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Height-based equations as screening tools for elevated blood pressure in the SAYCARE study

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Abstract

This study evaluated the accuracy of four height-based equations: blood pressure to height ratio (BPHR), modified BPHR (MBPHR), new modified BPHR (NMBPHR), and height-based equations (HBE) for screening elevated BP in children and adolescents in the SAYCARE study. We measured height and BP of 829 children and adolescents from seven South American cities. Receiving operating curves were used to assess formula performance to diagnose elevated BP in comparison to the 2017 clinical guideline. Sensitivity, specificity, and positive and negative predictive values (PPV, NPV) were calculated for the four screening formulas. The diagnostic agreement was evaluated with the kappa coefficient. The HBE equation showed the maximum sensitivity (100%) in children, both for boys and girls, and showed the best performance results, with a very high NPV (>99%) and high PPV (>60%) except for female children (53.8%). In adolescents, the highest sensitivity (100%) was achieved with the NMBPHR for both sexes. Kappa coefficients indicated that HBE had the highest agreement with the gold standard diagnostic method (between 0.70 and 0.75), except for female children (0.57). Simplified methods are friendlier than the percentile gold standard tables. The HBE equation showed better performance than the other formulas in this Latin American pediatric population.

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1 | INTRODUCTION

High blood pressure (BP) in children and adolescents is one of the main predictive factors of hypertension in adults, a significant risk factor for cardiovascular events[1]; Latin America has the highest prevalence in this age-group (23.4%).[2] Despite the clinical relevance of this condition, hypertension in childhood is under-diagnosed.[3] Several factors contribute to this, one of which is that BP measurement is not often included in routine clinical assessments of these age-groups. The procedure to obtain the diagnosis of high BP in children is also quite complex.[3] As BP varies according to age, sex, and height, diagnosis requires the determination of height percentiles and comparison of the systolic BP (SBP) and diastolic BP (DBP) with values provided by sex- and age-specific reference values.[4] To simplify the diagnosis of hypertension in children and adolescents, several simple methods have been described for screening elevated BP in clinical practice.[5] Some of these methods use simplified tables,[6,7] others use cutoff points based on the ratio between BP and height,[8-11] and some authors have developed age- and height-based formulas to screen high BP.[12,13] Several studies have compared these simplified methods to screen hypertension in youth, considering the Fourth Report (2004)[14] as the reference method and showing different results.[8-11] Since the publication of the 2017 Clinical Practice Guidelines,[4] currently the most widely used approach for diagnosing hypertension in children and adolescents, some new simplified tables have been designed,[15,16] and the performance of some formulas have been tested: the Blood Pressure to Height Ratio (BPHR)[17] proposed by Lu and colleagues,[18] the Modified Blood Pressure to Height Ratio (MBPHR)[17,19] proposed by Mourato and colleagues,[20] the new modified blood pressure to height ratio (NMBPHR)[17,19] proposed by Ma and colleagues[21] and the height-based equations (HBE) proposed by Mourato and colleagues.[13] Although the simplified tables are more comfortable to use than the ones in the original guidelines, we consider that the application of formulas is less complicated than searching in tables. Electronic applications have been developed to avoid consulting so many percentile tables, but the usage of electronic devices in Latin American countries is often not possible. The aim of this study was, therefore, to evaluate the feasibility and accuracy of four height-based equations (BPHR, MBPHR, NMBPHR, and HBE) for screening children and adolescents with elevated BP in the SAYCARE study[22] using the 2017 "Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents" as the reference method.[4]

2 | MATERIALS AND METHODS

We analyzed data collected in the South American Youth/Child Cardiovascular and Environmental (SAYCARE) study. SAYCARE is an observational multicenter, feasibility study designed to develop valid and reliable indicators to investigate health-related behaviors and nutritional status in children and adolescents. The study was carried out in seven cities from six countries of South America: Buenos Aires (Argentina), Lima (Perú), Medellin (Colombia), Montevideo (Uruguay), Santiago (Chile), and São Paulo and Teresina (Brazil). The fieldwork was carried out during the academic years of 2015 and 2016.[22]

The patients were selected in each city in two steps: (a) schools were selected based on the students' age stratified into two groups: children (3-10 years) and adolescents (11-18 years) and school types (public or private), and (b) random sampling was conducted by using student lists. Each sex was represented by 50% of participants. The sample size was calculated based on the experience of other multicenter studies in which feasibility pilot studies were previously conducted, and the reliability and validity of the used methods were evaluated.[23-25] The study's exclusion criteria were pregnancy, the inability to complete the questionnaires, and the inability/rejection of the parents, guardians, and/or students to sign the informed consent form. A total of 1067 children and 495 adolescents were invited to take part in the study. After losses and rejections, 521 children and 308 adolescents agreed to participate in the anthropometric and blood pressure measurements.[22]

The project followed the ethical standards of the Declaration of Helsinki and Good Clinical Practice recommendations. The study was approved by the Ethics Committee of each participating center. The volunteer and/or guardian provided fully informed written consent to participate.

