Original Article

Reference Values for Blood Pressure of Healthy Schoolchildren in Shiraz (Southern Iran) using Quantile Regression

SMT Ayatollahi[1], MA Vakili[1], J Behboodian[2], N Zare[1]

[1]Department of Biostatistics, Shiraz University of Medical Sciences, [2]Department of Mathematics, Shiraz Islamic Azad University, Shiraz, Iran

Background: The Reference values of systolic and diastolic Blood Pressure (BP) levels of school children aged 6–11 years by two different analytic strategies are presented and compared.
Methods: From the cross-sectional study a total of 2064 children (52.3% boys and 47.7% girls) aged 6–11 years living in Shiraz (southern Iran) and considering their sex and height were used for this analysis. Polynomial Regression (PR) and Quantile Regression (QR) models based on Restricted Cubic Spline (RCS) were performed to calculate age and height specific reference ranges. To assess comparability of the two techniques, a chi-square goodness-of-fit within sex and age groups was preformed for each method.
Results: Both statistical methods generated reference values of systolic and diastolic BP using data from apparently healthy children. Analysis of data by two approaches reflected an increase in BP measurements with age and height in both sexes based on a nonlinear manner up to age 11. We found 50th and 95th percentile differences by two methods in BP level between the tallest and the shortest individuals, ranging from 2-7 mmHg.
Conclusion: Using the QR model based on RCS offered the most flexible and better fit than PR model. The advantages of the QR led to a better adaptation of reference limits to the original data. This statistical approach might be preferable for the calculation of reference ranges in particular by non-normal distributed variables. Our results might help clinicians reach a consensus on the definition of hypertension in Iranian children living in Shiraz, south of Iran.

Keywords: Reference Values, Quantile Regression, Polynomial Regression, Blood pressure, School Children.

Introduction

High blood pressure (BP) in infants is always indicative of an underlying condition which requires attention. Children may present essential elevated BP, which is usually detected by regular BP monitoring. Currently, this is the main cause of arterial hypertension in this age group.[1-3]

Screening for high BP in children and adolescents which has been recommended since the 1977 Report of the Task Force on BP Control in Children is important in implementing preventive diet and exercise programs or pharmacologic treatment and to identify those at increased risk of cardiovascular disease as adults.[4-7]

Correspondence:
Mohammad Ali Vakili
Department of Biostatistics, School of Medicine, Shiraz University of Medical Sciences, P.O. Box 71345-1847, Shiraz, Iran
E-mail: vakilima@sums.ac.ir

The prevalence of hypertension among children ranges from 5.4% to 19.4% which has been reported previously.[8] Although prevalence is lower than those seen in adults, this condition is not rare in children, thus stressing the importance of evaluating BP.[9]

Numerous studies have shown that the underlying condition of high BP in adults may have its origins in childhood or adolescence, making early preventive intervention a tool to reduce the risks of cardiovascular disease and target organ damage in later stages of human life. Elevated BP in children is becoming an emerging public health problem and it seems that screening in children is important for the early detection and prevention of adult cardiovascular sequelae.[1, 10-13]

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Data from diverse populations show that BP in children could be affected by various factors such as environmental, cultural, social and genetic components, also BP levels vary with age, sex, and increase in growth and development.[13-14]

This association between elevated BP with other factors suggests that the reference values of BP is dynamic and varies from each society or era to another. Thus, application of the available reference for BP in children to other populations whose demographic factors are different may not be valid.[10]

To estimate Reference Values of Blood Pressure (RVBP) in children, we need to establish a range of values that systolic BP or diastolic BP may normally take in a target population. The corresponding ranges are often referred to as norms or reference values. Several methods, such as regression analysis, mixed models, polynomial regression (PR), fractional polynomial regression, and HRY nonparametric as well as LMS parametric techniques are available for estimating references values.[15] But to the best of our knowledge, except one, no report has ever dealt with the RVBP by Quantile Regression (QR) model. Rosner et al. examined three different analytical approaches on 11 large pediatric BP studies and showed that the use of the QR model the most flexible and best fits.[16]

Finally, because height is identified as more appropriate than weight for determination of BP in children and adolescence and also, there is no data available on local children BP standards adjusted for height, this study was conducted to estimate and compare RVBP by two different analytical techniques including PR and QR methods in 6-11 elementary school children in Shiraz (Southern Iran), by sex adjusting for age and height.

