Age at First Childbirth and Hypertension in Postmenopausal Women

Sangshin Park

Abstract—Whether age at first childbirth has an effect on hypertension incidence is unclear. The objectives of this study were to examine the relationship between age at first childbirth and hypertension and to examine whether degree of obesity, measured as body mass index, mediates age at first childbirth-related hypertension in postmenopausal women. This study analyzed 4779 postmenopausal women data from the Korea National Health and Nutrition Examination Survey 2010 to 2012. Logistic regression analyses were used to investigate relationship between age at first childbirth and hypertension. Mediation analysis was performed to examine the contribution of body mass index to age at first childbirth-related hypertension. Mean of participants' age at first childbirth and current age were 23.8 and 63.4 years, respectively. The prevalence of hypertension was 51.1%. Age at first childbirth was significantly associated with the prevalence of hypertension (odds ratio, 0.963; 95% confidence interval, 0.930–0.998; P=0.036). Women with age at first childbirth ≤19 years had significantly higher risk of hypertension (odds ratio, 1.61; 95% confidence interval, 1.17–2.23; P=0.004) compared with those >19 years. Multivariable-adjusted prevalence of hypertension was significantly lower in women who delivered the first infant at 20 to 24 (45.5%), 25 to 29 (46.1%), and ≥30 (39.9%) years compared with those at ≤19 years (58.4%). Body mass index completely mediated age at first childbirth–hypertension relationship (indirect effect: odds ratio, 0.992; 95% confidence interval, 0.987–0.998; P=0.008). Age at first childbirth was significantly associated with hypertension in postmenopausal women. Body mass index mediated the effects of age at first childbirth on hypertension. **(*Hypertension*. 2017;69:821-826. DOI: 10.1161/HYPERTENSIONAHA.117.09182.)**

Key Words: blood pressure ■ body mass index ■ hypertension ■ maternal age ■ pregnancy

High blood pressure and hypertension is the leading cause of cardiovascular disease and death worldwide: 13.5% of premature deaths, 47% of ischemic heart disease, and 54% of stroke are caused by high blood pressure.[1] People with hypertension have 63.3% lifetime risk for cardiovascular disease at 30 years of age, whereas those with normal blood pressure have 46.1%.[2] In 2010, globally 1.39 billion people (31.1% of total) had hypertension: 349 million (28.5% of total) in high-income countries and 1.04 billion (31.5% of total) in low- and middle-income countries.[3] Global age-standardized prevalence of hypertension increased by 4.9% from 2000 to 2010: 2.6% decrease in high-income countries but 7.7% increase in low- and middle-income countries.[3] Hypertension is consistently expected to be an important public health problem worldwide. In 2025, prevalence of hypertension is predicted to increase by 1.56 billion people (60% of total) worldwide in 2025.[4]

The extensive physical changes of childbearing have an effect on women's health status in their later life,[5–12] although pregnancy is a temporary stage unlike long-term chronic disease conditions (eg, diabetes mellitus). In South Korea, the mean maternal age at delivery was 31.5 years in 2013, and the fertility rate for women aged 15 to 19 was 1.7 births per 1000 women.[13] Previous studies have demonstrated the relationship between the timing of childbearing and health status in women's later life.[5–12] Early first childbirth has the relationship with the increased risks of osteoporosis,[5] diabetes mellitus,[6] metabolic syndrome,[7,8] coronary heart disease,[11] and cardiovascular disease mortality[10] in postmenopausal women. Relevant to hypertension, Lind et al[9] found that women who gave birth at the later age had lower odds of treatment for high blood pressure compared with those at the younger age. Another study also showed the negative relationship between age at first childbirth and high blood pressure, as a component of metabolic syndrome.[7] Recently, Parikh et al[12] found that younger age at first childbirth was associated with higher systolic and diastolic blood pressure and hypertension in women at age close to 40 years.

Most of the previous studies speculated that additional pregnancy and parity and exposure to circulating estrogen, caused by the early first childbirth, are likely to increase the risks of these chronic diseases.[5–9,14] In the basis of adverse effects of early childbirth, this study hypothesized that age at first childbirth was negatively associated with hypertension. In addition, we hypothesized that this association was mediated by degree of obesity, as measured by body mass index (BMI), because several lines of evidence support associations of

Received February 01, 2017; first decision February 19, 2017; revision accepted February 26, 2017.