2.1 | Measurements

Height was measured with a portable stadiometer (Cardiomed WSC, Paraná, Brazil) to the nearest 0.1 cm, with the patient having bare feet and head in the Frankfort plane.

Blood pressure was determined with an Omron HEM-7200 electronic device with automatic inflation and deflation, oscillometric measurement method, and a pressure variation of 0-299 mm Hg. Because correct measurement requires appropriate cuff size to avoid overestimating or underestimating the valid BP values,[14] three different cuff sizes were used according to arm circumference measurements: 12-21 cm (small), 22-32 cm (medium), and 33-42 cm (large). Before starting the measurement, the automatic device was adequately calibrated with a mercury sphygmomanometer. Calibration was done before each collection with all automatic devices. The validity of the automatic devices used for this study has been already tested and published elsewhere.[26]

The BP measurement was taken on the right arm of seated participants, who had their backs resting on the back of a chair, their arm resting on a rigid surface at the heart level, and uncrossed feet resting on the floor. After 5 minutes of rest, the measurement was initiated. Two consecutive measures were performed with a 2-minute interval between them; if the difference between the two measurements was >5 mm Hg (either for the SBP or DBP), a third measurement was carried out. The BP was established as the mean of the two closest readings.

The following height-based equations were tested to determine their accuracy in the detection of elevated BP (BP level > P90th) according to the 2017 Clinical Practice Guideline for the management of High Blood Pressure in Children and Adolescents (considered the gold standard)[4]:

(i)Blood pressure to height ratio (BPHR)[18] = BP (mm Hg)/Height (cm)

(ii) Modified BP to height ratio (MBPHR)[20] = BP/(Height (cm) + 7 × (13 − age in years)

(iii) New modified blood pressure to height ratio (NMBPHR)[21] = BP/(Height (cm) + 3 × (13 − age in years)

(iv) Elevated BP cutoffs from the height-based equations (HBE)[13]: SBP P90th = 70 + 0.3 × height (cm); DBP P90th = 35 + 0.25 × height (cm)

Although the new guidelines have defined cutoff points for the detection of high BP in adolescents (aligned with the new adult guideline to facilitate the management of adolescents with high BP[27]), the percentile tables are more precise, so the formulas were compared with the percentile tables.

2.2 | Statistical analysis

Descriptive statistics for sex, height, BMI, SBP, and DBP for children and adolescents were expressed as means ± standard deviation (SD). Student's *t* test was used to compare means between sexes. For equations (i), (ii), and (iii), receiver operating curves (ROC) were performed to assess their accuracy as diagnostic tests for elevated SBP and DBP in boys and girls, both in children and adolescents. The sex- and age-specific optimal thresholds of systolic and diastolic BP were determined by the Youden index,[28] and the values corresponding to the maximum of the Youden index were selected as predictive values of elevated BP, either for systolic or diastolic BP. The obtained cutoff points from the four equations were then used to classify the children as either having elevated BP or not (either SBP or DBP). Next, to compare these equations with the gold standard method for identification of elevated BP,[4] sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for the four screening methods. The areas under the curve (AUC) and 95% confidence interval for the BP to height equations were performed to assess the discrimination power of the tests. AUC 0.5, AUC 0.5-0.65, and AUC 0.65-1.0 were interpreted as equal to chance, moderately, and highly accurate tests, respectively.[29] The diagnostic agreement between each method and the gold standard method[4] was evaluated with the kappa coefficient, categorizing the agreement as poor

TABLE 1 Descriptive characteristics of the study participants by age-group and sex

	Children (3-10.9 y)		Adolescents (11-18 y)	
	Boys	Girls	Boys	Girls
n	250	271	148	160
Age (y)	6.9 ± 2.3	7.0 ± 2.2	14.7 ± 2.2	14.6 ± 2.1
Height (cm)	120.8 ± 1.5	121.3 ± 1.5	163.0 ± 1.2	156.5 ± 0.7
BMI (kg/m^2)	17.7 ± 3.5	17.8 ± 3.6	21.9 ± 4.7	21.5 ± 3.4
SBP (mm Hg)	98 ± 10.0	97 ± 10.0	112 ± 12.0	106 ± 9.0
DBP (mm Hg)	63 ± 7.0	63 ± 7.0	64 ± 8.0	65 ± 7.0

Note: Data are presented as mean ± SD.
Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure.
*P value for difference between boys and girls using Student's *t* test.