Materials and Methods

The data for this study were obtained from a previous survey involving children from forty- three schools of the four educational districts of Shiraz, during the academic period of 2003-2004. Sampling was done by multi-stage random method, a 10% systematic random sample of schools was taken from each district including public and private schools. Within each selected school, a 1 in 5 samples of students aged between 6 and 11 years old were selected using a table of random numbers. Applying this procedure, 2,237 healthy school attendees were selected in a cross-sectional study, representing a 2% sample of school children in the city. A child is considered healthy if he or she is free from any congenital, chronic, or malnutrition disorders. A total of 2,064 healthy students (1,080 boys, 984 girls) aged 6-11 (6≈6.00-6.99, 7≈7.00-7.99, 8≈8.00-8.99, 9≈9.00-9.99, 10≈10.00-10.99, and 11≈11.0-11.99) with valid BP and anthropometric measurements were selected and used for deriving BP distribution.

Children's height were measured by two trained auxologists using a digital stadiometer (SECA model 707, Germany) and methods given by Cameron[17] and recorded to the nearest 0.1 cm. The subjects' ages were calculated exactly as the differences between the dates of interview and the birthdates in days as recorded accurately in their birth certificates. An informed consent was sought from the subject's parents and guardians and the procedure was explained to the child before measuring his/her BP by the trained nurses or health workers of the research team. Standard and calibrated aneroid manometers (Model 500-c, Japan) (to avoid mercury toxicity) were used for all readings. BP was measured with the child sitting quietly for at least 5 minutes, feet on the floor and right arm supported, cubital fossa at heart level. Children were excluded if they had stress or were taking any stimulant foods or drugs (eating any food or drinking tea or coffee before the measurement or having any activity).

BP measurements are based on auscultatory method. An appropriate cuff size was used with an inflatable bladder length that was covering at least 80 percent of the arm circumference at the point midway. The stethoscope was placed over the brachial artery pulse and below the bottom edge of the cuff without any contact between cuff and stethoscope. The cuff was being inflated until brachial pulse disappeared. Systolic BP and Diastolic BP were determined by the onset of the tapping Korotkoff sounds (K1) and established the fifth Korotkoff sound (K5), respectively. BP of each school children was measured once. However, they were randomly checked for second or third time. Length between two measurements was at least 30 minutes. The detailed design and methodology is available in previous publication.[18]

Statistics

In order to fit appropriate models, PR and QR based on restricted cubic splines were considered to estimate BP percentiles in relation to sex, age, and height. Also to assess and compare these two models, a chi-square goodness-of-fit within sex and age groups was preformed for each method.

Polynomial Regression models

Sometimes, during data analysis with linear regression model, we may notice that the relationship between independent variable (X) and dependent variable (Y) does not follow a straight line; instead it appears as a curved line. In these cases, linear regression would not be a good model for prediction of relationships between variables. Hence we use polynomial regression in which different powers of independent variable X (X, X2, X3, X4…) are added to an equation to find the best-fitting equation. Our PR model, which were supported by the National High Blood Pressure Education Program (NHBPEP),[19] was a fourth degree polynomial model to estimate adjusted BP as a sex-specific function of age and height Z score. More technical details are found in appendix1.

The advantage of using PR model is that, although the distribution of height varies greatly with age, the distribution of height Z scores does not, thus allowing one to estimate BP percentiles as a function of age and height with a relatively simple polynomial model across a wide age range.[10,16, 21] However, a disadvantage of equation 1 is the assumption that the difference in measurement of BP between two children of the same age with height z scores of Z1 and Z2 is independent of age which may or may not be true (appendix 1).

Quantile Regression models

Any statistical test assumes some assumptions. Violation of these assumptions will change the conclusion of research. Hence any research must follow these presumptions e.g. assumption of normality. When PR was applied, we used Ordinary Least Squares (OLS) regression with three major speculations: (1) normality, i.e. for any value of X, variations of dependent variable Y has a normal or Gaussian distribution (like a bell-shaped graph) (2) homoscedasticity, that is, the width (standard deviation) of that distribution is identical for all values of age and height (X), and (3) nonlinearity. OLS regression model is often used for representation of continuous variables (e.g. BP distribution). For any statistical method, if these assumptions are violated, the results may be inaccurate or incorrect. [22-24]

When the first two assumptions are met, OLS regression describes how independent variables (vector of X) are associated with the conditional mean of BP measurements (Y).