From the Center for International Health Research, Rhode Island Hospital, and Department of Pediatrics, The Warren Alpert Medical School of Brown University, Providence, RI.

Correspondence to Sangshin Park, Department of Pediatrics, The Warren Alpert Medical School of Brown University, 55 Claverick St, Suite 101, Providence, RI 02903. E-mail dvm.spark@gmail.com

obesity with both age at first childbirth[15] and hypertension.[16] In this study, the above 2 hypotheses were tested in postmenopausal women using nationally representative population data.

Methods

This study used the data from the Korea National Health and Nutrition Examination Survey (KNHANES) from 2010 to 2012. This survey is a nationwide cross-sectional survey based on a stratified multistage probability sampling design, consisting of the health interview, behavioral and nutritional survey, and health examination. The KNHANES followed the Ethical Principles for Medical Research Involving Human Subjects defined by the Declaration of Helsinki. Each participant of KNHANES provided informed consent form. The approval of the institutional review board was not required because this survey is deidentified public data. Detailed information is available elsewhere.[17] Of the 13918 women participated in KNHANES 2010 to 2012, this study used data acquired from 4779 postmenopausal participants who had history of childbirth and were measured for blood pressure. We included only participants whose menopause occurred before their current age.

In KNHANES, medical staffs underwent a spirometry training course organized by the Korea Center for Disease Control and Prevention. They measured systolic and diastolic blood pressure using a standard mercury sphygmomanometer (Baumanometer; WA Baum Co, Inc, Copiague, NY) in the sitting position with 5-minute intervals. Blood pressure was measured 3×: the second and third measurements of blood pressure were recorded and averaged, whereas the first measurement was discarded. KNHANES implemented a stringent program for quality assurance and quality control of the blood pressure measurements. Hypertension was defined as systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or the use of antihypertensive medication.[18] Blood samples were collected from each KNHANES participant in the morning after overnight fast. Blood glucose, triglyceride, and cholesterol levels were analyzed using enzymatic methods with an autoanalyzer (Hitachi Automatic Analyzer 7600; Hitachi, Tokyo, Japan). Diabetes mellitus was defined as glucose ≥126 mg/dL or the use of antidiabetic medication (insulin or oral agents).[18] Dyslipidemia was defined as total cholesterol ≥240 mg/dL, high-density lipoprotein cholesterol <40 mg/dL, low-density lipoprotein cholesterol ≥160 mg/dL, triglyceride ≥200 mg/dL, or the use of antidyslipidemia medication.[18] This survey measured height to 0.1 cm in the upright position using a portable stadiometer (SECA 225; seca Deutschland, Hamburg, Germany) and body weight to 0.1 kg on a balanced scale (GL-6000-20; CAS, Seoul, South Korea). BMI was calculated as weight (in kilograms) divided by the squared of height (in meters). This study used variables acquired from self-reported questionnaires: current smoking status, current alcohol consumption, regular physical activity, education level, household income, age at menarche, age at menopause, duration of contraceptive use, duration of hormone therapy, age at first childbirth, age at last childbirth, and parity.