TABLE 2 Cutoff points and their performance in three height-based equations

	SBPHR		DBPHR		MSBPHR	
	Boys	Girls	Boys	Girls	Boys	Girls
Children						
AUC (95% CI)	0.869 (0.816-0.922)	0.833 (0.766-0.900)	0.960 (0.939-0.981)	0.906 (0.865-0.947)	0.933 (0.900-0.966)	0.944 (0.913-0.974)
Cutoff points	0.85	0.84	0.56	0.56	0.64	0.63
Sensitivity (%)	90.6	90.0	0.98	84.9	90.6	100
Specificity (%)	72.5	67.3	86.4	80.3	85.8	80.1
Adolescents						
AUC (95% CI)	0.970 (0.944-0.996)	0.976 (0.949-1.00)	0.994 (0.983-1.00)	0.975 (0.941-1.00)	0.882 (0.819-0.945)	0.852 (0.766-0.939)
Cutoff points	0.74	0.74	0.47	0.48	0.82	0.74
Sensitivity (%)	95.5	100	100	88.9	81.8	100
Specificity (%)	89.7	87.2	98.6	97.4	84.9	59.0

Abbreviations: AUC, area under the curve; BPHR, blood pressure to height ratio; HBE, height-based equation; MBPHR, modified BPHR; NMBPHR, new MBPHR; S and D before each formula stand for the abbreviation of Systolic and Diastolic, respectively. Sensitivity and specificity were computed for their corresponding optimal cutoff points independently for SBP and DBP in the different formulas.

(kappa < 0.20), fair (kappa between 0.21 and 0.40), moderate (kappa between 0.41 and 0.60), substantial (kappa between 0.61 and 0.80), and almost perfect (>0.8).[30] All the statistical analyses were done using the Statistical Package for the Social Sciences (SPSS Inc, 22.0). The statistical significance was set at $P < .05$.

3 | RESULTS

A total of 521 children and 308 adolescents were included in the present study. Table 1 shows the main characteristics of the study population, including body mass index (BMI), SBP, and DBP by age and sex. The prevalence of elevated blood pressure (BP > P90th) was 26.8% in children and 13.6% in adolescents.

Performance of the optimal thresholds to determine high SBP and DBP for the equations BPHR, MBPHR, and NMBPHR, both in children and adolescents in this study, are shown in Table 2 and Figure S1 (the HBE directly determines the threshold for the 90th percentile for SBP and DBP). The abilities of these formulas to accurately define elevated BP were assessed by the AUC, which ranged from 0.906 to 0.996 for most formulas. The BPHR showed lower AUC values in children (but not in adolescents), although they were still high values: 0.833 and 0.869 for girls and boys, respectively. The AUC of the MBPHR equation showed more differences between groups, being lower in adolescents. The NMBPHR showed high AUC in all groups. Table 2 also shows the sensitivity and specificity of the cutoff points both for SBP and DBP. In most of the formulas, sensitivity was higher than specificity both in children and adolescents (74.6%-100%), and it was highest in adolescents (reaching 100%).

Table 3 shows the PPV and NPV for the four evaluated equations and the sensitivity and specificity of the BP diagnosis using each equation. Figure 1 shows the area under the curve for the cutoff points of the four equations, compared with the gold standard diagnosis (2017 Clinical Practice Guidelines of the American Academic of Pediatrics), by age-group and sex.

In children, the HBE equation showed maximum sensitivity (100%), both for boys and girls, while in adolescents, the NMBPHR was the equation with the highest sensitivity (100%), also for both sexes. PPV was generally low in all cases, ranging from 21.2% to 72.6%. The HBE formula showed the best performance results, except for female children, for whom the PPV was lower (53.8%). NPV was high both in children and adolescents (>90%). Kappa coefficient results indicated that HBE showed the highest agreement with the gold standard[4] diagnostic method (between 0.70 and 0.75), except for female children (0.57). The lowest agreement was observed for the MBPHR equation (0.20-0.53).

