## JKMS

## Original Article Preventive & Social Medicine

Check for updates

## Blood Pressure Curve for Children Less than 10 Years of Age: Findings from the Ewha Birth and Growth Cohort Study

Hye Ah Lee <sup>(D)</sup>,<sup>1</sup> Bohyun Park <sup>(D)</sup>,<sup>2</sup> Eun Ae Park <sup>(D)</sup>,<sup>3</sup> Su Jin Cho <sup>(D)</sup>,<sup>3</sup> Hae Soon Kim <sup>(D)</sup>,<sup>3</sup> Eun Jeong Choi <sup>(D)</sup>,<sup>2</sup> Nam-eun Kim <sup>(D)</sup>,<sup>2</sup> and Hyesook Park <sup>(D)</sup>,<sup>2</sup>

<sup>1</sup>Clinical Trial Center, Mokdong Hospital, Ewha Womans University, Seoul, Korea <sup>2</sup>Department of Preventive Medicine, Ewha Womans University School of Medicine, Seoul, Korea <sup>3</sup>Department of Pediatrics, Ewha Womans University School of Medicine, Seoul, Korea

## ABSTRACT

**Background:** Routine blood pressure (BP) measurement is recommended to begin at 3 years of age, but there are no national BP reference values for Korean children less than 7 years of age. Therefore, we developed sex-, age-, and height-specific BP reference values for non-overweight children aged 3–9 years.

**Methods:** We analyzed the data of 416, 340, 321, 323, and 332 subjects aged 3, 5, 7, 8, and 9 years, respectively, who participated in the Ewha Birth and Growth Cohort Study. BP percentile curves were generated using generalized additive models for location, scale, and shape. Reference values for the 50th, 90th, and 95th percentiles of BP were determined according to sex, age, and height percentiles.

**Results:** In both boys and girls, a gradual increase in systolic blood pressure (SBP) with age was more pronounced than that in diastolic blood pressure (DBP). In boys, the reference values for 90th percentile of SBP/DBP at median height for children aged 3 and 9 years were 105/69 and 118/70, respectively. In girls, the reference values corresponding to the above conditions were 105/69 and 116/70, respectively. Among children aged 7–9 years of median height, the 90th percentile of SBP in the current study was lower and that of DBP was similar to the national reference values of Korea. For children aged < 7 years of median height, the reference value for SBP, but not that for DBP, was similar to that developed in the European study. **Conclusion:** Although further research is needed, our findings could be used to help identify high BP in children less than 10 years of age.

Keywords: Blood Pressure; Children; Hypertension

## INTRODUCTION

According to the 2018 Korea Hypertension Fact Sheet, the number of people in Korea with hypertension in 2016 was 11 million, compared to 7.6 million in 1998.<sup>1</sup> The prevalence of high blood pressure (BP), which promotes the development of cardiovascular and cerebrovascular diseases,<sup>1</sup> is considerable (around 30% of the Korean population aged  $\geq$  30 years).<sup>2</sup> The World Health Organization reported that 9 million people die annually due to hypertension.<sup>3</sup> High BP is a modifiable factor, so early intervention and prevention are important to reduce the burden of disease.

### OPEN ACCESS

Received: Sep 30, 2019 Accepted: Jan 28, 2020

#### Address for Correspondence: Hyesook Park, MD, PhD

Department of Preventive Medicine, Ewha Womans University School of Medicine, 25 Magokdong-ro 2-gil, Gangseo-gu, Seoul 07804, Korea.

E-mail: hpark@ewha.ac.kr

© 2020 The Korean Academy of Medical Sciences.

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (https:// creativecommons.org/licenses/by-nc/4.0/) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

#### ORCID iDs

Hye Ah Lee 厄 https://orcid.org/0000-0002-4051-0350 Bohyun Park 🕩 https://orcid.org/0000-0002-8538-9662 Eun Ae Park 厄 https://orcid.org/0000-0002-1685-4276 Su Jin Cho 🕩 https://orcid.org/0000-0002-3851-9073 Hae Soon Kim 厄 https://orcid.org/0000-0002-6976-6878 Eun Jeong Choi 匝 https://orcid.org/0000-0002-7698-3424 Nam-eun Kim 🕩 https://orcid.org/0000-0002-8826-7644 Hyesook Park 问 https://orcid.org/0000-0002-9359-6522

# JKMS

#### Funding

This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (NRF-2017R1D1A1B03030088).

#### Disclosure

The authors have no potential conflicts of interest to disclose.

#### **Author Contributions**

Conceptualization: Park H. Data curation: Park B, Choi EJ, Kim NE. Formal analysis: Lee HA. Methodology: Lee HA. Writing - original draft: Lee HA. Writing - review & editing: Park EA, Cho SJ, Kim HS, Park H. Although the prevalence of pediatric hypertension is low (< 5%),<sup>4</sup> it is reportedly associated with chronic diseases in later life, 5-7 so monitoring of the BP of children is important. A recent study that used data from the Bogalusa Heart Study, which involved a 36-year followup, reported that children with elevated BP and hypertension had 45% and 66% higher risks, respectively, of developing hypertension as adults compared to normotensive children.<sup>5</sup> In addition, elevated BP during childhood is associated with risk for metabolic syndrome and left ventricular hypertrophy in later life.<sup>5</sup> A systematic meta-analysis reported a strong correlation of childhood and adult BP across a diverse population.<sup>6</sup> Therefore, to prevent hypertension in adulthood it is necessary to maintain normal BP from early childhood. monitor BP regularly, and initiate interventions when required. In 2017, the American Academy of Pediatrics (AAP) published new guidelines for the screening and management of high BP in children and adolescents. Those guidelines recommend routine BP measurement beginning at 3 years of age and that monitoring of the BP of children with low birth weight, premature birth, or congenital heart disease should begin measuring earlier than 3 years of age.<sup>8,9</sup> National BP reference values for Korean children and adolescents were published in 2007 but do not apply to children less than 7 years old.<sup>10</sup> Improved Korean Children and Adolescent National Growth Charts were also published in 2017, but did not include BP charts. Although there are BP reference values for children in the United States and Europe,<sup>9,11</sup> these may not be applicable to Korean children. In addition, differences in the relationship between body size and BP according to ethnicity have been reported.12,13

Using data from the Ewha Birth and Growth Cohort Study, we developed sex-, age-, and height-specific BP reference values for children aged 3–9 years. Current reference values used to determine cutoff values for identifying children with elevated BP with high sensitivity are typically based on data from non-overweight children.<sup>9,11</sup> Therefore, we created a BP reference curve for non-overweight children.