Table 1. Characteristics of Study Participants

Variable	Nonhypertension (n=2250)	Hypertension (n=2529)	*P* Value
Age, y	59.9 (59.3–60.4)	66.7 (66.2–67.2)	<0.001
Lifestyle variable			
Current smoking, %	5.8 (4.5–7.1)	3.8 (2.8–4.7)	0.013
Alcohol consumption (≥1× drink/mo), %	29.9 (27.6–32.2)	23.3 (21.2–25.4)	<0.001
Regular physical activity (≥20 min in each time and ≥3×/wk), %	11.5 (9.8–13.2)	7.2 (5.9–8.6)	23.3±1.1
Socioeconomic status variable			
Education level, %			
≤Elementary school	49.1 (46.1–52.1)	71.6 (69.3–73.9)	<0.001
Middle school	20.1 (17.7–22.4)	13.2 (11.4–14.9)	<0.001
≥High school	30.8 (28.1–33.5)	15.2 (13.3–17.1)	<0.001
Income (≥3000 US$/mo), %	41.1 (38.3–43.9)	29.7 (27.2–32.2)	<0.001
Disease variable			
Diabetes mellitus, %*	8.4 (6.9–9.9)	20.5 (18.4–22.6)	<0.001
Dyslipidemia, %†	40.0 (37.5–42.5)	51.4 (48.8–54.0)	<0.001
Body mass index, kg/m^2	23.7 (23.5–23.9)	25.0 (24.8–25.2)	<0.001
Reproductive variable			
Age at menarche, y	16.0 (15.9–16.1)	16.2 (16.1–16.3)	<0.001
Age at menopause, y	48.4 (48.1–48.7)	48.8 (48.5–49.1)	<0.001
Duration of contraceptive use, mo	4.3 (3.3–5.2)	6.6 (5.6–7.6)	<0.001
Duration of hormone therapy, mo	5.6 (4.8–6.5)	4.2 (3.4–5.0)	<0.001
Age at first childbirth, y	24.4 (24.2–24.6)	23.3 (23.1–23.4)	<0.001
Age at last childbirth, y	30.0 (29.8–30.3)	31.1 (30.8–31.3)	<0.001
Parity, n	3.0 (2.9–3.1)	3.6 (3.6–3.7)	<0.001

Data are presented as mean or % (95% confidence interval).

*Defined as fasting glucose ≥126 mg/dL or under ongoing treatments.

†Defined as high-density lipoprotein cholesterol <40 mg/dL, low-density lipoprotein cholesterol ≥160 mg/dL, total cholesterol ≥240 mg/dL, triglyceride ≥200 mg/dL, or under ongoing treatments.

This study followed the analytic guidelines for KNHANES which considered survey complex sampling structure with stratification, cluster, and sampling weights to extrapolate the study findings to the entire South Korean population.[17] Nonhypertensive and hypertensive groups were compared using *t* test for continuous variables and the use of Pearson χ^2 test for categorical variables with taking consideration into survey design. Survey logistic regression analyses were performed to address the relationship between age at first childbirth and hypertension. As the predictor, age at first childbirth was analyzed with both continuous (unit, year) and dichotomized (≤19 versus >19 years) formats. Survey models adjusted for age (<55, 55–59, 60–64, 65–69, 70–74, versus ≥75 years), smoking status (current smoking versus nonsmoking), alcohol consumption (≥1× per month versus <1× per month), regular physical activity (≥20 min in each time or ≥3× per week versus <20 minutes in each time and <3× per week), education level (≤elementary, middle, versus ≥high school), household income (≥3000 versus <3000 US$/mo), diabetes mellitus (yes versus no), dyslipidemia (yes versus no), age at menarche (unit, year), age at menopause (unit, year), duration of contraceptive use (unit, months), duration of hormone therapy (unit, months), age at last childbirth (unit, year), and parity (unit, n). The multivariable-adjusted prevalence of hypertension were compared among 4 groups of participants aggregated according to the age at first childbirth: ≤19, 20 to 24, 25 to 29, and ≥30 years. Because age at first childbirth may be highly correlated with age at last childbirth, it is not clear whether hypertension status is affected by age at first or last childbirth. Therefore, to observe the effects of timing of last childbirth, this study additionally performed logistic regression analyses for the age at last childbirth (both continuous and dichotomized [≤24 versus >24 years] formats), as a predictor, with an adjustment for age at first childbirth and other confounders. Cutoff points for age at first (19 years) and last childbirth (24 years) were determined based on the relationship between mothers' early first (≤19 years)[5,11] and last (≤24 years)[19,20] childbirth and increased risks of other chronic diseases. Mediation analysis using structural equation modeling was performed to address whether age at first childbirth–hypertension was explained by BMI (Mplus 7.3 statistical software; Muthén and Muthén 1998–2014). The mediation analysis accommodated the complex sampling structure of the KNHANES and adjusted for the same confounders used in multivariable regression models. Complete mediation was defined as a significance of indirect effect with nonsignificance of direct effect between age at first childbirth and hypertension.[21] This study statistically analyzed the data using SAS 9.4 statistical software (SAS Institute, Cary, NC), with the exception of the mediation analysis. The *P* value <0.05 was considered to be statistically significant.

