, %	8.1 ± 0.9	20.3 ± 1.3	<0.001
Pregnancy and breastfeeding variable			
No. of pregnancies, *n*	4.7 ± 0.1	5.4 ± 0.1	<0.001
Breastfeeding information			
No. children breastfed, *n*	2.8 ± 0.1	3.4 ± 0.1	<0.001
Duration of breastfeeding, months	46.4 ± 1.5	65.4 ± 1.7	<0.001

Data present % and mean ± SE. Abbreviations: BMI, body mass index; HOMA-IR, homeostasis model assessment of insulin resistance.

Table 2. Odds ratios (95% confidence intervals) of hypertension according to number of children breastfed

	Quintiles of number of children breastfed (Range, no.)					
	Q1 (0–1)	Q2 (2)	Q3 (3)	Q4 (4)	Q5 (5 to 11)	*P* for trend
No. of participants	410	816	748	497	648	
No. of hypertension (%)	184 (44.9)	340 (41.7)	430 (57.5)	302 (60.8)	420 (64.8)	
Model 1	Reference	0.74 (0.55–0.99)*	0.96 (0.71–1.31)	0.81 (0.55–1.17)	0.73 (0.51–1.04)	0.24
Model 2	Reference	0.73 (0.54–1.00)*	0.86 (0.61–1.19)	0.69 (0.46–1.04)	0.60 (0.41–0.87)*	0.018
Model 3	Reference	0.67 (0.48–0.94)*	0.77 (0.54–1.09)	0.55 (0.35–0.86)*	0.49 (0.31–0.75)*	0.002

Model 1 adjusted for age. Model 2 adjusted for covariates in model 1: alcohol consumption, regular physical activity, education level, and income. Model 3 adjusted for covariates in model 2: obesity, diabetes mellitus, and number of pregnancies. *$P < 0.05$.

Table 3. Odds ratios (95% confidence intervals) of hypertension according to duration of breast feeding

	Quintiles of duration of breastfeeding (Range, mo)					
	Q1 (0–17)	Q2 (18–35)	Q3 (36–52)	Q4 (54–92)	Q5 (96–324)	*P* for trend
No. of participants	600	557	684	563	681	
No. of hypertension (%)	248 (41.3)	239 (42.9)	378 (55.3)	342 (60.8)	444 (65.2)	
Model 1	Reference	0.82 (0.61–1.11)	1.05 (0.79–1.40)	1.03 (0.73–1.44)	0.84 (0.60–1.17)	0.74
Model 2	Reference	0.80 (0.58–1.10)	0.92 (0.67–1.26)	0.83 (0.58–1.20)	0.69 (0.48–0.99)*	0.10
Model 3	Reference	0.75 (0.53–1.04)	0.77 (0.55–1.07)	0.73 (0.50–1.07)	0.55 (0.37–0.82)*	0.010

Model 1 adjusted for age. Model 2 adjusted for covariates in model 1: alcohol consumption, regular physical activity, education level, and income. Model 3 adjusted for covariates in model 2: obesity, diabetes mellitus, and number of pregnancies. *$P < 0.05$.

Some studies have investigated that women who breastfed for longer period had significantly lower risks of having hypertension[8,14] or high blood pressure,[37] comparing to parous women who never breastfed. Zang *et al.* found 13%, 17%, and 21% lowered risks of hypertension in women who breastfed for 0 to 6 months, 6 to 12 months, and more than 12 months, respectively, comparing to parous women who did not breastfeed.[14] Schwarz *et al.* showed that women who breastfed more than 12 months were less likely to have hypertension by 12% than women who never breastfed.[8] Another study also demonstrated the decreased risk of having high blood pressure in women who breastfed for longer than 6 months or 3 months per child, comparing to parous women who never breastfed.[37] Consistent with these findings, a review study documented that disruption of breastfeeding after pregnancy is related to long-term adverse consequences of maternal health outcome, and thus never or early termination of breastfeeding is related to an increased risk of hypertension.[15]