## **METHODS**

#### **Study subjects**

This study used data from the Ewha Birth and Growth Cohort Study, a longitudinal birth cohort established at Mokdong Hospital, Ewha Womans University, Seoul, Korea, from 2001 to 2006 (baseline n = 940). This cohort was established for the purpose of identifying risk and preventive factors related to growth and disease susceptibility. Beginning in 2005, the subjects underwent follow-up evaluations at 3 and 5 years of age, and annually after the age of 7 years. On average, about half of the subjects were contacted and three-quarters participated in the follow-up program. Detailed information on the cohort composition and methodology has been reported elsewhere.<sup>14,15</sup> Of the subjects, 471, 400, 364, 382, and 400 aged 3, 5, 7, 8, and 9 years, respectively, participated in the follow-up program. We excluded subjects with missing data for height or BP. Accordingly, complete data were available for 453, 391, 361, 380, and 390 subjects aged 3, 5, 7, 8, and 9 years, respectively. We excluded overweight and obese subjects (body mass index [BMI] ≥ 85th percentile based on the 2007 Korean Children and Adolescent National Growth Charts). The proportions of those who were overweight or obese at 3, 5, 7, 8, and 9 years of age were 7.3, 13.0, 11.1, 14.6, and 14.4%, respectively (boys, 12.9% and girls, 11.0%). Thus, the data for 416, 340, 321, 323, and 332 subjects aged 3, 5, 7, 8, and 9 years, respectively, were analyzed. Of these, 26.9, 17.4, 8.7, 9.6, and 13.0% of the subjects were born preterm at each age, respectively.

#### **Measurements**

When subjects visited the hospital for follow-up, their anthropometric measurements and BP were evaluated by trained researchers. Height and weight were measured with no shoes while wearing light clothing using a stadiometer and a calibrated scale (DS-102; Dong Sahn Jenix Co. Ltd., Seoul, Korea). BMI was calculated as weight divided by height in meters squared. The sex- and age-specific *z*-scores of height, weight, and BMI were calculated based on the 2007 Korean Children and Adolescent National Growth Charts.<sup>10</sup>

Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured twice using an automated instrument (Dinamap Procare 200; GE Inc., Milwaukee, WI, USA) with the correct cuff size with the subject in a stable position. The correct cuff size was determined based on the circumference of the upper arm. Two measurements, taken within 5 minutes of each other, were averaged. Generally, a BP between the 90th and 94th percentiles in children is considered prehypertension and a BP  $\geq$  95th percentile is considered hypertension.<sup>16</sup> In this study, children with an average SBP or DBP  $\geq$  90th percentile or > 120/80 mmHg were defined as having elevated BP.

#### **Statistical analyses**

Using the generalized additive model for location, scale, and shape (GAMLSS) package in R software (ver. 3.5.0 for Microsoft Windows<sup>™</sup>; R Foundation, Vienna, Austria),<sup>17</sup> we generated a BP percentile curve for non-overweight children, stratified by sex and age. The GAMLSS method is an extension of the Lambda-Mu-Sigma (LMS) method for modeling the distribution of the outcome of interest depending on multiple covariates, while accounting for the dispersion, skew, and kurtosis of the distribution.<sup>18</sup> We evaluated various distribution models (e.g., Box-Cox Cole-Green, Box-Cox power exponential, and Box-Cox t) to choose the best one. Goodness of fit was assessed using the generalized Akaike information criterion and by generating Q-Q plots. Based on the selected model, the reference 50th, 90th, and 95th percentile values of BP for boys and girls were estimated for the 5th, 10th, 25th, 50th, 75th, 90th, and 95th percentiles of height for age.

Based on the definition of prehypertension, the 90th percentile of BP was compared to that in the 2017 Pediatric Hypertension Guidelines of the AAP,<sup>9</sup> the Identification and Prevention of Dietary- and Lifestyle-Induced Health Effects in Children and Infants (IDEFICS) study in Europe,<sup>11</sup> the international BP reference values from a multinational study,<sup>19</sup> and the national growth chart released in 2007 by the Korea Centers for Disease Control and Prevention (KCDC).<sup>10</sup>

#### **Ethics statement**

The study protocol was approved by the Institutional Review Board (IRB) of Ewha Womans University Hospital (IRB No. EUMC 2018–03–017, EUMC 2018–02–019). The parents or guardians of the subjects provided informed consent for participation in the follow-up program.