An alternative way to assess how X affects the central region of the conditional distribution of Y is median regression. (Distribution of values of Y for a specific or a narrow range of values of X, is called conditional distribution of Y on X).[24] “Because medians are less influenced by outlying values than means, the median has advantages for tracking typical values, that is, the central tendency. QR is a method that assesses how Y relates to X for any conditional percentile of Y, that is, for individuals whose value of Y tends to be the lower end, higher end, midrange, or anywhere within the observed conditional distribution of Y. Median regression is a specific case of QR, for the 50th percentile”.[24] Despite OLS regression, there is no need to assume normality or homoscedasticity for median regression. If our data satisfy the normality supposition, then the conditional mean and conditional median are comparable. As for median regression, QR does not assume normality or homoscedasticity.[24-26] It should be noted that QR has greater power for finding a statistically significant effect of X on Y for an extreme percentile (e.g. <10 or >90) than for more central percentiles.[24, 26]

Another important issue in regression relationships is nonlinearity, which can be assessed by several methods, such as, logarithms, polynomials,

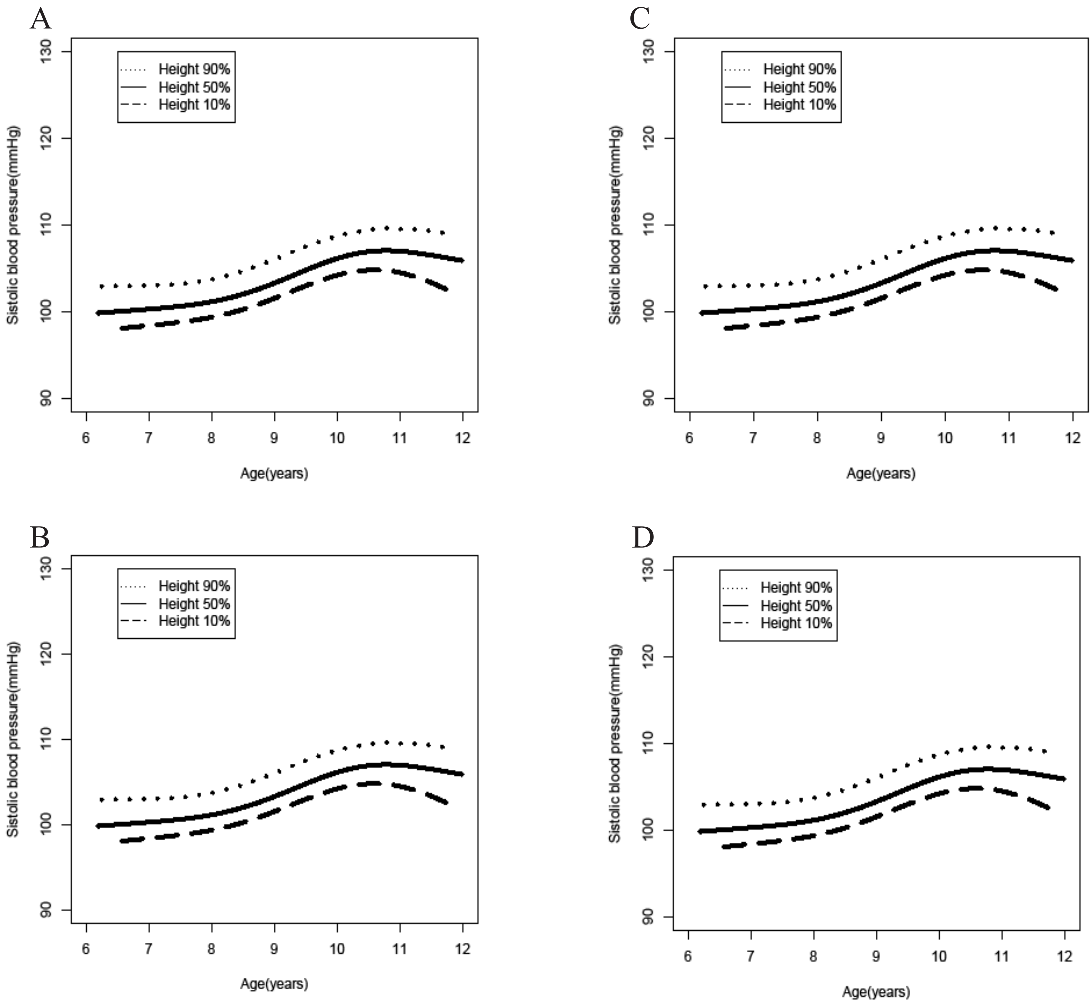

Figure1. 90th percentile of blood pressure by age and percentile of height (10%, 50%, or 90%) among children, obtained from polynomial regression models. A) Polynomial systolic blood pressure for boys, by age; B) Polynomial diastolic blood pressure for boys, by age; C) Polynomial systolic blood pressure for girls, by age; D) Polynomial diastolic blood pressure for girls, by age.

cubic splines, and Restricted Cubic Splines.[26-28] A common approach is dividing a continuous independent variable into a number of categories. A powerful and flexible method that can fit almost any relationship is RCS.[24, 29] The steps in creating RCS include: (1) Dividing the observed range of the X variable using k breakpoints, called knots, at $X_{knot\#j}$, for j=1 to k; (2) For each of these k knots, creating a new variable that is a third order polynomial in X above that knot (i.e. $X\text{-}X1)^3$, and zero below it; (3) constraining of these "piecewise" polynomials or functions (In mathematics, A piecewise function is usually defined by more than one formula (i.e. a formula for each interval.), and X itself, to smoothly fit together at each knot, and to be linear both below the first knot and above the last knot. This process produces k – 1 variables (the linear variable X itself, and k - 2 piecewise cubic variables). The knots are usually located at fixed percentiles of X. The number of knots is more important than their location; k=5 usually gives a good fit, although fewer knots is adequate for small data sets.[16, 29-30]

In this study, a fitted QR using RCS was applied to relax the assumption of normality and homoscedasticity, and also to build a more flexible model ,.

To implement these methods, first, we constructed an OLS regression model of each BP measurement (Appendix 2). Each predictor variable was modeled using a restricted cubic spline representation with five knots located at the 5th, 27.5th, 50th, 72.5th, and 95th percentiles, respectively, as suggested by Harrell.[16, 27]

Secondly, we used QR for each quantile τ (Appendix2). The regression is estimated using

