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Height-based equations as screening tools for high blood pressure in pediatric practice, the GENOBOX study

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Abstract

Due to the absence of easily applicable cut-off points to determine high blood pressure or hypertension in children, as in the adult population, blood pressure is rarely measured in the pediatrician's clinical routine. This has led to an underdiagnosis of high blood pressure or hypertension in children. For this reason, the present study evaluate the utility of five equations for the screening of high blood pressure in children: blood pressure to height ratio, modified blood pressure to height ratio, new modified blood pressure to height ratio, new simple formula and height-based equations. The authors evaluated 1599 children between 5 and 18 years. The performance of the five equations was analyzed using the receiver-operating characteristics curves for identifying blood pressure above P90th according to the American Academy of Pediatrics Clinical Practice Guideline 2017. All equations showed an area under the curve above 0.882. The new modified blood pressure to height ratio revealed a high sensitivity whereas the height-based equations showed the best performance, with a positive predictive value above 88.2%. Finally, all equations showed higher positive predictive values in children with overweight or obesity. The height-based equation obtained the highest PPV values above 71.1% in children with normal weight and above 90.2% in children with overweight or obesity. In conclusions, the authors recommend the use of the height-based equations equation because it showed the best positive predictive values to identify children with elevated blood pressure, independently of their sex, pubertal and weight status.

KEYWORDS
children, height-based equations, high blood pressure, pediatrician, screening

1 | INTRODUCTION

High blood pressure is the most important risk factor contributing to worldwide deaths.[1,2] Data indicate that its prevalence has continued to rise in the recent years,[3] and Europe is the region with the highest prevalence, where 55% of the adults have hypertension.[4] In adults in Spain, hypertension prevalence is estimated at 42.6%.[5] However, hypertension is not only present in adulthood, but also in children and adolescents. In the last two decades, hypertension has earned importance in terms of its appearance in young populations.[6] One meta-analysis[7] and a study done in Greece[8] found a prevalence of hypertension of 16.2% among 10–19 year-old and a 18.5% among 9–13 year-old children, respectively.

In adults, high blood pressure stands out as one of the most important risk factors for cardiovascular diseases (CVD).[9] Whereas this relationship is more difficult to establish in childhood, since cardiovascular complications usually appear over time and together with additional risk factors.[6] It has been shown that hypertension tracks from childhood to adulthood.[10–12] Among the developmental time frame, puberty is a key period for hypertension development.[10] The development of childhood hypertension should be avoided since it is a risk factor that can cause organic damage.[13]

Indeed, given its early role in long-term cardiovascular risk, blood pressure needs to be monitored, even in asymptomatic children and adolescents.[14] Despite its increase,[15] high blood pressure it is still underdiagnosed in the pediatric routines.[16] There are several reasons why hypertension may be underdiagnosed. One of these reasons could be the different cuts-off values that need to be applied in the process of diagnosis, depending on age and sex, height percentiles.[14] Although there are tables based on these percentiles, some authors have proposed the use of different methods to simplify the screening of blood pressure reducing the health care visits time,[17] which is usually insufficient.[16]

Some authors developed formulas[18–21] based on simple measurements, to be used to identify hypertension defined by the 2004 Fourth report of the American of Academy of Pediatrics guidelines.[18–21] However, in 2017 this guideline was updated using only children with normal weight.[14] For this reason, only some authors have tested the usefulness of these formulas based on the 2017 guideline.[22] While other authors have proposed new formulas adapted to the 2017 guideline.[23,24] Nevertheless, no study has been found in a pediatric Spanish population using any of the mentioned formulas.

Therefore, the aim of this study was to identify the formula with the best performances to classify a sample of Spanish children and adolescents according to their blood pressure levels, based on the American Academy of Pediatrics (AAP) Clinical Practice Guideline (CPG).[14]

2 | MATERIALS AND METHODS

2.1 | Study sample

A sample of 1599 children and adolescents (48.5% males and 70.6% with overweight/obesity) participated in the GENOBOX multicenter case control study, carried out in three Spanish cities: Córdoba, Santiago de Compostela and Zaragoza. The participants and their families were informed about the aim of the study. Children were classified in two groups: cases with overweight or obesity, and controls with normal weight. The case group was recruited from children who came to the hospitals to confirm the diagnosis of overweight or obesity or for identification of minor gastrointestinal disorders that were discarded after clinical and laboratory tests. Whereas, the control group were children who came to the emergency departments owing to a common infection, that were not confirmed after laboratory tests. We included in the study children from 5 to 18 years. Those children having a chronic or inflammatory disease, a congenital disease or psychomotor disability and taking drugs for treatment of alterations in blood pressure, hormonal, glucose or lipid metabolism and those who did intensive exercise in the 24 h previous to the examination or had been involved in other studies 3 month before, were excluded from the study. The present study was approved by the Ethics Committees of each center (Code IDs: Santiago 2011/198, Zaragoza 10/2010, Córdoba 01/2017) involved in the project and was carried out following the Declaration of Helsinki principles.