## RESULTS

The characteristics of the subjects are listed in **Table 1**. Among non-overweight children (n = 416, 340, 321, 323, and 332 subjects aged 3, 5, 7, 8, and 9 years, respectively), the sex ratio was close to 1.0 (boys, 49.9% and girls, 50.1%). Compared with the anthropometric measurements of all Korean children (presented as z-scores), the heights of children aged 3

| Gender | Subjects               |                | 3 yr               |                 | 5 yr                 |                 | 7 yr                 |                 | 8 yr                 |                 | 9 yr                 |
|--------|------------------------|----------------|--------------------|-----------------|----------------------|-----------------|----------------------|-----------------|----------------------|-----------------|----------------------|
|        |                        | Mean ± SD      | Median (range)     | Mean ± SD       | Median (range)       | Mean ± SD       | Median (range)       | Mean ± SD       | Median (range)       | Mean ± SD       | Median (range)       |
| Boys   | No. of subjects        |                | 209                |                 | 171                  |                 | 153                  |                 | 167                  |                 | 164                  |
|        | Height, cm             | $97.8 \pm 4.5$ | 97.7 (87.0, 117.1) | $111.6 \pm 5.0$ | 111.9 (94.5, 128.6)  | $123.8 \pm 5.3$ | 123.9 (110.8, 139.8) | $129.5 \pm 5.2$ | 129.7 (117.2, 144.8) | $134.2 \pm 5.4$ | 134.0 (119.7, 149.0) |
|        | Z value of             | $-0.3 \pm 1.1$ | -0.3 (-3.1, 3.9)   | $-0.1 \pm 1.1$  | 0.0 (-4.0, 3.7)      | $0.0 \pm 1.0$   | 0.0 (-2.7, 2.9)      | $0.1 \pm 0.9$   | 0.1 (-2.2, 2.6)      | $0.0 \pm 0.9$   | 0.0(-2.5, 2.4)       |
|        | height                 |                |                    |                 |                      |                 |                      |                 |                      |                 |                      |
|        | Weight, kg             | $14.6 \pm 1.7$ | 14.6 (10.6, 20.7)  | $19.2 \pm 2.2$  | 19.1 (14.2, 25.4)    | $23.8 \pm 3.4$  | 23.3 (15.5, 36.7)    | $27.0 \pm 4.0$  | 26.4 (18.7, 40.4)    | $30.6 \pm 4.6$  | 29.8 (20.4, 45.6)    |
|        | Z value of             | $-0.5 \pm 1.1$ | -0.4 (-3.5, 2.5)   | $-0.3 \pm 1.0$  | -0.2 (-3.3, 1.6)     | $-0.4 \pm 1.0$  | -0.4 (-4.3, 1.9)     | $-0.3 \pm 0.9$  | -0.3 (-2.8, 1.7)     | $-0.2 \pm 0.8$  | -0.3 (-2.6, 1.6)     |
|        | weight                 |                |                    |                 |                      |                 |                      |                 |                      |                 |                      |
|        | BMI, kg/m <sup>2</sup> | $15.3 \pm 1.1$ | 15.2 (12.0, 17.3)  | $15.4 \pm 1.0$  | 15.4 (13.2, 17.4)    | $15.5 \pm 1.4$  | 15.4 (10.4, 18.8)    | $16.1 \pm 1.6$  | 16.0 (12.8, 19.7)    | $16.9 \pm 1.9$  | 16.8 (12.3, 20.8)    |
|        | Z value of BMI         | $-0.6 \pm 1.1$ | -0.6 (-4.5, 1.0)   | $-0.3 \pm 0.8$  | -0.2 (-2.6, 1.0)     | $-0.6 \pm 0.9$  | -0.6 (-6.2, 1.0)     | $-0.5 \pm 0.8$  | -0.5 (-2.7, 1.0)     | $-0.4 \pm 0.8$  | -0.3 (-3.1, 1.0)     |
|        | SBP, mmHg              | $93.2 \pm 9.9$ | 93.5 (64.0, 126.0) | $99.4 \pm 8.7$  | 99.0 (76.0, 128.0)   | $100.3 \pm 8.7$ | 99.0 (77.0, 129.0)   | $104.4 \pm 9.6$ | 104.0 (82.0, 134.0)  | $106.9 \pm 9.4$ | 105.0 (84.0, 137.0)  |
|        | DBP, mmHg              | $59.4 \pm 8.0$ | 60.0 (41.0, 80.0)  | $58.7 \pm 6.2$  | 59.0 (42.0, 85.0)    | $58.3 \pm 6.4$  | 58.5 (42.0, 82.0)    | $60.4 \pm 6.6$  | 60.0 (47.0, 80.0)    | $63.0 \pm 6.0$  | 63.0 (50.0, 79.0)    |
| Girls  | No. of subjects        |                | 207                |                 | 169                  |                 | 168                  |                 | 156                  |                 | 168                  |
|        | Height, cm             | $96.2 \pm 4.2$ | 95.8 (87.0, 106.3) | $111.2 \pm 4.7$ | 110.9 (101.7, 123.5) | $122.7 \pm 4.9$ | 122.4 (112.1, 141.9) | $129.3 \pm 4.8$ | 129.2 (117.6, 141.2) | $134.1 \pm 5.3$ | 134.0 (115.6, 145.9) |
|        | Z value of             | $-0.2 \pm 1.0$ | -0.3 (-2.6, 2.2)   | 0.1 ± 1.1       | 0.0 (-2.1, 2.9)      | $0.0 \pm 0.9$   | 0.0 (-2.1, 3.5)      | $0.3 \pm 0.8$   | 0.2 (–1.9, 2.2)      | $0.1 \pm 0.8$   | 0.1 (-3.1, 1.9)      |
|        | height                 |                |                    |                 |                      |                 |                      |                 |                      |                 |                      |
|        | Weight, kg             | $14.1 \pm 1.5$ | 14.0 (10.2, 18.1)  | $18.8 \pm 2.1$  | 18.8 (14.1, 24.3)    | $23.2 \pm 3.1$  | 22.8 (16.7, 30.4)    | $26.7 \pm 3.5$  | 26.3 (18.7, 36.5)    | $29.8 \pm 4.2$  | 29.1 (18.3, 41.2)    |
|        | Z value of             | $-0.5 \pm 1.0$ | -0.4 (-3.7, 1.7)   | $-0.2 \pm 1.0$  | 0.0 (–3.0, 1.7)      | $-0.3 \pm 0.9$  | -0.3 (-2.8, 1.3)     | $-0.1 \pm 0.8$  | -0.1 (-2.4, 1.5)     | $-0.2 \pm 0.8$  | -0.3 (-3.1, 1.4)     |
|        | weight                 |                |                    |                 |                      |                 |                      |                 |                      |                 |                      |
|        | BMI, $kg/m^2$          | $15.2 \pm 1.1$ | 15.1 (12.5, 17.1)  | $15.2 \pm 1.0$  | 15.3 (12.7, 17.0)    | $15.3 \pm 1.4$  | 15.2 (11.9, 18.3)    | $15.9 \pm 1.5$  | 15.7 (13.0, 18.8)    | $16.5 \pm 1.7$  | 16.5 (13.2, 19.9)    |
|        | Z value of BMI         | $-0.5 \pm 0.9$ | -0.5 (-3.3, 1.0)   | $-0.3 \pm 0.8$  | -0.1 (-2.7, 0.9)     | $-0.5 \pm 0.9$  | -0.5 (-3.5, 1.0)     | $-0.4 \pm 0.8$  | -0.4 (-2.3, 1.0)     | $-0.3 \pm 0.8$  | -0.3 (-2.2, 1.0)     |
|        | SBP, mmHg              | $92.9 \pm 8.8$ | 93.0 (72.0, 120.0) | $97.9 \pm 9.2$  | 98.0 (75.0, 131.0)   | $97.6 \pm 8.8$  | 98.0 (74.0, 127.0)   | $101.6 \pm 9.8$ | 102.0 (74.0, 138.0)  | $104.5 \pm 9.8$ | 104.0 (82.0, 131.0)  |
|        | DBP, mmHg              | $59.5 \pm 7.2$ | 59.0 (45.0, 81.0)  | $59.1 \pm 6.5$  | 59.0 (45.0, 90.0)    | $58.4 \pm 6.3$  | 58.0 (44.0, 81.0)    | $60.0 \pm 6.7$  | 60.0 (45.0, 77.0)    | $62.5 \pm 7.3$  | 62.0 (47.0, 88.0)    |