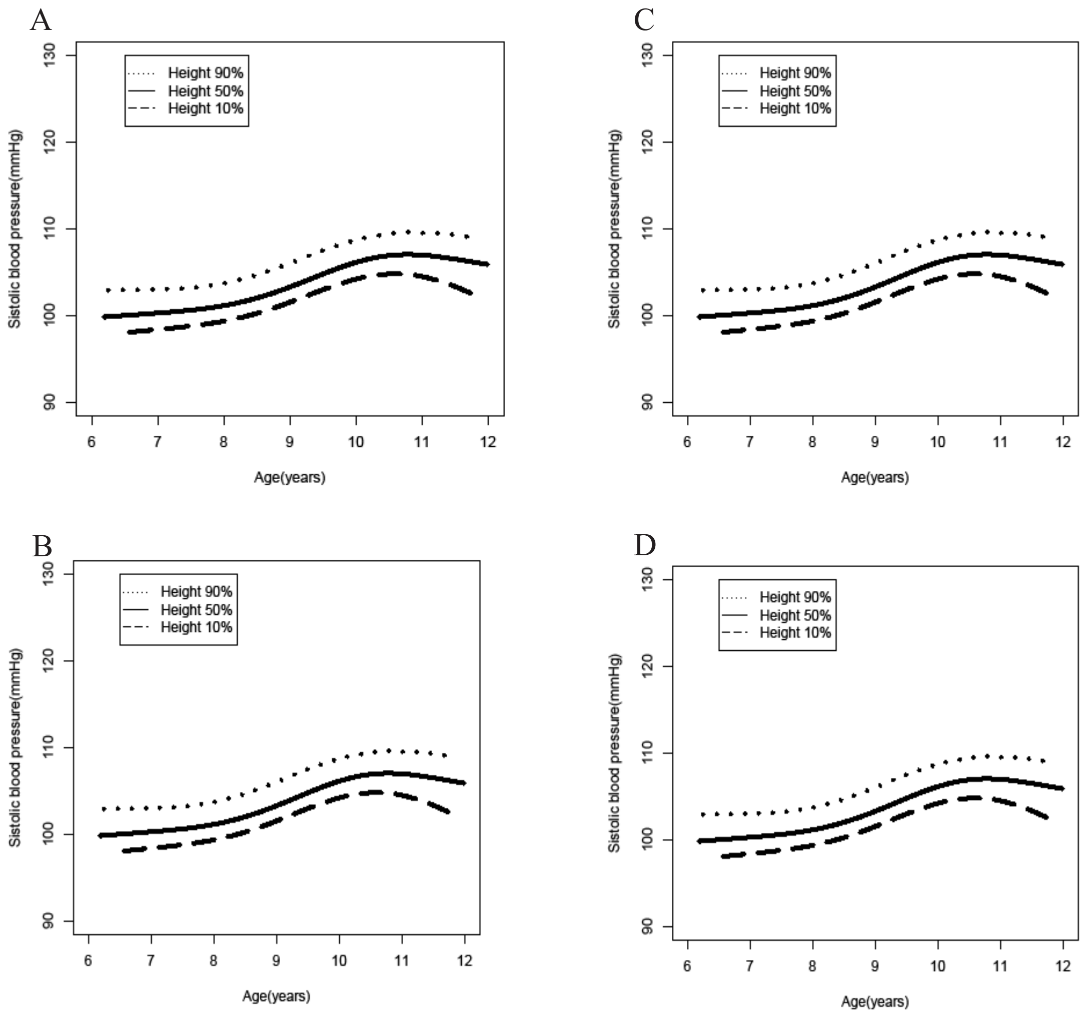

Figure2. 90th percentile of blood pressure by age and percentile of height (10%, 50%, or 90%) among children, obtained from quantile regression models. A) Systolic blood pressure for boys (quantile regression); B) diastolic blood pressure for boys (quantile regression); C) Systolic blood pressure for girls (quantile regression); D) diastolic blood pressure for girls (quantile regression).

QUANTREG in R software.[31] We ran these regressions for each quantile of τ =0.05, 0.1, 0.25, 0.5, 0.75, 0.9 and 0.95. The QR approach using separate restricted cubic splines because prediction for quantile offers the most flexibility in terms of both specification of the regression function for a specific quantile and allowing for separate regression equations for different quantiles.[16, 24]

Assessing goodness of fit

When assessing the goodness of fit of the PR and the QR approaches, we subdivided the data for each age according to sex-specific predicted BP percentile, divided at 5 percent, 10 percent, 25 percent, 50 percent, 75 percent, 90 percent, and 95 percent, where the cut points were included in the upper segment. For each sex, we then compared the observed distribution of children in these BP percentile groups with the expected distribution for each 2-year age group, combined the