Results

Of 4779 study population, the mean age was 63.4 years (Table 1). Mean of participants' age at their first and last childbirth were 23.8 and 30.6 years, respectively. The prevalence of hypertension was 51.1% (n=2529). Hypertensive participants were older, less smoking and alcohol consumption, less exercise, less educated, and more obese and had lower income than nonhypertensive. Hypertensive participants delivered the first infant in younger age and the last infant in older age than nonhypertensive.

In the age-adjusted model, the risk of hypertension significantly decreased by 3.5% for every 1-year increase in the age at first childbirth (odds ratio [OR], 0.965; 95% confidence interval [CI], 0.943–0.987; *P*=0.002; Table 2). Women who delivered the first infant in younger age ≤19 years had higher risk for hypertension (OR, 1.63; 95% CI, 1.22–2.18; *P*<0.001), compared with those at first childbirth >19 years. After further adjustments for all other confounders, both continuous (OR, 0.963; 95% CI, 0.930–0.998; *P*=0.036) and dichotomized (OR, 1.61; 95% CI, 1.17–2.23; *P*=0.004) predictors remained significant. Multivariable-adjusted prevalence of hypertension was significantly lower in women who delivered the first infant in 20 to 24 (45.5%), 25 to 29 (46.1%), and ≥30 (39.9%) years, compared with those who delivered the first infant in ≤19 years (58.4%; Figure 1).

Table 2. ORs (95% CIs) of Hypertension According to Age at First or Last Birth

Predictor	Model	OR (95% CI)	*P* Value
Age at first childbirth			
Age at first childbirth, y	1	0.965 (0.943–0.987)	0.002
	2	0.964 (0.942–0.987)	0.002
	3	0.966 (0.940–0.992)	0.012
	4	0.963 (0.930–0.998)	0.036
Age at first childbirth ≤19 y (vs >19 y)	1	1.63 (1.22–2.18)	<0.001
	2	1.65 (1.24–2.19)	<0.001
	3	1.66 (1.21–2.28)	0.002
	4	1.61 (1.17–2.23)	0.004
Age at last childbirth			
Age at last childbirth, y	1	0.985 (0.968–1.002)	0.090
	2	0.985 (0.968–1.002)	0.088
	3	0.984 (0.962–1.007)	0.185
	4	1.003 (0.974–1.034)	0.834
Age at last childbirth ≤24 y (vs >24 y)	1	1.32 (0.97–1.80)	0.082
	2	1.33 (0.98–1.81)	0.071
	3	1.36 (0.96–1.91)	0.081
	4	1.19 (0.83–1.71)	0.334

CI indicates confidence interval; and OR, odds ratio. Model 1, adjusted for age. Model 2, model 1 plus smoking status, alcohol consumption status, regular physical activity. Model 3, model 2 plus education level, household income, diabetes mellitus, dyslipidemia, age at menarche, age at menopause, duration of contraceptive use, duration of hormone therapy, and parity. Model 4: model 3 plus age at last childbirth (only for age at first childbirth predictor) or age at first childbirth (only for age at last childbirth predictor).

In mediation analysis, the total effect of age at first childbirth on hypertension was significant (OR, 0.977; 95% CI, 0.957–0.998; *P*=0.030; Figure 2). BMI completely mediated the relationship between age at first childbirth and hypertension, which indicates the significant indirect effect (OR, 0.992; 95% CI, 0.987–0.998; *P*=0.008) but nonsignificant direct effect (OR, 0.984; 95% CI, 0.965–1.005; *P*=0.137).

Discussion

This study demonstrates that women who delivered the first infant in younger age were likely to have high risk of hypertension. BMI was an important mediator of the association between age at first childbirth and hypertension. Because hypertension is an important risk factor for cardiovascular disease and mortality, our findings suggest that careful observation for hypertension is required for postmenopausal women who delivered the first infant in younger age, in particular <20 years.