4 | DISCUSSION

This study evaluated the performance of different available height-based equations for screening elevated BP in children and adolescents from the SAYCARE study. In this sample of Latin American children and adolescents, all of the studied formulas performed well in the identification of elevated BP. The HBE equation showed better performance than the other formulas in this pediatric population. In epidemiology, classification bias is common and can considerably diminish the validity of study results.[31] These formulas were developed to simplify the screening of elevated BP in children and adolescents, avoiding the use of complicated and time-consuming percentile tables. Specifically, the 2017 Clinical Practice Guidelines of the American Academic of Pediatrics[4] entail almost 500 sex-,

MDBPHR		NMSBPHR		NMDBPHR	
Boys	Girls	Boys	Girls	Boys	Girls
0.835 (0.779-0.891)	0.929 (0.899-0.958)	0.971 (0.953-0.990)	0.952 (0.925-0.979)	0.983 (0.971-0.995)	0.970 (0.952-0.989)
0.40	0.41	0.74	0.75	0.48	0.48
74.6	92.5	100	100	96.6	96.2
78.0	85.3	85.3	86.1	89.5	86.7
0.955 (0.915-0.995)	0.891 (0.823-0.960)	0.955 (0.923-0.987)	0.965 (0.936-0.993)	0.996 (0.987-1.00)	0.971 (0.942-1.00)
0.49	0.49	0.75	0.76	0.49	0.47
100	100	100	100	100	100
87.9	76.8	83.3	89.9	97.2	88.1

age-, and height-specific cutoffs to assess SBP and DBP in children and adolescents.

Although there are applications or web sites that can identify blood pressure percentiles, inequalities in Internet access and insecurity problems in Latin American countries make simplified methods a quick option to screen high blood pressure in children and adolescents.

Many equations had been tested with the 2004 Fourth Report of the American Academic of Pediatrics guidelines,[14] starting with the BPHR developed by Lu and colleagues[18] and followed by the MBPHR[32] and the NMBPHR,[21] which improved the performance of the first one.

In 2017, the new guidelines[4] changed the BP percentile values, based on a population that excluded children and adolescents with overweight or obesity. This meant a change in the cutoff points for all formulas.

Zhang and colleagues[17] compared the performance of three height-based formulas (BPHR, MBPHR, and NMBHR) in Chinese and American children using the 2017 guidelines as the diagnosis method. He found that NMBPHR performed better than BPHR and MBPHR in both child populations, although the three formulas had low PPV (<50%) compared to the gold standard guidelines. Our study showed better PPV and similar NPV than the three formulas tested by Zhang and colleagues[17] in the Chinese and American populations. The Kappa coefficient also showed a better agreement in most of the formulas in our population. Mourato and colleagues[19] calculated the new cutoff points for the same three height-based formulas using the 2017 guidelines in a population of Brazilian and American children aged 8-13 years old. He found that the NMBPHR showed better specificity and PPV for the screening of high BP in both populations. Our study showed better PPV than the three formulas tested by Mourato and colleagues[19] in the Brazilian and American populations. NPV in our population was similar to these values in the mentioned study. Based on the current 2017 guidelines, this author built a simple height-based equation (HBE)[13] for the detection of high BP and compared it with the previously reported screening methods in the mentioned samples of Brazilian and American children. His study showed that the HBE had a higher ability to detect high BP and better agreement with the 2017 guidelines than the previous ones. We tested all of the mentioned formulas in the SAYCARE Latin American children and adolescents, comparing them with the new 2017 guidelines. All of the equations showed a good performance based on the AUC, sensibility, specificity, and NPV. Although the PPV values were low in all of the formulas, the HBE equation showed the highest PPV (>60%) in both age and sex groups, except for female children (53.8%). This means that 47% of the female children identified as having elevated BP using the HBE equation would not actually have elevated BP based on the new guidelines (false positives). However, the chances of false positives (low PPV) were higher when using the other equations, highlighting the lowest PPV values of the MBPHR and NMBPHR among female adolescents. These results involve the need for these children to be more closely monitored to confirm or rule out the diagnosis, something that may result in unnecessary tests and consequent psychological stress for these children and their families. On the other hand, the NPV was above 90% for all of the equations and reached 100% with the HBE equation for both age and sex groups, except for female adolescents, which almost reached this value (99.2%). This means that the simplified methods to assess high BP perform well when the purpose is to exclude the presence of elevated BP.