years tended to be slightly lower (boys,  $-0.3 \pm 1.1$  standard deviation [SD]; girls,  $-0.2 \pm 1.0$  SD), while those of children of other ages were similar.

The 50th, 90th, and 95th percentiles for SBP and DBP were calculated according to the percentile of height for age of boys and girls (**Tables 2** and **3**, respectively). For non-overweight children, the best-fit model for the SBP and DBP of boys was the log-linked versions of BCCG (**Table 2**), and that for girls was the BCCG model (**Table 3**). Overall, BP

| Table 2. BP distribution by percentil | es in non-overweig | ht boys < 10 years old |
|---------------------------------------|--------------------|------------------------|
|---------------------------------------|--------------------|------------------------|

|         | Boys  |        |     | Sy   | stolic BP | by percen | tiles, mm | Hg   |      | Diastolic BP by percentiles, mmHg |      |      |      |      |      |      |  |
|---------|-------|--------|-----|------|-----------|-----------|-----------|------|------|-----------------------------------|------|------|------|------|------|------|--|
| Age, yr | Heigh | nt, cm | 5th | 10th | 25th      | 50th      | 75th      | 90th | 95th | 5th                               | 10th | 25th | 50th | 75th | 90th | 95th |  |
| 3       | 50th  | 96     | 90  | 91   | 92        | 93        | 95        | 96   | 96   | 59                                | 59   | 59   | 58   | 58   | 58   | 58   |  |
|         | 90th  | 102    | 102 | 103  | 104       | 105       | 106       | 107  | 108  | 70                                | 70   | 69   | 69   | 68   | 68   | 68   |  |
|         | 95th  | 103    | 106 | 106  | 107       | 108       | 109       | 110  | 111  | 74                                | 73   | 73   | 72   | 72   | 71   | 71   |  |
| 4       | 50th  | 104    | 93  | 94   | 95        | 96        | 97        | 98   | 99   | 58                                | 58   | 58   | 58   | 58   | 58   | 58   |  |
|         | 90th  | 110    | 105 | 106  | 107       | 108       | 109       | 109  | 110  | 69                                | 69   | 68   | 68   | 68   | 68   | 67   |  |
|         | 95th  | 111    | 108 | 109  | 110       | 111       | 112       | 113  | 114  | 72                                | 72   | 71   | 71   | 71   | 70   | 70   |  |
| 5       | 50th  | 111    | 96  | 97   | 97        | 98        | 99        | 100  | 100  | 58                                | 58   | 58   | 58   | 58   | 59   | 59   |  |
|         | 90th  | 118    | 108 | 108  | 109       | 110       | 111       | 111  | 111  | 68                                | 68   | 68   | 67   | 67   | 67   | 67   |  |
|         | 95th  | 120    | 111 | 112  | 112       | 113       | 114       | 115  | 115  | 71                                | 71   | 70   | 70   | 70   | 70   | 70   |  |
| 6       | 50th  | 117    | 98  | 98   | 99        | 100       | 101       | 101  | 102  | 58                                | 58   | 58   | 59   | 59   | 59   | 60   |  |
|         | 90th  | 123    | 109 | 110  | 111       | 111       | 112       | 113  | 114  | 68                                | 67   | 67   | 67   | 67   | 68   | 68   |  |
|         | 95th  | 124    | 113 | 113  | 114       | 115       | 116       | 117  | 118  | 70                                | 70   | 70   | 70   | 70   | 70   | 71   |  |
| 7       | 50th  | 123    | 99  | 100  | 100       | 101       | 103       | 104  | 104  | 58                                | 59   | 59   | 59   | 60   | 61   | 61   |  |
|         | 90th  | 128    | 111 | 111  | 112       | 113       | 115       | 116  | 117  | 67                                | 67   | 67   | 68   | 68   | 69   | 69   |  |
|         | 95th  | 131    | 114 | 115  | 116       | 117       | 119       | 120  | 121  | 70                                | 70   | 70   | 70   | 71   | 71   | 72   |  |
| 8       | 50th  | 129    | 100 | 101  | 102       | 103       | 105       | 107  | 107  | 59                                | 59   | 60   | 60   | 62   | 62   | 63   |  |
|         | 90th  | 136    | 112 | 112  | 114       | 115       | 118       | 120  | 121  | 67                                | 67   | 68   | 69   | 70   | 71   | 71   |  |
|         | 95th  | 139    | 116 | 116  | 118       | 120       | 122       | 125  | 126  | 70                                | 70   | 71   | 71   | 72   | 73   | 74   |  |
| 9       | 50th  | 135    | 101 | 102  | 104       | 105       | 107       | 109  | 110  | 59                                | 60   | 61   | 62   | 63   | 64   | 64   |  |
|         | 90th  | 142    | 113 | 114  | 116       | 118       | 121       | 123  | 124  | 68                                | 68   | 69   | 70   | 71   | 72   | 72   |  |
|         | 95th  | 143    | 117 | 118  | 120       | 122       | 126       | 128  | 129  | 70                                | 71   | 71   | 72   | 74   | 74   | 75   |  |