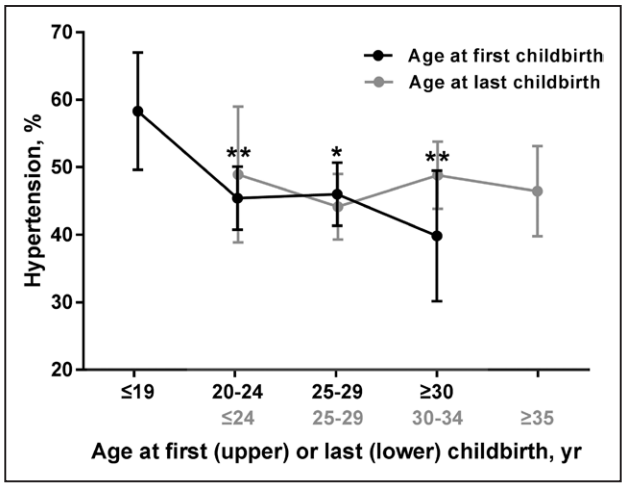

Figure 1. Adjusted prevalence of hypertension according to age at first and last childbirth. The error bars show 95% confidence interval. Participants aggregated according to the age at first childbirth of ≤19 (n=420), 20 to 24 (n=2517), 25 to 29 (n=1597), and ≥30 (n=245) y and the age at last childbirth of ≤24 (n=325), 25 to 29 (n=1807), 30 to 34 (n=1676), and ≥35 (n=971) y. Multivariable logistic regression models were used to estimate prevalence with adjustments for age, smoking status, alcohol consumption status, regular physical activity, education level, household income, diabetes mellitus, dyslipidemia, age at menarche, age at menopause, duration of contraceptive use, duration of hormone therapy, parity, and age at last childbirth (only for age at first childbirth predictor) or age at first childbirth (only for age at last childbirth predictor). *P value <0.05 and **P value <0.001 in comparisons with age at first childbirth ≤19 y. Any significant differences among age at last childbirth were found.

This study showed that age at first childbirth influenced BMI. Several mechanisms may be suggested to explain an increased BMI in postmenopausal women who delivered the first infant early. First, weight retention during pregnancy and changes of lifestyle caused by pregnancy at early age (eg, increased food intakes and physical activities toward a more sedentary)[22] may increase the degree of obesity in their later life. Second, child-rearing from earlier age may make women to carry out restricted physical activities focusing on nurturing and housework from earlier age, which may increase their BMI.[23] Third, earlier exposure to high levels of estrogen by early pregnancy may lead to an increase in body fat because early pregnancy make fat storage of energy to be more efficient in preparation for fetal development and lactation.[24] Fourth, women who delivered the first childbirth at early age are more likely to have higher number of parity, which may accumulate weight retention and contribute to obesity in their later life accordingly.[15,25–27]

Expectedly, this study found the significant relationship between BMI and hypertension. Although biological mechanisms of BMI–hypertension relationship are not clearly explained, BMI is speculated to influence on hypertension through complex interactions between oxidative stress, inflammation, hyperleptinemia, insulin resistance, the renin–angiotensin–aldosterone system, and the renal sympathetic nervous system.[28,29]

Complete mediation of BMI on age at first childbirth–hypertension association indicates that this association may not be explained by other mechanisms. However, it should be noticed that diabetes mellitus or dyslipidemia, which were adjusted in the models, also can play a role as a mediator in the association between age at first childbirth and hypertension. This study did not perform mediation analysis for these potential mediators because these and hypertension frequently occur at the same time whereas obesity is prone to occur earlier than hypertension and other metabolic disturbances.[30,31]

Another interesting point of this study was that effect of age at first childbirth was consistently significant even after adjusting for parity and age at last childbirth. We expected that late pregnancy might increase the risk of hypertension in postmenopausal period because of oxidative stress and inflammation in late pregnancy, but any significant trends across age at last childbirth were not observed. Early first childbirth affecting increased BMI may be more influential on hypertension in menopause women than late last childbirth inducing adverse health effects. Future studies should clarify which mechanisms are involved in the associations of hypertension with age at both first and last childbirth.