2.2 | Anthropometric measurements

Trained researchers weighed and measured all the participants. The participants were measured in their underwear and without shoes. An electronic scale and a stadiometer were used to measure weight and height, respectively. Then, body weight in kg was divided by the square of height in meters to obtain the body mass index (BMI). Cole and coworkers, International Obesity Task Force criteria were used to classify participants as children with normal weight or overweight/obesity according to their sex and age specific cut-offs equivalent to adult values of 25 kg/m^2 and 30 kg/m^2.[25] Children with underweight were exclude for the study. In addition, the pubertal stage was determined according to Tannert's criteria by an expert pediatrician and confirmed with sexual hormone measurements.[26] Children in Tanner stage I were considered prepubertal, and children with stages II-V were considered pubertal. Despite the participants with tanner V presented clinical signs and hormones similar to adults, they were grouped as pubertal because they still had a growth velocity around 2 cm/year.

2.3 | Blood pressure

In all participating centers, an electronic manometer (M6, HEM-7001-E, Omron, Tokio, Japan), which has been approved by the British Hypertension Society,[27] was used to measure systolic and diastolic blood pressure (SBP, DBP). The cuff-size was adapted to the arm circumference of each child. The blood pressure measure was taken by a trained personal in a quiet room. The child was seated on a chair with the back supported and feet undercrossed on the floor and waited 5 min until the first measurement of BP. The measures were repeated twice with a 5 min interval on the right arm and in sitting position. If the first two measures differed by more than 20% the measure was repeated a third time. Children were classified as having elevated SBP or DBP (> P90th for sex, age and height) or not, according to the AAP CPG.[14] In order to avoid the risk of white coat hypertension (WCH), the BP levels of 154 of that children (77 with normal weight and 77 with obesity or overweight) were measured too by ambulatory blood pressure monitoring.

2.4 | Height-based equations

The following five height-based equations,[18–20,23,24] were used to check their usefulness as tools for the detection of high blood pressure as compared with the AAP CPG (≥ P90th both systolic and diastolic). Each one of the first three equations were calculated both for SBP and DBP.

I. Blood pressure to height ratio (BPHR)[18] = BP /Height (cm).
II. Modified blood pressure to height ratio (MBPHR)[19] = BP/(Height (cm) + 7 × (13 – age in years).
III. New modified blood pressure to height ratio (NMBPHR)[20] = BP/(Height (cm) + 3 × (13 – age in years).
IV. New simple formula (NSF)[23] = [1.5 × systolic blood pressure + diastolic blood pressure] – [(26 × height (m)] – age (years).
V. Elevated blood pressure cut-offs from the "Height-based equation" (HBE)[24]: SBP P90th = 70 + 0.33× height (cm); DBP P90th = 35 + 0.25× height (cm).

2.5 | Statistical analyses

The sample sized estimation was calculated with a 95% degree of confidence (type I error alpha = 0.05) and a power of 80% (type II beta error = 0.20) according to the estimation equation of n by comparison of two proportions of one variable in two independent groups. The sample size under these conditions was raised to a total of 300 to be sure that significant differences could be found for a minimal difference of 20% in each parameter between children with obesity and normal weight. Descriptive statistics for sex, height, BMI, SBP and DBP for children and adolescents were expressed as means ± standard deviation (SD). Studentt's t-test was used to compare normally distributed variables between children of different sex and weight status. The proportion of normal SBP and DBP and those with elevated SBP and DBP were reported by frequency. Due to the observed differences between males and females, further analyses were done separated by sex.

Receiver operating characteristics curves (ROC) analyses were applied for the equations i to iv in children and adolescents with normal weight to assess their accuracy as diagnostic test for elevated SBP and DBP in the study population. The area under the curve (AUC) was used as indicator of overall ability of using i to iv and equations cut-off points to discriminate children and adolescents with elevated SBP or DBP. To assess the performance of ROC analyses we used the AUC with its 95% confidence intervals. A perfect test will have an AUC of 1.0, and an AUC of 0.5 is equivalent to random guessing.[28] From these data, the cut-off point with the highest sensitivity and specificity were selected.[29] The cut-off point obtained in children with normal weight were then used to classify the total population using both systolic and diastolic cut-off points. Due to the peculiar of blood pressure diagnoses, children and adolescents are prehypertension or have elevated blood pressure when either SBP or DBP are above P90th.[14] In this line new categorical variables were created unifying the presence of either elevated SBP or DBP of each equation (i to iv). For the last equation (v), no ROC analyses was needed since the formula itself gives a cut-off point to compare with each patient blood pressure level. Hence, the whole sample was classified according to have or not either SBP or DBP above or below its own cut-off point. Then, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), real prevalence and apparent prevalence and their confidence intervals, using the exact binomial statistical method, were calculated from the new categorical variable compared with the AAP CPG (≥ P90th both systolic and diastolic).

All analyses were carried out with IBM SPSS Statistics (IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY, USA: IBM Corp.) and statistical significance was considered when $p < .05$.