data into three age groups (6–7 years, 8–9 years, and 10–12 years) separately done for boys and girls, and performed a chi-square goodness-of-fit test for each method within each of the six age-sex groups.

Results

Table 1 summarizes statistics of BP by sex, age and height. An increasing trend in systolic and diastolic BP can be seen by age and height for both sexes.

There was a strong positive correlation of systolic and diastolic BP with height and age in both sexes. In boys, the respective coefficients of correlation of systolic and diastolic BP in height were

Table 1. Summary statistics of BP by sex, age, and height

Parameter		Boys					Girls				
		SBP (mmHg)			DBP (mmHg)		SBP (mmHg)			DBP (mmHg)	
		n	Mean (SD)	CI (95%)	Mean (SD)	CI (95%)	n	Mean (SD)	CI (95%)	Mean (SD)	CI (95%)
Age (years)	6-7	296	89(9)	88-90	56(8)	55-57	283	89(10)	88-91	58(9)	57-59
	8-9	434	92(10)	91-92	59(8)	59-60	379	93(11)	91-94	60(9)	60-61
	10-11	350	95(12)	94-97	61(10)	60-63	322	95(12)	93-96	62(10)	61-63
Height (cm)	<120	153	88(9)	86-89	56(8)	54-57	142	85(10)	84-87	55(8)	54-57
	120-30	357	90(9)	89-91	57(8)	56-58	326	91(10)	90-92	60(9)	59-61
	130-140	391	93(10)	92-94	60(9)	59-61	328	94(11)	93-95	61(9)	60-62
	>= 140	179	98(12)	96-100	64(10)	62-65	188	97(13)	95-99	64(10)	62-65
	Total	1080	92(11)	91-93	59(9)	58-60	984	92(11)	92-93	60(9)	60-61