To our knowledge, this is the first study to address the relationship between age at first childbirth and hypertension and the underlying mechanism in this relationship. Another strength of this study was that our hypotheses were examined using a nationally representative sample of Korean postmenopausal women. However, this study has several limitations. First, because KNHANES is a cross-sectional survey, causality

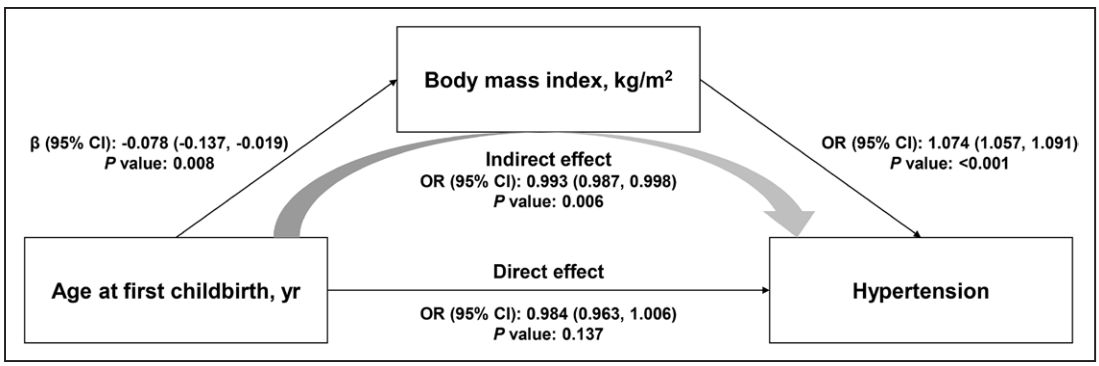

Figure 2. Mediation analysis to determine the relationship between age at first childbirth (unit, y) and hypertension through body mass index (unit, kg/m^2). Odds ratio (OR; 95% confidence interval [CI]; P value) of total effect was 0.977 (0.957–0.998; 0.030). Adjusted for age, smoking status, alcohol consumption status, regular physical activity, education level, household income, diabetes mellitus, dyslipidemia, age at menarche, age at menopause, duration of contraceptive use, duration of hormone therapy, parity, and age at last childbirth.

cannot be clearly drawn. In particular, because this study used participants' current BMI instead of weight gain from the first childbirth, we were unable to confirm that hypertension was affected by increased BMI caused by early childbirth. Second, reproductive factors, including age at first childbirth, were determined by self-report questionnaires, which may induce recall bias, but recall of reproductive factors is expected to be valid and reliable.[32] Third, statistical models of this study did not adjust for some confounders, such as women's birth weight at pregnancy. Fourth, extrapolation of our findings to today's reproductive-aged women should be cautious because current pregnancy-related environments and cultures are difference from the past in which study population of this study was childbearing age.

Perspectives

Age at first childbirth is significantly associated with hypertension in Korean postmenopausal women. In this population, BMI was a significant mediator in the timing of first childbirth–hypertension association. These findings indicate that more attention should be paid to postmenopausal women with pregnancy at younger age of first childbirth for effective prevention of their hypertension. Further prospective studies are needed to elucidate the timing of first childbirth–hypertension association and the role of degree of obesity in this association.

Disclosures

None.