3 | RESULTS

Table 1 shows their main characteristics of the participants according to age and weight status. Both boys and girls with normal weight showed significant differences with lower values in height, BMI, SBP

TABLE 1 Descriptive characteristics of the participants including blood pressure distribution according to the American Academy of Pediatrics Clinical practice guideline 2017

	Normal weight				Overweight/Obesity			
	Boys		Girls		Boys		Girls	
	248		222		528		601	
N	Median	(p25–p75)	Median	(p25–p75)	Median	(p25–p75)	Median	(p25–p75)
Age (years)	9.8[a]	(8.2–11.5)	10.1[c]	2.5	10.4[a]	2.4	10.3[c]	2.6
Height (m)	1.39[a]	0.15	1.39[c]	0.14	1.45[b]	0.14	1.44[d*]	0.14
Weight (kg)	33.5[a]	11.0	33.5[c]	10.6	56.3[b]	18.1	54.7[d]	17.9
BMI	17.03[a]	2.0	17.22[c]	2.2	26.21[b]	4.4	25.98[d]	4.6
BMI-z	−0.27[a]	0.58	−0.23[c]	0.49	2.90[b]	1.54	2.38[d*]	1.25
SBP (mm Hg)	100[a]	13	100[c]	12	111[b]	14	110[d]	13
DBP (mm Hg)	60[a]	10	62[c*]	10	67[b]	11	67[d]	11
SBPHR	0.721[a]	0.10	0.726[c]	0.10	0.768[b]	0.1	0.770[d]	0.1
DBPHR	0.435[a]	0.07	0.451[c,*]	0.08	0.465[b]	0.08	0.470[d]	0.09
MSBPHR	0.626[a]	0.09	0.629[c]	0.08	0.681[b]	0.1	0.679[d]	0.09
MDBPHR	0.377[a]	0.06	0.391[c,*]	0.07	0.412[b]	0.07	0.414[d]	0.07
NMSBPHR	0.675[a]	0.09	0.679[c]	0.08	0.726[b]	0.09	0.725[d]	0.08
NMDBPHR	0.407[a]	0.06	0.422[c,*]	0.07	0.439[b]	0.07	0.443[d]	0.07
NSF	183.2[a]	25.7	185.9[c]	24.5	206.7[b]	27.8	205.2[d]	25.8
HBE SBP	115.8[a]	5.0	115.8[c]	4.7	118.0[b]	4.6	117.5[d]	4.6
HBE DBP	69.7[a]	3.8	69.7[c]	3.6	71.3[b]	3.5	70.97[d]	3.7
	n	(%)	*n*	(%)	*n*	(%)	*n*	(%)
Elevated SBP	26	10.5	25	11.3	200	37.9	211	35.1
Elevated DBP	14	5.6	31	14	120	22.7	142	23.6

Abbreviations: BMI, Body mass index; BMI-z, Body mass index z-score; DBP, Diastolic blood pressure; DBPHR, diastolic blood pressure (BP/Height); HBE, Elevated blood pressure cut-offs from the "Height-based equation MDBPHR", Modified diastolic blood pressure to height ratio (DBP/Height+7x(13-age); MSBPHR, Modified systolic blood pressure to height ratio (SBP/Height+7x(13-age); NMSBPHR, New modified diastolic blood pressure to height ratio (DBP/Height+3x(13-age); NMSBPHR, New modified systolic blood (SBP/Height+3x(13-age); NSF, New simple formula, (1.5xSBP+DBPD)-(26xheight)-age; SBP, systolic blood pressure; SBPHR, systolic blood pressure to height ratio (BP/Height); SD, standard deviations.
*Indicates significant differences $p < 0.05$ between sex in children with the same weight status. (a and b) indicates differences $p < 0.050$ between boys with normal-weight versus those with overweight/obesity; (c and d) indicates differences $p < 0.05$ between girls with normal-weight versus those with overweight/obesity.

and DBP than children with overweight/obesity. In addition, girls with normal weight showed significantly higher DBP values than boys with normal weight. Also, boys with overweight or obesity were significantly taller than girls with overweight or obesity. Regarding BP classification, a 29.1% of boys and 28.7% of girls showed elevated SBP. Similarly, elevated DBP was observed in 17.3% of boys and 21.0% of girls. In addition, in the subsample of 154 children the measure of BP by ambulatory blood pressure monitoring showed a 6.5% and a 13% of WCH in children with normal weight and overweight or obesity, respectively.

The performance in the identification of the optimal cut-off points for elevated BP, both in systolic and diastolic blood pressure, using the first four equations (BPHR, MBPHR, NMBPHR and NSF) is shown in Table 2. Moreover, Figure 1 shows the AUC for equations (BPHR, MPHBR and NMBPHR) compared to the AAP CPG. All equations showed an AUC with a range of 0.915–0.992 in boys. Whereas in girls the AUC range was 0.882–0.985. In addition, AUC showed better values for boys than for girls, except in the SBPHR and NSF equations. The best AUC for the identification of elevated blood pressure was the obtained by the NMBPHR equation, both for SBP and DBP. Regarding sensitivity and specificity of cut-off points obtained, all equations showed high values (between 73.3 and 100%). In addition, in boys all equations showed a sensitivity of 100%, except BPHR for systolic blood pressure and NSF.