Abbreviation: SBP = Systolic Blood Pressure; DBP =Diastolic Blood pressure; SD = Standard Deviation; CI = Confidence Interval

0.33 (P<0.0001) and 0.31 (P<0.0001), and in age 0.24 (P<0.0001) and 0.25 (P<0.0001). In girls, the coefficients of correlation of systolic and diastolic BP in height were 0.33 (P<0.0001) and 0.26 (P<0.0001), and with age 0.22 (P<0.0001) and 0.19 (P<0.0001), respectively.

Given these results, first, we estimated the age and height dependent reference values for BP measurements by PR models. The regression coefficients from PR model were demonstrated for both sexes separately (Table 2). As expected, the age and height Z score and some of their powers were strong predictors of systolic BP and diastolic BP for both of the boys and girls (P<0.05). In Figure 1, we plot the predicted 90th percentile of blood pressure (pre-hypertensive level) by age for children at the 10th, 50th, and 90th height percentiles obtained from PR models. As shown in Figure1, the shapes of the pre-hypertensive level in nonlinear manner by age are different for the boys and girls. The predicted 90th percentile of BP increased gradually by age in girls, but in boys, this trend was followed up

Table 2. Results from polynomial regression models relating blood pressure to age and height Z score (Zht) among children in Shiraz-Iran

Parameter	Systolic blood pressure				Diastolic blood pressure			
	Boys		Girls		Boys		Girls	
	β*	P value	β	P value	β	P value	β	P value
Intercept	92.14	<0.001	94.73	<0.001	59.71	<0.001	61.75	<0.001
$(Age-9)^1$	3.19	<0.001	0.99	0.075	2.48	<0.001	0.98	0.04
$(Age-9)^2$	0.88	0.071	- 0.90	0.099	0.05	0.909	-0.81	0.082
$(Age-9)^3$	- 0.36	0.003	0.17	0.003	-0.22	0.030	0.05	0.625
$(Age-9)^4$	- 0.16	0.055	0.12	0.055	-0.04	0.621	0.12	0.111
$(Zht)^1$**	3.37	<0.001	3.08	<0.001	2.68	<0.001	1.71	<0.001
$(Zht)^2$	0.70	0.134	-0.59	0.107	0.51	0.217	-0.13	0.670
$(Zht)^3$	-0.23	0.418	-0.08	0.324	-0.36	0.149	0.002	0.978
$(Zht)^4$	-0.08	0.420	0.04	0.145	-0.11	0.210	0.01	0.633
Residual standard Deviation	9.93		10.74		8.69		9.13	
ρ^{***}	0.351		0.348		0.317		0.271	

*Regression coefficient; **Zht: height Z score; ***Intra-class correlation coefficient (It shows whether values from the same group tend to be similar, the greater the coefficient, the more tendency for similarity).

Table3. Blood Pressure (BP) percentile values for boys in relation to age and height percentiles by polynomial and quantile regression models.