References

1. Lawes CM, Vander Hoorn S, Rodgers A; International Society of Hypertension. Global burden of blood-pressure-related disease, 2001. *Lancet*. 2008;371:1513–1518. doi: 10.1016/S0140-6736(08)60655-8.
2. Rapsomaniki E, Timmis A, George J, Pujades-Rodriguez M, Shah AD, Denaxas S, White IR, Caulfield MJ, Deanfield JE, Smeeth L, Williams B, Hingorani A, Hemingway H. Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1·25 million people. *Lancet*. 2014;383:1899–1911. doi: 10.1016/S0140-6736(14)60685-1.
3. Mills KT, Bundy JD, Kelly TN, Reed JE, Kearney PM, Reynolds K, Chen J, He J. Global disparities of hypertension prevalence and control: a systematic analysis of population-based studies from 90 countries. *Circulation*. 2016;134:441–450. doi: 10.1161/CIRCULATIONAHA.115.018912.
4. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. *Lancet*. 2005;365:217–223. doi: 10.1016/S0140-6736(05)17741-1.
5. Cho GJ, Shin JH, Yi KW, Park HT, Kim T, Hur JY, Kim SH. Adolescent pregnancy is associated with osteoporosis in postmenopausal women. *Menopause*. 2012;19:456–460. doi: 10.1097/gme.0b013e3182337150.
6. Kim JH, Jung Y, Kim SY, Bae HY. Impact of age at first childbirth on glucose tolerance status in postmenopausal women: the 2008-2011 Korean National Health and Nutrition Examination Survey. *Diabetes Care*. 2014;37:671–677. doi: 10.2337/dc13-1784.
7. Sim JH, Chung D, Lim JS, Lee MY, Chung CH, Shin JY, Huh JH. Maternal age at first delivery is associated with the risk of metabolic syndrome in postmenopausal women: from 2008-2010 Korean National Health and Nutrition Examination Survey. *PLoS One*. 2015;10:e0127860. doi: 10.1371/journal.pone.0127860.
8. Cho GJ, Park HT, Shin JH, Kim T, Hur JY, Kim YT, Lee KW, Kim SH. The relationship between reproductive factors and metabolic syndrome in Korean postmenopausal women: Korea National Health and Nutrition Survey 2005. *Menopause*. 2009;16:998–1003. doi: 10.1097/gme.0b013e3181a03807.
9. Lind JM, Hennessy A, Chiu CL. Association between a woman's age at first birth and high blood pressure. *Medicine*. 2015;94:e697. doi: 10.1097/MD.0000000000000697.
10. Chang HS, Odongua N, Ohrr H, Sull JW, Nam CM. Reproductive risk factors for cardiovascular disease mortality among postmenopausal women in Korea: the Kangwha Cohort Study, 1985-2005. *Menopause*. 2011;18:1205–1212. doi: 10.1097/gme.0b013e31821adb43.
11. Beard CM, Fuster V, Annegers JF. Reproductive history in women with coronary heart disease. A case-control study. *Am J Epidemiol*. 1984;120:108–114.
12. Parikh NI, Norberg M, Ingelsson E, Cnattingius S, Vasan RS, Domellöf M, Jansson JH, Edstedt Bonamy AK. Association of pregnancy complications and characteristics with future risk of elevated blood pressure: the Västerbotten Intervention Program. *Hypertension*. 2017;69:475–483. doi: 10.1161/HYPERTENSIONAHA.116.08121.
13. Organisation for Economic Co-operation and Development. OECD Family Database: SF2.3. Age of Mothers at Childbirth and Age-Specific Fertility. http://www.oecd.org/els/soc/SF_2_3_Age_mothers_childbirth.pdf. Accessed February 23, 2017.
14. Tian Y, Wu J, Xu G, Shen L, Yang S, Mandiwa C, Yang H, Liang Y, Wang Y. Parity and the risk of cataract: a cross-sectional analysis in the Dongfeng-Tongji cohort study. *Br J Ophthalmol*. 2015;99:1650–1654. doi: 10.1136/bjophthalmol-2015-306653.
15. We JS, Han K, Kwon HS, Kil K. Effect of maternal age at childbirth on obesity in postmenopausal women: a nationwide population-based study in Korea. *Medicine*. 2016;95:e3584. doi: 10.1097/MD.0000000000003584.
16. Shihab HM, Meoni LA, Chu AY, Wang NY, Ford DE, Liang KY, Gallo JJ, Klag MJ. Body mass index and risk of incident hypertension over the life course: the Johns Hopkins Precursors Study. *Circulation*. 2012;126:2983–2989. doi: 10.1161/CIRCULATIONAHA.112.117333.
17. Korea Center for Disease Control and Prevention. Korea National Health and Nutrition Examination Survey. http://knhanes.cdc.go.kr. Accessed September 23, 2016.
18. National Cholesterol Education Program Expert Panel on Detection E, and Treatment of High Blood Cholesterol in Adults. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation*. 2002;106:3143–3421.
19. Whiteman DC, Siskind V, Purdie DM, Green AC. Timing of pregnancy and the risk of epithelial ovarian cancer. *Cancer Epidemiol Biomarkers Prev*. 2003;12:42–46.
20. Setiawan VW, Pike MC, Karageorgi S, et al; Australian National Endometrial Cancer Study Group. Age at last birth in relation to risk of endometrial cancer: pooled analysis in the epidemiology of endometrial cancer consortium. *Am J Epidemiol*. 2012;176:269–278. doi: 10.1093/aje/kws129.
21. Baron RM, Kenny DA. The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. *J Pers Soc Psychol*. 1986;51:1173–1182.
22. Harris HE, Ellison GT, Clement S. Do the psychosocial and behavioral changes that accompany motherhood influence the impact of pregnancy on long-term weight gain? *J Psychosom Obstet Gynaecol*. 1999;20:65–79.
23. Gunderson EP, Murtaugh MA, Lewis CE, Quesenberry CP, West DS, Sidney S. Excess gains in weight and waist circumference associated with childbearing: The Coronary Artery Risk Development in Young Adults Study (CARDIA). *Int J Obes Relat Metab Disord*. 2004;28:525–535. doi: 10.1038/sj.ijo.0802551.
24. O'Sullivan AJ. Does oestrogen allow women to store fat more efficiently? A biological advantage for fertility and gestation. *Obes Rev*. 2009;10:168–177. doi: 10.1111/j.1467-789X.2008.00539.x.
25. Weng HH, Bastian LA, Taylor DH Jr, Moser BK, Ostbye T. Number of children associated with obesity in middle-aged women and men: results from the health and retirement study. *J Womens Health*. 2004;13:85–91. doi: 10.1089/154099904322836492.
26. Koch E, Bogado M, Araya F, Romero T, Díaz C, Manriquez L, Paredes M, Román C, Taylor A, Kirschbaum A. Impact of parity on anthropometric measures of obesity controlling by multiple confounders: a cross-sectional study in Chilean women. *J Epidemiol Community Health*. 2008;62:461–470. doi: 10.1136/jech.2007.062240.
27. Hajiahmadi M, Shafi H, Delavar MA. Impact of parity on obesity: a cross-sectional study in Iranian women. *Med Princ Pract*. 2015;24:70–74. doi: 10.1159/000368358.
28. Hall JE, do Carmo JM, da Silva AA, Wang Z, Hall ME. Obesity-induced hypertension: interaction of neurohumoral and renal mechanisms. *Circ Res*. 2015;116:991–1006. doi: 10.1161/CIRCRESAHA.116.305697.
29. Kotsis V, Stabouli S, Papakatsika S, Rizos Z, Parati G. Mechanisms of obesity-induced hypertension. *Hypertens Res*. 2010;33:386–393. doi: 10.1038/hr.2010.9.