When participants were divided by pubertal status, the AUC range for all equations was 0.936–0.999 for prepubertal and 0.845–1.00 for pubertal children (Table S1). NMBPHR equation was found to be the best for identifying prepubertal children with elevated SBP (AUC = 0.969 for boys and AUC = 0.965 for girls) and elevated DBP (AUC = 0.999 for boys and AUC = 0.994 for girls) with a sensitivity of 100%, except for girls in the systolic category (95.2%). However, in pubertal children the equation with the best AUC was BPHR, particularly SBPHR, with an AUC of 0.981 for boys and 1.00 for girls.

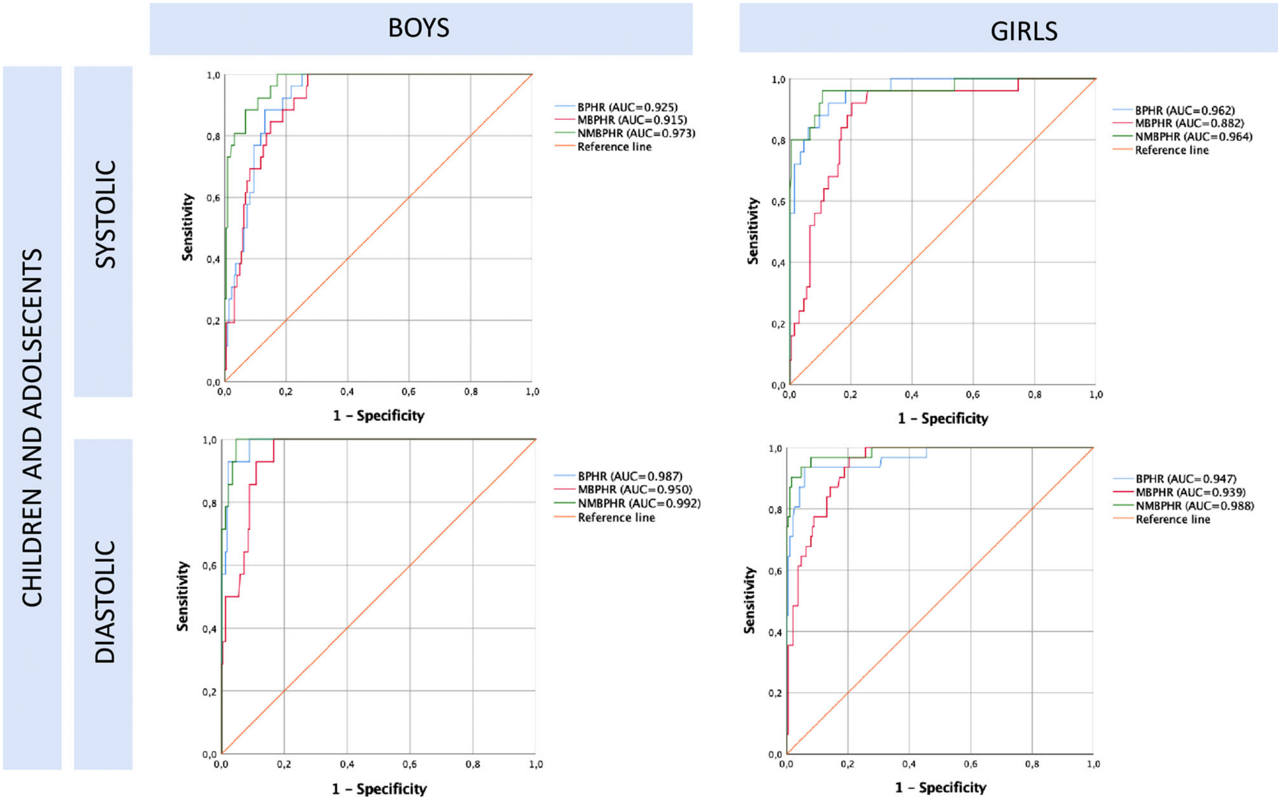

FIGURE 1 ROC curves for children and adolescents with normal weight, both systolic and diastolic blood pressure

In addition, BPHR for pubertal children showed an AUC with a high sensitivity (100%), except for girls in the diastolic category (87.5%).

Once we obtained the new categories regarding the presence or absence of elevated blood pressure according to the identified cut-offs from the studied equations, these were compared with the Gold standard classification in the whole sample. Table 3 shows sensitivity, specificity, PPV, NPV, true prevalence and apparent prevalence for the all studied equations. MBPHR showed the best sensitivity in boys (98.2%). Whereas NSF showed the best sensitivity for girls (96.7%). NMBPHR showed a high sensitivity both in girls and boys, (96.7% and 95.0%, respectively). Regarding specificity, the HBE equation showed the highest value both in boys (93.2%) and girls (93.5%). In addition, the HBE equation obtained the best PPV (87.5% for boys and 88.2% for girls). As for prevalence, the true prevalence in boys was 35.2% and 36.5% in girls. BPHR, MBPHR, NMBPHR and NSF equations showed a higher apparent prevalence, and the HBE equation showed a lower apparent prevalence, than the true prevalence. The HBE equation showed the most similar apparent prevalence to the true prevalence (35.1% and 35% in boys and girls, respectively).