BP = blood pressure.

#### Table 3. BP distribution by percentiles in non-overweight girls < 10 years old

|         | Girls |        |     | S    | ystolic BP | by percer | ntile, mm | Hg   |      | Diastolic BP by percentile, mmHg |      |      |      |      |      |      |  |
|---------|-------|--------|-----|------|------------|-----------|-----------|------|------|----------------------------------|------|------|------|------|------|------|--|
| Age, yr | Heigh | it, cm | 5th | 10th | 25th       | 50th      | 75th      | 90th | 95th | 5th                              | 10th | 25th | 50th | 75th | 90th | 95th |  |
| 3       | 50th  | 96     | 89  | 90   | 92         | 93        | 94        | 95   | 96   | 56                               | 57   | 58   | 59   | 60   | 60   | 60   |  |
|         | 90th  | 102    | 99  | 101  | 103        | 105       | 106       | 107  | 108  | 66                               | 67   | 68   | 69   | 69   | 70   | 69   |  |
|         | 95th  | 103    | 103 | 104  | 106        | 108       | 109       | 111  | 111  | 69                               | 70   | 71   | 72   | 73   | 73   | 73   |  |
| 4       | 50th  | 104    | 93  | 94   | 95         | 96        | 96        | 97   | 97   | 59                               | 59   | 60   | 60   | 59   | 59   | 59   |  |
|         | 90th  | 110    | 105 | 105  | 107        | 108       | 108       | 109  | 109  | 69                               | 69   | 70   | 69   | 69   | 68   | 68   |  |
|         | 95th  | 111    | 108 | 109  | 110        | 111       | 112       | 112  | 112  | 72                               | 73   | 73   | 73   | 72   | 72   | 71   |  |
| 5       | 50th  | 111    | 96  | 96   | 96         | 97        | 97        | 97   | 98   | 60                               | 59   | 59   | 59   | 58   | 58   | 58   |  |
|         | 90th  | 118    | 108 | 108  | 108        | 109       | 109       | 109  | 110  | 69                               | 69   | 69   | 68   | 68   | 67   | 67   |  |
|         | 95th  | 120    | 111 | 111  | 112        | 112       | 113       | 113  | 113  | 73                               | 73   | 72   | 72   | 71   | 71   | 70   |  |
| 6       | 50th  | 117    | 97  | 97   | 97         | 98        | 98        | 99   | 100  | 59                               | 59   | 59   | 58   | 58   | 58   | 58   |  |
|         | 90th  | 123    | 109 | 109  | 109        | 109       | 110       | 111  | 111  | 69                               | 68   | 68   | 67   | 67   | 67   | 68   |  |
|         | 95th  | 124    | 112 | 112  | 113        | 113       | 113       | 114  | 115  | 72                               | 72   | 71   | 70   | 70   | 70   | 71   |  |
| 7       | 50th  | 123    | 97  | 97   | 98         | 99        | 100       | 101  | 102  | 58                               | 58   | 58   | 58   | 59   | 60   | 60   |  |
|         | 90th  | 128    | 109 | 109  | 110        | 111       | 112       | 113  | 114  | 68                               | 67   | 67   | 67   | 68   | 69   | 69   |  |
|         | 95th  | 131    | 113 | 113  | 113        | 114       | 115       | 117  | 118  | 71                               | 71   | 70   | 70   | 71   | 72   | 72   |  |
| 8       | 50th  | 129    | 98  | 98   | 100        | 101       | 103       | 104  | 105  | 58                               | 58   | 58   | 59   | 61   | 62   | 62   |  |
|         | 90th  | 136    | 110 | 110  | 111        | 112       | 115       | 117  | 119  | 67                               | 67   | 68   | 68   | 70   | 71   | 72   |  |
|         | 95th  | 139    | 113 | 113  | 115        | 116       | 119       | 121  | 122  | 70                               | 70   | 71   | 71   | 73   | 74   | 75   |  |
| 9       | 50th  | 135    | 99  | 100  | 101        | 103       | 105       | 107  | 108  | 58                               | 59   | 60   | 61   | 62   | 63   | 64   |  |
|         | 90th  | 142    | 111 | 112  | 113        | 116       | 119       | 120  | 122  | 67                               | 68   | 69   | 70   | 72   | 73   | 74   |  |
|         | 95th  | 143    | 114 | 115  | 117        | 120       | 122       | 124  | 126  | 70                               | 71   | 72   | 73   | 75   | 76   | 77   |  |

BP = blood pressure.

percentiles tended to be higher in boys than in girls at any age (**Tables 2** and **3**), and BP for height tended to be lower in non-overweight children than in all children (including overweight and obese children) (data not shown). **Fig. 1** shows the sex- and age-specific BP percentiles (5th, 10th, 25th, 50th, 75th, 90th, and 95th) at median height of non-overweight children. In both boys and girls, the gradual increase in SBP with age was more pronounced than that in DBP.