When we tested the agreement between the formulas and the diagnosis by the 2017 guidelines through the kappa coefficient, the HBE formula showed the best agreement, above 70%, although,

TABLE 3 Performance of height-based equations

Screening method	BPHR Boys	BPHR Girls	MBPHR Boys	MBPHR Girls	NMBPHR Boys	NMBPHR Girls	HBE Boys	HBE Girls
Children								
Cutoff points	0.85/0.56	0.84/0.56	0.64/0.40	0.63/0.41	0.74/0.48	0.75/0.48	N/A	N/A
Sensitivity (%)	94.8	87.3	84.4	93.7	97.4	98.4	100	100
Specificity (%)	75.6	66.8	65.3	72.1	79.2	77.9	83.2	74.0
AUC (95% CI)	0.853 (0.804-0.902)	0.771 (0.708-0.833)	0.749 (0.685-0.813)	0.829 (0.776-0.881)	0.883 (0.840-0.926)	0.881 (0.841-0.922)	0.916 (0.881-0.951)	0.870 (0.830-0.911)
PPV (%)	63.5	44.4	52.0	50.4	67.6	57.4	72.6	53.8
NPV (%)	97.0	94.6	90.4	97.4	98.6	99.4	100	100
Kappa coefficient	.62	.41	.42	.51	.68	.61	.75	.57
Adolescents								
Cutoff points	0.74/0.47	0.74/0.48	0.82/0.49	0.74/0.49	0.75/0.49	0.76/0.47	N/A	N/A
Sensitivity (%)	95.8	94.4	87.5	100	100	100	100	94.4
Specificity (%)	89.5	85.9	82.3	52.8	79.8	79.6	88.7	92.3
AUC (95% CI)	0.927 (0.870-0.983)	0.902 (0.831-0.973)	0.849 (0.763-0.935)	0.764 (0.682-0.847)	0.899 (0.851-0.948)	0.898 (0.849-0.946)	0.944 (0.908-0.979)	0.933 (0.867-1.00)
PPV (%)	63.9	45.9	48.8	21.2	49.0	38.3	63.2	60.7
NPV (%)	99.1	99.2	97.1	100	100	100	100	99.2
Kappa coefficient	.71	.55	.53	.20	.56	.47	.72	.70

Note: Sensitivity and specificity were computed for the diagnosis based on elevated SBP and/or DBP. Kappa coefficient was calculated for the diagnosis of elevated BP derived from each method against the one derived from the 2017 Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents.

Abbreviations: AUC, area under the curve; BPHR, blood pressure to height ratio; CI, confidence interval; HBE, height-based equation; MBPHR, modified BPHR; N/A, nonapplicable; NMBPHR, new MBPHR; NPV, negative predictive value; PPV, positive predictive value.