Table S2 shows the sensitivity, specificity, PPV and NPV of all height-based equations compared with AAP CPG divided by pubertal status in the all the participants. Sensitivity values were between 80.4 and 97.4% in children with prepubertal status and between 59.5 and 95% in children with pubertal status. Similarly, specificity range was 73.9–91.2% and 79.3–97.8% in children with prepubertal and pubertal status, respectively. Respect PPV the HBE equation showed the highest values in prepubertal and pubertal children.

Finally, Table 4 shows the sensitivity, specificity, PPV, NPV, real prevalence and apparent prevalence when the analysis was stratified by BMI status. Participants with higher BMI showed higher PPV than those with normal BMI. Both in children with normal weight and children with overweight or obesity the HBE equations obtained the best PPV (71.1 and 71.4% for boys and girls with normal weight, respectively; and 90.2 and 91.6% for boys and girls with overweight or obesity).

4 | DISCUSSION

The present study shows the usefulness of different height-based equations for the detection of elevated blood pressure in Spanish children. All equations (i to iv) were found to be useful for the identification of elevated blood pressure (AUC above 0.882). However, some of them revealed better results than others. This is the case for the HBE equation,[24] which showed the best PPV in the identification of children with blood pressure above the P90th both in children with normal weight and children with overweight or obesity. On the other hand, the NMBPHR equation turned out to be the best equation for the identification of children with blood pressure above the P90th (with the highest AUC and sensitivity).

TABLE 2 Identification of the optimal cut-off points in children with normal weight using four height-based equations, according to systolic and diastolic blood pressure

	BPHR				MBPHR				NMBPHR				NSF	
	SBP ≥ 90th		DBP ≥ 90th		SBP ≥ 90th		DBP ≥ 90th		SBP ≥ 90th		DBP ≥ 90th		BP ≥ 90th	
All	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls
N	248	222	248	222	248	222	248	222	248	222	248	222	248	222
AUC(95% CI)	0.925 (0.889–0.960)	0.962 (0.931–0.994)	0.987 (0.973–1.00)	0.965 (0.931–1.00)	0.915 (0.876–0.955)	0.882 (0.818–0.946)	0.950 (0.917–0.983)	0.940 (0.908–0.972)	0.973 (0.952–0.994)	0.964 (0.921–1.00)	0.992 (0.982–1.00)	0.985 (0.967–1.00)	0.916 (0.858–0.974)	0.938 (0.908–0.968)
Cut-off points	0.805	0.788	0.505	0.523	0.659	0.679	0.422	0.418	0.732	0.738	0.485	0.474	200.3	200.1
Sensitivity% (95% CI)	88.5 (69.9–97.6%)	92.3 (74.0–99.0%)	100 (76.8–100.0%)	93.5 (78.6–99.2%)	100 (86.8–100.0%)	92.0 (74.0–99.0%)	100 (76.8–100.0%)	96.8 (83.3–99.2%)	100 (86.8–100.0%)	96.0 (79.7–99.9%)	100 (76.8–100.0%)	96.8 (83.3–99.2%)	88.2 (72.6–96.7%)	90.7 (77.9–97.4%)
Specificity% (95% CI)	86.7 (81,3–90.7%)	87.3 (81.8–91.6%)	91.0 (86.6–94.4%)	94.2 (89.3–96.7%)	73.3 (66.2–78.3%)	79.7 (73.4–85.1%)	83.3 (77.5–87.5%)	79.6 (72.6–84.6%)	83.0 (77.3–87.6%)	89.3 (83.6–92.9%)	95.3 (91.7–97.6%)	92.1 (87.4–95.5%)	86.4 (81.1–90.7%)	86.6 (80.7–91.2%)

Abbreviations: AUC, area under the curve; BPHR, Blood Pressure to Height Ratio; CI, Confident Interval HBE, Height-Based Equation; MBPHR, modified BPHR; NMBPHR, new modified BPHR, for the abbreviation of Systolic and Diastolic respectively; NSF, New Simple Formula.

Sensitivity and specificity were computed for their corresponding optimal cutoff points independently for SBP and DBP in the different equations.

Reference according to the American Academy of Pediatrics Clinical practice guideline 2017 as the gold standard (≥ P90th both systolic and diastolic blood pressure)

Due to the high number of cut-off points that have to be considered in the diagnosis of hypertension using the AAP CPG, and the time needed to search for the appropriate cut-off point of each child, some authors have developed simple tools to facilitate the correct classification of children according to the their blood pressure levels.[18–20,23,24] Using the AAP CPG, Zhang and coworkers,[30] found that the NMBPHR equation had a better performance in the identification of high blood pressure (above P95th) compared with the BPHR and MBPHR equations, in American children. However, the MBPHR was the equation with the best performance in Chinese children.[30] Similarly, Yazdi and coworkers observed that the NMBPHR equation had a better performance than the BPHR and MBPHR equations in the identification of high blood pressure in Iranian children (7–12 years).[31] In our study, among the equations used in that studies, the NMNPHR was the best for the identification of elevated blood pressure in Spanish children. Compared with the studies of Zhang and Yazdi,[30,31] we obtained a moderately higher PPV. In a study similar to ours, Mourato and coworkers[32] in American and Brazilian children, observed NMBPHR as the equation with the best performance. Thus, our study seems to confirm the best results for the NMBPHR equation. In addition, these results were observed with similar cut-off points to those obtained in previous studies.[22,30,31]