The reference values for 90th percentile of BP by sex at median (i.e., 50th percentile) height for age from the US (2017 AAP guidelines), Europe (IDEFICS study), a multinational study, and the KCDC are shown in **Fig. 2**. The aforementioned multinational study reported the lowest 90th percentile SBP value, and our findings were most similar to those of the European IDEFICS study. The DBP values were higher than the US reference values for children < 6 years old, but that trend was reversed in older children. The reference SBP value of the KCDC was higher than that in the current study while the reference DBP value was similar.

Based on our reference values, 18.5% of children 3 to 9 years old had an elevated BP (boys, 19.5% and girls, 17.5%). Among children 7–9 years old, 17.7% had an elevated BP (boys, 19.2% and girls, 16.1%), which is similar to the proportion determined using the KCDC reference values (total, 18.4%; boys, 18.6%; and girls, 18.1%) (data not shown).

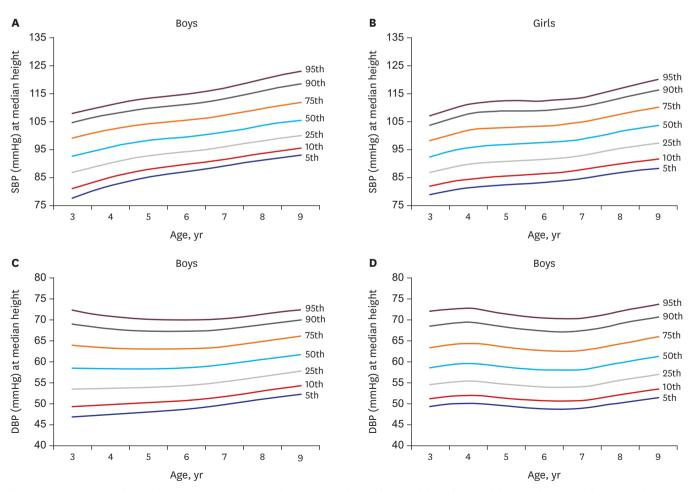
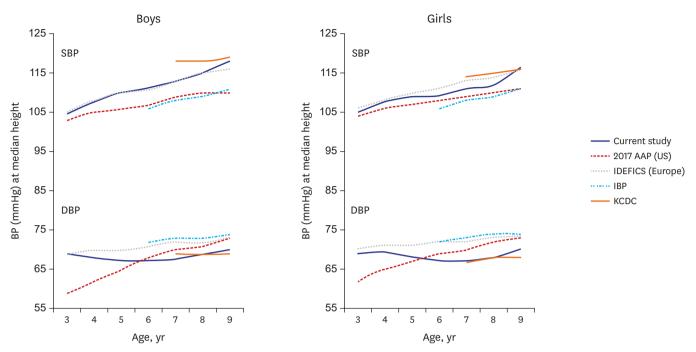


Fig. 1. BP percentiles at median height for age in non-overweight boys and girls. (A) SBP for boys, (B) SBP for girls, (C) DBP for boys, and (D) DBP for girls. BP = blood pressure, SBP = systolic blood pressure, DBP = diastolic blood pressure.



**Fig. 2.** Comparison of the 90th percentile BP values in prior reports and the current study. BP values are for the median height for age. BP = blood pressure, SBP = systolic blood pressure, DBP = diastolic blood pressure, AAP = American Academy of Pediatrics, IDEFICS = Identification and Prevention of Dietary- and Lifestyle-Induced Health Effects in Children and Infants, IBP = international blood pressure derived from a multinational data, KCDC = Korean Center for Disease Control and Prevention.

### DISCUSSION

We propose sex-, age-, and height-specific BP reference values for children aged 3–9 years using data from the Ewha Birth and Growth Cohort Study. To the best of our knowledge, this study is the first to propose BP reference values for children aged 3–9 years in Korea using the data of non-overweight children.

The life-course approach to the prevention of chronic disease has led to an emphasis on the need for early intervention for risk factors during childhood. Although there is insufficient evidence of the benefit of screening for elevated BP among children,<sup>7</sup> the American Heart Association and the European Society of Hypertension recommend routine BP measurement in children older than 3 years in a medical setting.<sup>8,20</sup> To determine cutoff BP values for identifying children with elevated BP with greater sensitivity, BP reference values for non-overweight children were recently proposed.<sup>11,19,21,22</sup> Pediatric BP is closely related to anthropometric measurements and the reference BP is typically based on height rather than weight. This may be because the relationship between changes in BP and in weight is, at least in part, a consequence of a physiopathological process.<sup>11</sup> Indeed, BMI, which is closely correlated with weight, is an independent predictor of hypertension in children and in adults. <sup>11,23</sup> In the same context, the BP reference values in the fourth report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents in 2004 were in 2017 updated based on the normative BP values for non-overweight children.<sup>9</sup>