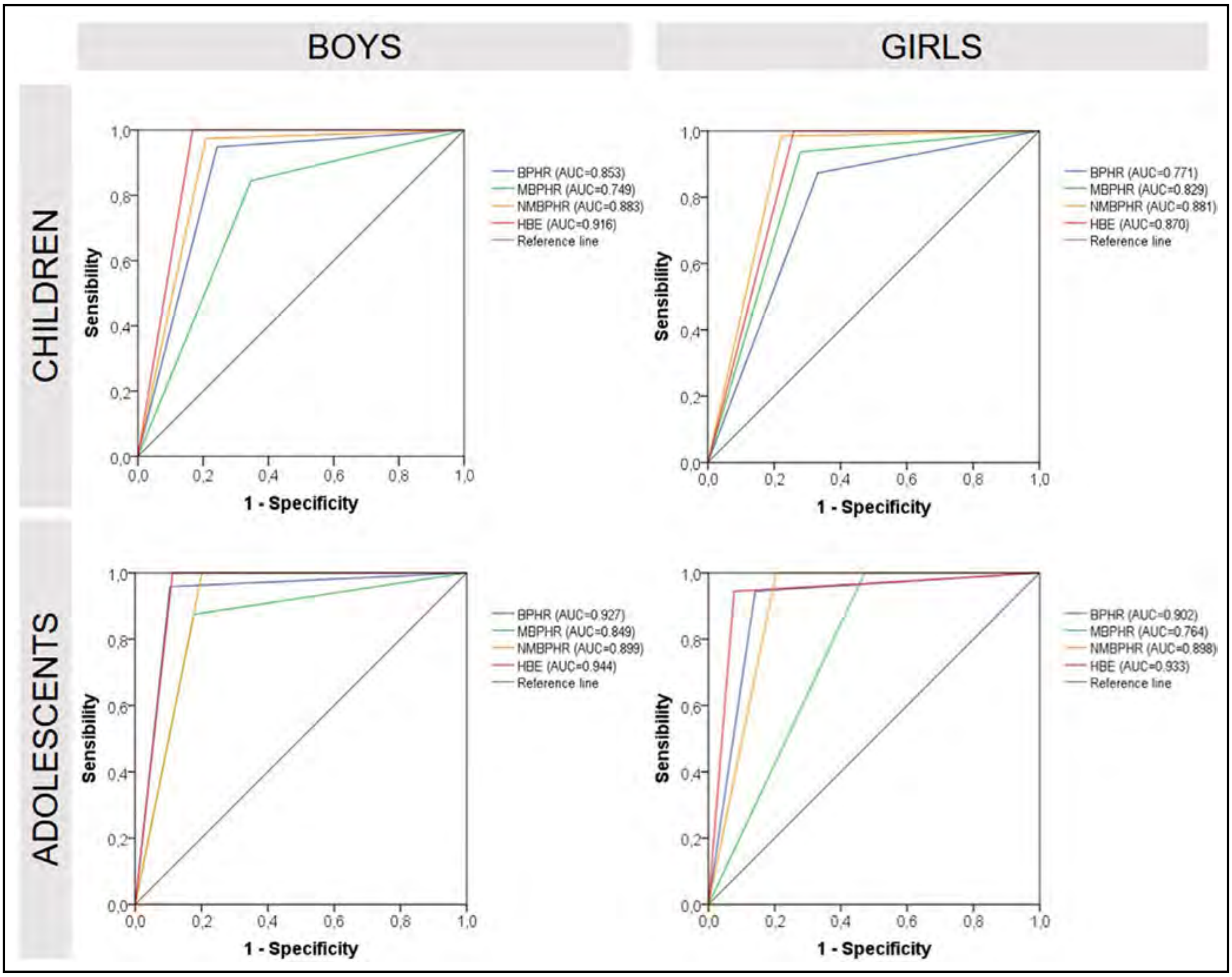

FIGURE 1 Receiver operating characteristic curves with the cutoff points of the four equations in children and adolescents

again, it was lower in female children. We tried to find possible causes for this to happen because, in the rest of the groups (male children and adolescents of both sexes), the kappa coefficient performed very well in the HBE formula. These results could be related to differences in growth pattern, since pubertal development begins earlier in girls than in boys. In a study carried out with more than five thousand Croatian children and adolescents, trunk height growth velocity increased in girls and decreased in boys between 7 and 11 years old. The authors mention that their findings are similar to others found in several European countries, regardless of the mean height of each population.[33] In a study about components of height and blood pressure in children, published in 2014, the authors found that trunk length, but not leg length, was positively related to SBP and DBP.[34] However, we did not measure the trunk length in this study. A possible explanation for the difference in kappa values between girls and boys in children could be that, in this stage of growth, the trunk growth rates differ by sex. [34]

The simplified methods are friendlier than the diagnosis percentile tables. The most practical formulas to apply were the BPHR and the HBE equations because they do not require age in their calculation. The BPHR equation involves the calculation of four different cutoff points (boys and girls in children and adolescents), whereas the HBE formula implies two equations, one for the SBP and one for the DBP. It is likely that the HBE formula showed a better performance in the present Latin American population given the similar origin (Brazilian and American) of the children from the study in which the author designed the equation.[13] Compared to the performance in the Brazilian population of the mentioned study, the HBE equation performed equal to or better in our Latin American population.

The use of this equation can be useful in those instances where the health professional does not have access to the applications that can simplify the diagnosis. The data provided by this research is not intended to replace the diagnosis of high blood pressure; it aims to facilitate the approach to a diagnosis in those children and adolescents who may be hypertensive.

The present work has few limitations that must be acknowledged, we were not working with a representative sample of each of the different participating countries, and we did not have information regarding comorbidities or use of medication. A strength is that we could test the equations using the new 2017 guidelines in a diverse population of children and adolescents from seven cities in six Latin American countries.

5 | CONCLUSION

In this Latin American pediatric population, the use of the HBE equation proved to be a useful tool to screen elevated blood pressure in children and adolescents. As it is easy to apply, we encourage health professionals and epidemiologists to consider it in their routine clinical assessments and determine which patients require from a closer and more thorough evaluation to confirm (or rule out) the diagnosis.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

AUTHOR CONTRIBUTIONS

ES, KAM, ACFDeM, HBC, and JCA involved in the data collection. ES, AIR, JCA, and LAM involved in the conducting, analysis and writing of the manuscript. All authors involved in writing the paper and had final approval of the submitted and published versions.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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