Di Bonito and coworkers[23] created the NSF based on the 2017 AAP CPG especially for children with overweight or obesity and obtained a good PPV (84–83%).[23] In our study, although we found a lower PPV both in boys and girls, when data were analyzed by weight status, the analysis in children with overweight or obesity showed an increase in PPV compared to children with normal weight (69.4–69.1% vs. 50.8–61.9%).

The HBE is the most practical equation because it showed the best performance and it does not require age to be introduced in the calculation. It is very useful in clinical practice where the pediatricians can measure blood pressure and classify children accordingly. If the blood pressure levels (SBP and DBP) are above the data obtained with the HBE, it indicates that children have elevated blood pressure.[24] In a recent study performed in South America, the HBE was the equation with the best performance to identify elevated blood pressure (> P90th, according to the AAP CPG), showing also a high sensitivity, NPV and a PPV above 53.8, with male children and adolescents showing the maximum PPV values (72.6 and 63.2, respectively).[22]

It is well known that children with overweight or obesity have higher prevalence of hypertension than children with normal weight.[33] For this reason, when other studies studied the performance of the different equations according to weight status, the subgroups with overweight or obesity showed better PPV.[30,31] In our study, when the analyses were stratified by weight status we found higher PPV in children with overweight or obesity than in children with normal weight. In children with normal weight we obtained the higher PPV in the HBE equation (71.1% and 71.4%, in boys and girls, respectively). Whereas in children with overweight or obesity the PPV increased until (90.2% and 91.6%, in boys and girls, respectively). This suggests that although children with normal weight obtained a high PPV percentage in the HBE

TABLE 3 Performance of all height-based equations in the whole sample using the cut-off points obtained in participants with normal weight, considering the American Academy of Pediatrics Clinical practice guideline 2017 diagnosis as the gold standard (≥ P90th both systolic and diastolic blood pressure)

	BPHR		MBPHR		NMBPHR		NSF		HBE*	
	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls
n	776	823	776	823	776	823	776	823	776	823
Cut-off points	0.805 /0.505	0.788 /0.523	0.659 /0.422	0.679 /0.418	0.732 /0.485	0.738 /0.474	200.29	200.1	N/A	N/A
Sensitivity% (95% CI)	80.2 (75.0–84.8%)	85.3 (80.8–89.1%)	98.2 (95.8–99.4%)	92.0 (88.3–94.8%)	96.7 (93.8–98.5%)	95.0 (91.9–97.2%)	92.3 (88.5–95.2%)	96.7 (94–98.4%)	87.2 (82.6–90.9%)	84.7 (80.1–88.6%)
Specificity% (95% CI)	86.3 (83.0–89,2%)	84.9 (81.5–87.9%)	61.4 (57.0–65.7%)	66.5 (62.3–70.6%)	81.3 (77.6–84.6%)	84.7 (81.3–87.7%)	74.8 (70.7–78.5%)	74.0 (70.0–77.7%)	93.2 (90.7–95.3%)	93.5 (91–95.5%)
PPV% (95% CI)	76.0 (70.7–80.9%)	76.4 (71.5–80.9%)	58.0 (53.4–62.6%)	61.2 (56.5–65.7%)	73.7 (68.9–78.2%)	78.1 (73.5–82.2%)	66.5 (61.5–71.2%)	68.1 (63.4–72.5%)	87.5 (83.0–91.2%)	88.2 (83.9–91.7%)
NPV% (95% CI)	89.0 (85.8–91.6%)	91.0 (88.1–93.4%)	98.4 (96.3–99.5%)	93.5 (90.6–95.8%)	97.8 (96.0–99.0%)	96.7 (94.7–98.2%)	94.7 (92–96.7%)	97.5 (95.4–98.8%)	93.1 (90.5–95.1%)	91.4 (88.7–93.6%)
True prevalence% (95% CI)	35.2 (31.8–28.7%)	36.5 (33.2–39.8%)	35.2 (31.8–38.7%)	36.5 (33.2–39.8%)	35.2 (31.8–38.7)	36.5 (33.2–39.8%)	35.2 (31.8–38.7%)	36.5 (33.2–39.8%)	35.2 (31.8–38.7%)	36.5 (33.2–39.8%)
Apparent prevalence% (95% CI)	37.1 (33.7–40.6%)	40.7 (37.3–44.4%)	59.5 (56.0–63.0%)	54.8 (51.3–58.2%)	46.1 (42.6–49.7%)	44.3 (40.9–46.8%)	48.8 (45.3–52.4%)	51.8 (48.3–55.2%)	35.1 (31.7–38.5%)	35.0 (31.7–38.%)

Abbreviations: AUC, Area Under the Curve; PPV, Positive Predictive Value; NPV, Negative Predictive Value; BPHR, Blood Pressure to Height Ratio; CI, confidence interval; HBE, Height-Based Equation; MBPHR, Modified BPHR; NMBPHR, New MBPHR; NSF, New simple formula.