30. Cercato C, Mancini MC, Arguello AM, Passos VQ, Villares SM, Halpern A. Systemic hypertension, diabetes mellitus, and dyslipidemia in relation to body mass index: evaluation of a Brazilian population. *Rev Hosp Clin Fac Med Sao Paulo*. 2004;59:113–118. doi: /S0041-87812004000300004.
31. Schmidt MI, Watson RL, Duncan BB, Metcalf P, Brancati FL, Sharrett AR, Davis CE, Heiss G. Clustering of dyslipidemia, hyperuricemia, diabetes, and hypertension and its association with fasting insulin and central and overall obesity in a general population. Atherosclerosis Risk in Communities Study Investigators. *Metabolism*. 1996;45:699–706.
32. Bosetti C, Tavani A, Negri E, Trichopoulos D, La Vecchia C. Reliability of data on medical conditions, menstrual and reproductive history provided by hospital controls. *J Clin Epidemiol*. 2001;54:902–906.

Novelty and Significance

What Is New?

- This is the first study to show the association between age at first childbirth and hypertension in postmenopausal women.
- Body mass index mediated age at first childbirth–hypertension relationship.

What Is Relevant?

- To prevent hypertension in postmenopausal women, attention should be paid to women with pregnancy at younger age of first childbirth.

Summary

Age at first childbirth was significantly associated with hypertension in postmenopausal women; body mass index mediated this association.

Hypertension
Journal of the American Heart Association

Age at First Childbirth and Hypertension in Postmenopausal Women

Sangshin Park

Hypertension. 2017;69:821-826; originally published online March 27, 2017;
doi: 10.1161/HYPERTENSIONAHA.117.09182
Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0194-911X. Online ISSN: 1524-4563