We showed that increased breastfeeding affected lower risks of hypertension. The mechanisms of the relationship between breastfeeding and hypertension are not clearly understood, although it has been suggested that breastfeeding-induced reset of maternal adaptation during pregnancy may reduce cardiovascular risks including hypertension.[16] Alternatively or additively, the release of oxytocin in response to breastfeeding may be associated with lower hypertension.[20] The mechanisms of the oxytocin–blood pressure relationship are not known; however, in the periphery, oxytocin may increase blood pressure by its effects on the kidney, blood vessels, and heart, where it interacts notably with nitric oxide and atrial natriuretic peptide; in the central nervous system, oxytocinergic fibers reach several important areas such as the vagal nuclei and the locus coeruleus, and the interactions of these with alpha 2-adrenoreceptors may influence the relationship between oxytocin and blood pressure.[38] Breastfeeding may also increase plasma ghrelin levels, which decrease food intake and body weight by increasing the release of agouti-related protein and neuropeptide Y in the arcuate nucleus.[39,40] Another representative breastfeeding-induced gut-secreted hormone, protein peptide YY, may also inhibit food intake and reduce weight gain accordingly.[40] These hormones are associated with hypertension.[24,26]

Unexpectedly, we found moderation effects of BMI and HOMA-IR on the relationships between breastfeeding and hypertension. In specific, the positive relationships of BMI and HOMA-IR with hypertension were consistent with the documented evidence, but the positive relationships of breastfeeding with BMI and HOMA-IR contradicted our understanding. Moreover, several epidemiologic studies showed the protective effects of breastfeeding on obesity,[41] insulin resistance,[41,42] and diabetes mellitus.[6–9] Therefore, our study results are difficult to explain by any existing biological mechanisms.

However, the significant relationships between breastfeeding and hypertension did not disappear. Alternatively, we speculated that these findings might have been because the KNHANES investigated participants at a certain time point in their later lives in a cross-sectional design but that obesity

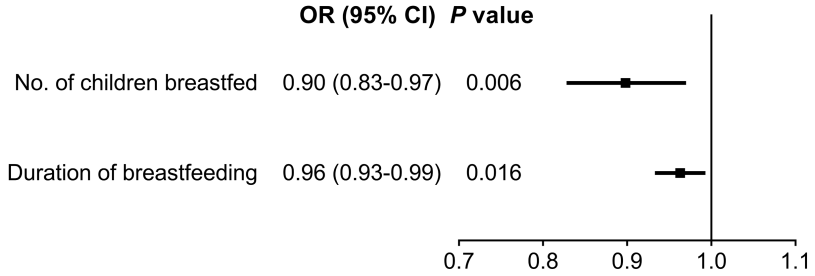

Figure 1. ORs (95% CIs) of hypertension according to number of children breastfed and duration of breastfeeding (unit, year). Each model adjusted for age, alcohol consumption, regular physical activity, education level, income, obesity, diabetes mellitus, and number of pregnancies. Abbreviations: CI, confidence interval; OR, odds ratio.