ROC analyses were performed to evaluate the usefulness of the cutoffs obtained from the different height-based equations to diagnose elevated BP according to the American Academy of Pediatrics Clinical practice guideline 2017.

* HBE cut-off points are not available due to the special characteristics of the HBE equation mentioned in the methodology section.

TABLE 4 Performance of all height-based equations in the whole sample divided by weight status, using the cut-off points obtained in participants with normal weight

	BPHR		MBPHR		NMBPHR		NSF		HBE*	
Normal weight	**Boys**	**Girls**	**Boys**	**Girls**	**Boys**	**Girls**	**Boys**	**Girls**	**Boys**	**Girls**
n	**248**	**222**	**248**	**222**	**248**	**222**	**248**	**222**	**248**	**222**
Sensitivity% (95% CI)	94.1 (80.3–99.3%)	90.7 (77.9–97.4%)	100 (89.7–100%)	95.3 (84.2–99.4%)	100 (89.7–100%)	93.0 (80.9–98.5%)	88.2 (72.6–96.7%)	90.7 (77.9–97.4%)	79.4 (62.1–91.3%)	81.4 (66.6–91.6%)
Specificity% (95% CI)	84.6 (79.0–89.1%)	89.0 (84.6–93.9%)	69.2 (62.5–75.3%)	69.8 (62.5–76.5%)	83.2 (77.5–87.9%)	87.2 (81.4–91.7%)	86.4 (81.1–90.7%)	86.6 (80.7–91.2%)	94.9 (91–97.4%)	92.2 (87.2–95.7%)
PPV% (95% CI)	49.2 (36.6–62.9%)	68.4 (54.8–80.1%)	34 (24.8–44.2%)	43.2 (33.0–53.7%)	48.6 (36.4–60.8%)	63.5 (50.4–75.3%)	50.8 (37.5–64.1%)	61.9 (48.8–73.9%)	71.1 (54.1–84.6%)	71.4 (56.7–83.4%)
NPV% (95% CI)	98.9 (97.4–100%)	97.6 (93.9–99.3%)	100 (97.5–100%)	98.4 (94.4–99.8%)	100 (98–100%)	98.1 (94.6–99.6%)	97.9 (94.7–99.4%)	97.5 (93.7–99.3%)	96.7 (93.3–98.7%)	95.4 (91.1–98.0%)
True prevalence% (95% CI)	13.7 (9.7–18.6%)	19.4 (14.4–25.2%)	13.7 (9.7–18.6%)	19.4 (14.4–25.2%)	13.7 (9.7–18.6%)	19.4 (14.4–25.2%)	13.7 (9.7–18.6%)	19.4 (14.4–25.2%)	13.7 (9.7–18.6%)	19.4 (14.4–25.2%)
Apparent prevalence% (95% CI)	26.2 (20.9 –32.2%)	25.7 (20.1–32.0%)	40.3 (34.2–46.7%)	42.8 (36.2–49.6%)	28.2 (22.7–34.3%)	28.4 (22.6–34.8%)	23.5 (18.6–29.6%)	28.4 (22.6–34–8%)	15.3 (11.1–20.4%)	22.1 (16.8–28.1%)
Overweight and Obesity										
n	**528**	**601**	**528**	**601**	**528**	**601**	**528**	**601**	**528**	**601**
Sensitivity% (95% CI)	78.2 (72.5–83.3%)	84.4 (79.4–88.6%)	97.9 (95.2–99.3%)	91.4 (87.3–94.6%)	96.2 (93.0–98.3%)	95.3 (92.0–97.6%)	92.9 (88.9–95.8%)	97.7 (95.0–99.1%)	88.3 (83.5–92.1%)	85.2 (80.3–89.3%)
Specificity% (95% CI)	87.5 (83.2–91.1%)	82.3 (77.8–86.2%)	55.7 (49.8–61.5%)	64.8 (59.5–69.9%)	79.9 (74.8–84.4 5)	83.4 (79.1–87.2%)	66.1 (60.3–71.5%)	67.4 (62.2–72.4%)	92.0 (88.3–94.9%)	94.2 (91.2–96.4%)
PPV% (95% CI)	83.9 (78.4–88.4%)	78.1 (72.7–82.8%)	64.6 (59.5–69.6%)	66.0 (60.8–70.9%)	79.9 (74.8–84.3%)	81.1 (76.3–85.4%)	69.4 (64.0–74.4%)	69.1 (64.1–73.9%)	90.2 (85.6–93.7%)	91.6 (87.4–92.5%)
NPV% (95% CI)	83.0 (78.3–87.0%)	87.6 (83.5–91.0%)	97.0 (93.1–99.0%)	91.0 (86.7–94.3%)	96.3 (93.0–98.3%)	96.0 (93.1–97.0%)	91.8 (87.2–95.2%)	97.5 (94.6–99.1%)	90.5 (86.5–93.6%)	89.5 (85.9–92.5%)
True prevalence% (95% CI)	45.3 (41.0–49.6%)	42.8 (38.8–46.8%)	45.3 (41.0–49.6%)	42.8 (38.8–46.8%)	45.3 (41.0–49.6%)	42.8 (38.8–46.8%)	45.3 (41.0–49.6%)	42.8 (38.8–64.3%)	45.3 (41.0–49.6%)	42.8 (38.8–46.8%)
Apparent prevalence% (95% CI)	42.2 (38.0–46.6%)	46.3 (42.2–50.3%)	68.6 (64.4–72.5%)	59.2 (55.2–63.2%)	54.5 (50.2–58.9%)	50.2 (46.2–54.3%)	60.6 (56.3–64.8%)	60.4 (56.4–64.3%)	44.3 (40.0–48.7%)	39.8 (35.8–43.8%)