A study by Sohn et al.<sup>24</sup> reported the BP percentiles according to sex, age, and height of children under 6 years of age, but overweight and obese children were included in the

analyses. Compared to our values for children aged 3-6 years, the SBP reference values in that study were 6–9 mmHg higher in boys and 3–8 mmHg higher in girls. A multinational study of non-overweight children, including Korean teenagers, proposed BP reference values only for those aged 6–17 years.<sup>19</sup> Compared to the national reference values of the KCDC, the 90th percentile of SBP at ages 7–9 years in our study was lower, and that of the DBP was similar. The cutoff values proposed in this study result in more boys than girls with high BP compared to those based on the national reference values of the KCDC. However, the national reference values were developed based in part on data from overweight and obese children. When the data for overweight and obese children were included, the BP reference values also increased in this study, but were lower than those of the KCDC. The difference may be due to the different statistical analysis methods used. The GAMLSS method is more flexible than the LMS method in terms of applying various distributions of the outcome of interest.<sup>18</sup> It is also able to incorporate a larger number of covariates to maximize the model fit. Because of these advantages, several studies have proposed BP reference values using the GAMLSS method.<sup>11,19,21</sup> Furthermore, the BP data in this study were obtained using the same instrument as the national reference values of the KCDC.<sup>25</sup> but there was bias caused by operator and measurement time.

The 90th percentiles of SBP for boys and girls were similar to the BP reference values for children younger than 7 years derived from the European IDEFICS study. The US DBP reference values of boys and girls are lower than those in this study for children aged < 6 years, and vice versa for older children. The US BP reference values are based on auscultatory measurements, and oscillometric devices systematically overestimate BP compared to the values determined by auscultation.<sup>9,26</sup> In addition, the median height for age differs among countries, and European children have a high median height for age. Although controversial, differences in the relationship between body size and BP according to ethnicity have been reported.<sup>12,13</sup> Therefore, it would be appropriate to develop and use population-based BP reference values to screen high-risk groups.<sup>21</sup>

Because the BP reference values were obtained from a statistical distribution rather than based on their associations with disease, they cannot be directly applied for diagnostic purposes. Thus, our results enable the identification of children who require BP monitoring, but are unsuitable as cutoff values for diagnostic purposes. Considering the variation in BP, multiple measurements are needed to diagnose hypertension. Identification of high-risk children with an elevated BP would enable early interventions, such as improvement of the diet or promotion of physical activity, to prevent hypertension in adulthood. A high BMI is an independent risk factor for hypertension, and in this study 39.6% (boys, 40.6% and girls, 38.3%) of overweight and obese children had an elevated BP, a higher frequency than that in normal-weight children (total, 15.7%; boys, 16.4%; and girls, 15.0%). Thus, it is important for overweight and obese children to return to a normal weight.

This study had several limitations. The sample was small and not representative of the Korean population, limiting the generalizability of the results. The cohort was established in a tertiary hospital, so the percentage of children with low birth weight or preterm birth was higher than in the general population. This may have influenced the results because the risk for high BP increases with the degree of immaturity at birth.<sup>27</sup> Considering the increasing number of low-birth-weight births, this factor should be considered in future studies. In addition, we did not assess external validity, and so further research is needed. The trends in body size among Korean children and adolescents have slowed, but the average height

of children in the 2016–2017 Korea National Health and Nutrition Examination Survey was increased compared to that in the 2005 survey by the Korean Pediatric Society<sup>28</sup>; indeed, the average height of children aged 3–6 years has recently increased by 2–5 cm (data not shown). Therefore, by reflecting the current body size of children, it is necessary to develop the normal ranges of BP for Korean children of all ages. Finally, regarding the accuracy of the device, the device used in this study can measure BP in children and adolescents, but was not sufficiently accurate to recommend for measuring DBP.<sup>29</sup> Therefore, it is not interchangeable with auscultatory measurements, so care must be taken when interpreting BP measurements. In addition, the intraclass correlation coefficient (ICC) values of intra-observer variability were 0.877 (95% confidence interval [CI], 0.833–0.906) for SBP and 0.767 (95% CI, 0.743–0.789) for DBP, while the ICC values of inter-observer variability could not be estimated. However, by minimizing the observer bias, which is an advantage of the oscillometric method, the issue of observer variability is not critical in the BP measurements.

In summary, we determined BP reference values for non-overweight children using an advanced statistical method. Routine BP measurement should begin at an early age, but there were no BP reference values for children under 7 years old in Korea; our findings bridge that gap in knowledge.

## REFERENCES

- Korean Society Hypertension (KSH); Hypertension Epidemiology Research Working Group, Kim HC, Cho MC. Korea hypertension fact sheet 2018. *Clin Hypertens* 2018;24(1):13.
   PUBMED | CROSSREF
- Statistics Korea. Prevalence of hypertension: sex, age 30 and over. http://kosis.kr/statHtml/ statHtml.do?orgId=117&tblId=DT\_11702\_N105&vw\_cd=&list\_id=117\_11702\_B01&seqNo=&lang\_ mode=ko&language=kor&obj\_var\_id=&itm\_id=&conn\_path=MT\_ZTITLE#. Updated 2017. Accessed January 4, 2018.
- 3. World Health Organization. A global brief on hypertension: silent killer, global public health crisis. http://apps.who.int/iris/bitstream/10665/79059/1/WHO\_DCO\_WHD\_2013.2\_eng.pdf?ua=1&bcsi\_ scan\_43167910db6ab4d9=0&bcsi\_scan\_filename=WHO\_DCO\_WHD\_2013.2\_eng.pdf. Updated 2013. Accessed January 4, 2018.
- 4. Bell CS, Samuel JP, Samuels JA. Prevalence of hypertension in children. *Hypertension* 2019;73(1):148-52. PUBMED | CROSSREF
- Du T, Fernandez C, Barshop R, Chen W, Urbina EM, Bazzano LA. 2017 pediatric hypertension guidelines improve prediction of adult cardiovascular outcomes. *Hypertension* 2019;73(6):1217-23.
   PUBMED | CROSSREF
- Chen X, Wang Y. Tracking of blood pressure from childhood to adulthood: a systematic review and metaregression analysis. *Circulation* 2008;117(25):3171-80.
   PUBMED | CROSSREF
- Chiolero A, Bovet P, Paradis G. Screening for elevated blood pressure in children and adolescents: a critical appraisal. *JAMA Pediatr* 2013;167(3):266-73.
  PUBMED | CROSSREF
- Pickering TG, Hall JE, Appel LJ, Falkner BE, Graves JW, Hill MN, et al. Recommendations for blood pressure measurement in humans: an AHA scientific statement from the Council on High Blood Pressure Research Professional and Public Education Subcommittee. *J Clin Hypertens (Greenwich)* 2005;7(2):102-9.
   PUBMED | CROSSREF
- Flynn JT, Kaelber DC, Baker-Smith CM, Blowey D, Carroll AE, Daniels SR, et al. Clinical practice guideline for screening and management of high blood pressure in children and adolescents. *Pediatrics* 2017;140(3):e20171904.
   PUBMED | CROSSREF
- Korean Center for Disease Control and Prevention. 2007 Korean children and adolescent growth standard.http://www.cdc.go.kr/CDC/cms/content/mobile/35/1235\_view.html. Updated 2007. Accessed November 7, 2019.