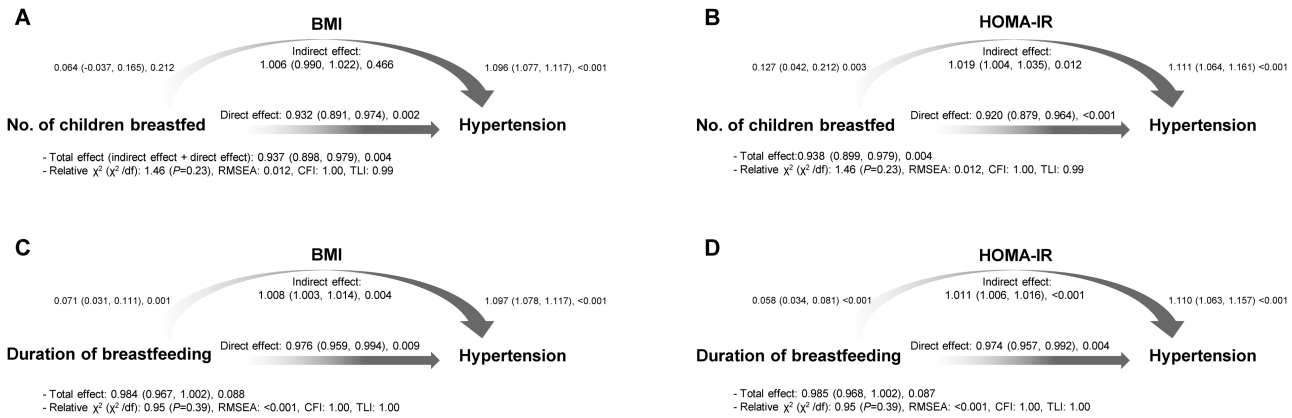

Figure 2. Direct, indirect, and total effects of breastfeeding on hypertension though body mass index (BMI) and homeostasis model assessment of insulin resistance (HOMA-IR). (**a**) predictor: number of children breastfed, mediator: BMI; (**b**) predictor: number of children breastfed, mediator: HOMA-IR; (**c**) predictor: duration of breastfeeding, mediator: BMI; (**d**) predictor: duration of breastfeeding, mediator: HOMA-IR. The numbers present unstandardized coefficients [95% confidence intervals (CIs)] and *P* values in the relationship between the predictors and mediators and odds ratios (95% CIs) and *P* values in other relationships. (a) and (c) adjusted for age, alcohol consumption, regular physical activity, education level, income, diabetes mellitus, and number of pregnancies, and (b) and (d) adjusted for age, alcohol consumption, regular physical activity, education level, income, obesity, and number of pregnancies. The relative χ^2 (χ^2/df) <3 with $P > 0.05$ of χ^2,[45] the root mean square error of approximation (RMSEA) ≤0.06, the comparative fit index (CFI) ≥0.95, and the Tucker Lewis index (TLI) ≥0.95 are accepted as indicating good model fit.[46] Therefore, all models showed overall good statistical fit.

can develop prior to some metabolic disturbances such as hypertension.[29,30] This study would have been unlikely to capture previous participants' BMI and HOMA-IR, which would lead to current blood pressure. Future prospective studies should clarify why our hypothetical mediators attenuated the relationship between breastfeeding and hypertension.

Of interest, we investigated whether number of pregnancies affected the risk of maternal hypertension through breastfeeding. Although the total effects of the number of pregnancies on maternal hypertension were not significant (OR of total effects = 1.00, 95% CI = 0.96–1.04, $P = 0.97$), women who was more pregnant had lower risks for hypertension either through increased number of children breastfed (OR of indirect effect = 0.98, 95% CI = 0.96–<1.00, $P = 0.021$) or extended duration of breastfeeding (OR of indirect effect = 0.99, 95% CI = 0.98–<1.00, $P = 0.023$) (data not shown). To our knowledge, this is the first study to attempt to find the mechanisms that underlie the breastfeeding-hypertension relationship, and another strength of the study was that our findings were results from a nationwide representative population. Nevertheless, our study has several limitations. First, because the KNHANES is a cross-sectional survey, it is unlikely to determine causative relationships. For example, we could not elucidate whether less breastfeeding-induced hypertension was actually moderated by past BMI or HOMA-IR. Second, we acquired our predictors of interest from self-reported questionnaires after a certain time had passed, which might have contributed to recall bias. However, the recall of breastfeeding tends to be both reliable and valid.[43,44] Third, it is necessary to be cautious in generalizing our study findings to women today because other breastfeeding-related cultures may differ from those of our study population.

In conclusion, breastfeeding fewer children and short-term breastfeeding were associated with higher risk of hypertension in parous postmenopausal women; 10.2% and 6.5% of the hypertension in our study population could be attributed 3 or fewer children breastfed and breastfeeding for 56 months or less, respectively. Our findings endorsed the current recommendations of breastfeeding for the benefit of maternal health in mothers' later lives. Greater attention should be paid to breastfeeding in developing more effective hypertension prevention strategies in parous

postmenopausal women. Prospective studies are required to address the mechanisms of breastfeeding-induced hypertension.

DISCLOSURE

All authors declared no conflict of interest.

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