Abbreviation: AUC Area Under the Curve, PPV Positive Predictive Value, NPV Negative Predictive Value, BPHR Blood Pressure to Height Ratio, CI confidence interval, HBE Height-Based Equation, MBPHR Modified BPHR, NMBPHR: New MBPHR, NSF: New simple formula.

ROC analyses were performed to evaluate the usefulness of the cutoffs obtained from the different height-based equations to diagnose elevated BP according to the American Academy of Pediatrics Clinical practice guideline 2017.

* HBE cut-off points are not available due to the special characteristics of the HBE equation mentioned in the methodology section.

Considering the American Academy of Pediatrics Clinical practice guideline 2017 diagnosis as the gold standard equation, this percentage was higher when compared with their counterparts with overweight/obesity.

To our knowledge, this is the first study to assess the performance of different height-based equations to identify children and adolescents with elevated blood pressure in Spain. Others studies have done the analyses with other populations (American, Sud-American, Chinese). It should be noted the importance of puberty since it is a factor to be asses in childhood. And it is the first study of this type in which puberty has been taken into account. For these reason these cut-off points obtained in Spanish children and adolescents could be used as a reference for Spanish population in order to screening children or adolescents with elevated blood pressure. Moreover, the study was performed in a large sample and considering three different subgroups for the analyses (sex, weight status and pubertal status). The results obtained in children with normal weight have been confirmed in the children and adolescents with higher risk of hypertension (children and adolescents with overweight or obesity). Also, the cut-off points were identified only in children with normal weight, following the AAP CPG recommendation, which may explain the better AUC obtained in the children with normal weight when compared with those with overweight/obesity.

However, the study has several limitations. First, the use of an oscillometric device instead of a mercury sphygmomanometer. Although the oscillometric device was validated and its use is recommended by the AAP CPG, most previous studies used a mercury sphygmomanometer as it is the most accurate method. The oscillometric device was the selected method to measure blood pressure because it does not need prior preparation and its measurements are reproducible in other contexts such as schools. So, its use in other settings could be adequate to detect children with elevated blood pressure. Second, blood pressure level was measured at one visit instead of three visits as recommended by the AAP CPG. One of the risks of performing a single auscultation visit is the masking of white coat hypertension, specifically in the group of children with hypertension. Taking into account this, a small subsample was measured by ambulatory blood pressure monitoring too and the percentage of WCH found was low compared with other studies.[34,35] Third, the terminal digit preference in the measure of BP levels, specifically in SBP, was zero. However, a recent study has shown how the use of automated devices decrease the percentage of BP recordings ending in zero. Although zero is still the terminal digit preference with the highest prevalence in the BP records.[36]

In conclusions, the HBE equation showed the best PPV to identify children with elevated blood pressure, independently of their sex and pubertal weight status. The HBE is a simple formula and it could be included in the pediatrician's clinical routine or in other public health activities.

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AUTHOR CONTRIBUTIONS

Conceptualization, Mercedes Gil-Campos, Rosaura Leis, Concepción M. Aguilera, Luis A. Moreno and Gloria Bueno-Lozano; methodology, Gloria Pérez-Gimeno, Azahara I. Ruperez, Mercedes Gil-Campos, Estela Skapino, Rosaura Leis, Concepción M. Aguilera, Luis A. Moreno and Gloria Bueno-Lozano; patient recruitment, Rocío Vázquez-Cobela, Mercedes Gil-Campos, Rosaura Leis, Gloria Bueno-Lozano; biochemical analyses: Concepción M. Aguilera, Augusto Anguita; data curation, Gloria Pérez-Gimeno, Azahara I. Ruperez, Estela Skapino, Augusto Anguita; writing original draft preparation, Gloria Pérez-Gimeno, Azahara I. Ruperez, Luis A. Moreno, Rosaura Leis, Gloria Bueno-Lozano; writing-review and editing, all authors.; funding acquisition, Mercedes Gil-Campos, Rosaura Leis, Concepción M. Aguilera, Luis A. Moreno and Gloria Bueno-Lozano.

CONFLICT OF INTEREST

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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