- Barba G, Buck C, Bammann K, Hadjigeorgiou C, Hebestreit A, Mårild S, et al. Blood pressure reference values for European non-overweight school children: the IDEFICS study. *Int J Obes* 2014;38(Suppl 2):S48-56.
   PUBMED | CROSSREF
- Ke L, Brock KE, Cant RV, Li Y, Morrell SL. The relationship between obesity and blood pressure differs by ethnicity in Sydney school children. *Am J Hypertens* 2009;22(1):52-8.
   PUBMED | CROSSREF
- Harding S, Whitrow M, Lenguerrand E, Maynard M, Teyhan A, Cruickshank JK, et al. Emergence of ethnic differences in blood pressure in adolescence: the determinants of adolescent social well-being and health study. *Hypertension* 2010;55(4):1063-9.
- Lee HA, Park EA, Cho SJ, Kim HS, Kim YJ, Lee H, et al. Mendelian randomization analysis of the effect of maternal homocysteine during pregnancy, as represented by maternal MTHFR C677T genotype, on birth weight. *J Epidemiol* 2013;23(5):371-5.
- Lee HA, Kim YJ, Lee H, Gwak HS, Hong YS, Kim HS, et al. The preventive effect of breast-feeding for longer than 6 months on early pubertal development among children aged 7–9 years in Korea. *Public Health Nutr* 2015;18(18):3300-7.
- National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. *Pediatrics* 2004;114(2 Suppl 4th Report):555-76.
   PUBMED
- 17. R Core Team. R: a language and environment for statistical computing. https://www.R-project.org. Updated 2018. Accessed August 29, 2019.
- Rigby RA, Stasinopoulos DM. Generalized additive models for location, scale and shape. *Appl Stat* 2005;54(3):507-54.
  - CROSSREF
- Xi B, Zong X, Kelishadi R, Hong YM, Khadilkar A, Steffen LM, et al. Establishing international blood pressure references among nonoverweight children and adolescents aged 6 to 17 years. *Circulation* 2016;133(4):398-408.
   PUBMED | CROSSREF
- Lurbe E, Cifkova R, Cruickshank JK, Dillon MJ, Ferreira I, Invitti C, et al. Management of high blood pressure in children and adolescents: recommendations of the European Society of Hypertension. *J Hypertens* 2009;27(9):1719-42.
   PUBMED | CROSSREF
- Yan W, Liu F, Li X, Wu L, Zhang Y, Cheng Y, et al. Blood pressure percentiles by age and height for non-overweight Chinese children and adolescents: analysis of the China Health and Nutrition Surveys 1991–2009. *BMC Pediatr* 2013;13(1):195.
   PUBMED | CROSSREF
- Rosner B, Cook N, Portman R, Daniels S, Falkner B. Determination of blood pressure percentiles in normal-weight children: some methodological issues. *Am J Epidemiol* 2008;167(6):653-66.
- Juonala M, Magnussen CG, Berenson GS, Venn A, Burns TL, Sabin MA, et al. Childhood adiposity, adult adiposity, and cardiovascular risk factors. *N Engl J Med* 2011;365(20):1876-85.
   PUBMED | CROSSREF
- 24. Sohn JA, Lee HS, Lim KA, Yoon SY, Jung JW, Kim NS, et al. Normal blood pressure values and percentile curves measured by oscillometric method in children under 6 years of age. *Korean J Pediatr* 2008;51(9):998-1006.

CROSSREF

- Lee CG, Moon JS, Choi JM, Nam CM, Lee SY, Oh K, et al. Normative blood pressure references for Korean children and adolescents. *Korean J Pediatr* 2008;51(1):33-41.
- Flynn JT, Pierce CB, Miller ER 3rd, Charleston J, Samuels JA, Kupferman J, et al. Reliability of resting blood pressure measurement and classification using an oscillometric device in children with chronic kidney disease. *J Pediatr* 2012;160(3):434-440.e1.
   PUBMED | CROSSREF
- 27. Johansson S, Iliadou A, Bergvall N, Tuvemo T, Norman M, Cnattingius S. Risk of high blood pressure among young men increases with the degree of immaturity at birth. *Circulation* 2005;112(22):3430-6. PUBMED | CROSSREF

- Moon JS. Secular trends of body sizes in Korean children and adolescents: from 1965 to 2010. *Korean J Pediatr* 2011;54(11):436-42.
  PUBMED | CROSSREF
- 29. Lee CG, Park HM, Shin HJ, Moon JS, Hong YM, Kim NS, et al. Validation study of the Dinamap ProCare 200 upper arm blood pressure monitor in children and adolescents. *Korean J Pediatr* 2011;54(11):463-9. PUBMED | CROSSREF