Age	BP percentiles/ Height	Height Percentiles 5		10		25		50		75		90		95	
		PR	QR	PR	QR	PR	QR	PR	QR	PR	QR	PR	QR	PR	QR
6.0	SBP50	86	85	86	86	87	87	87	88	88	89	89	89	89	90
	SBP90	99	95	99	95	99	96	100	98	101	98	102	99	102	99
	DBP50	54	51	54	52	54	53	55	55	55	56	56	57	56	57
	DBP90	65	61	65	62	65	63	66	63	66	64	67	64	67	64
	Height	110		111		113		115		117		118		119	
7.0	SBP50	86	87	87	88	87	89	88	90	88	90	89	90	89	90
	SBP90	99	96	99	97	100	98	100	100	101	100	101	100	101	100
	DBP50	55	56	55	56	55	57	55	58	56	59	56	59	56	59
	DBP90	66	66	66	66	66	66	66	66	67	67	67	67	67	67
	Height	114		116		118		120		121		122		122	
8.0	SBP50	87	88	88	89	88	90	89	90	90	90	90	90	90	90
	SBP90	100	98	100	100	101	100	101	100	102	100	103	100	103	100
	DBP50	56	58	56	59	56	60	57	60	58	60	58	60	58	60
	DBP90	67	66	67	66	68	67	68	67	69	68	69	68	69	69
	Height	118		120		123		125		127		127		128	
9.0	SBP50	90	90	91	91	91	91	92	91	93	91	93	92	93	92
	SBP90	103	101	103	103	104	103	105	104	106	104	106	105	106	105
	DBP50	59	59	59	60	59	60	59	60	60	60	60	60	60	60
	DBP90	70	68	70	70	70	71	70	71	71	71	72	71	72	71
	Height	122		125		128		130		132		133		133	
10.0	SBP50	93	91	93	91	94	91	95	92	95	93	96	93	96	94
	SBP90	106	106	106	107	107	107	107	109	108	110	108	111	108	111
	DBP50	60	60	60	60	60	60	61	60	61	60	62	60	62	60
	DBP90	71	71	71	71	72	72	72	72	73	72	73	73	73	73
	Height	127		129		133		135		137		137		138	
11.0	SBP50	91	88	92	89	92	90	93	91	94	92	94	93	94	93
	SBP90	104	103	105	105	105	106	106	107	106	108	107	108	107	108
	DBP50	59	60	60	60	60	60	60	60	61	60	61	60	61	60
	DBP90	71	68	71	69	71	70	71	70	72	71	72	71	72	71
	Height	131		133		135		137		139		140		140	
Total	SBP50	89	88	90	89	90	90	91	90	91	90	92	90	92	90
	SBP90	102	99	102	100	103	101	103	102	104	102	105	102	105	102
	DBP50	57	59	57	60	58	60	58	60	59	60	59	60	59	60
	DBP90	68	66	69	67	69	68	69	69	70	70	70	70	70	70
	Height	121		123		126		127		129		130		130	

Abbreviation: QR = Quantile Regression; PR = Polynomial Regression; BP = Blood Pressure; SBP50 = 50th Systolic Blood Pressure; SBP90 = 90th Systolic Blood Pressure; DBP50 = 50th Diastolic Blood pressure; DBP90 = 950th Diastolic Blood Pressure

to 10 years old. Also, the differences in pre-hypertensive level between the 10th and 90th percentiles of height were noticeably different by age for both systolic and diastolic BP in girls.

In addition, we conducted additional analyses including interaction terms of (age-9) × Zht^1, (age-9) × Zht^2, (age-9) × Zht^3, and (age-9) × Zht^4 for all of the models in Table 2. This was done with the idea that based on equation (2), we assumed the mean difference in blood pressure for two children with height z scores of Zht1 and Zht2 are the same for all ages. There were not any significant interaction effects for all of the four models supporting this assumption.

Table4. Blood Pressure (BP) percentile values for girls in relation to age and height percentiles by polynomial and quantile regression models.

Age	BP percen-tiles/ Height	Height Percentiles 5		10		25		50		75		90		95	
		PR	QR	PR	QR	PR	QR	PR	QR	PR	QR	PR	QR	PR	QR
6.0	SBP50	82	85	82	86	84	87	86	87	87	88	87	88	87	88
	SBP90	96	96	96	98	98	98	99	99	101	100	101	100	101	100
	DBP50	53	59	54	59	55	60	56	60	57	60	57	60	57	60
	DBP90	65	62	66	64	67	65	68	67	69	67	69	68	69	68
	Height	106		108		111		114		116		117		117	
7.0	SBP50	84	84	85	85	87	87	88	88	89	89	89	90	90	90
	SBP90	98	99	99	99	100	100	102	101	103	101	103	102	103	102
	DBP50	55	57	56	58	57	58	57	59	58	59	58	60	58	60
	DBP90	67	67	67	68	68	69	69	70	69	70	70	70	70	70
	Height	113		115		117		120		121		122		122	
8.0	SBP50	87	87	87	88	89	90	90	91	92	92	92	93	92	93
	SBP90	100	99	101	100	103	101	104	105	105	107	106	107	106	107
	DBP50	57	58	57	59	58	59	59	60	60	60	60	60	60	60
	DBP90	69	68	69	68	70	69	71	70	71	71	72	71	72	71
	Height	118		119		122		125		126		127		127	
9.0	SBP50	87	89	89	90	90	90	92	91	93	92	93	93	93	94
	SBP90	101	99	103	103	104	106	105	108	106	110	107	110	107	110
	DBP50	58	60	59	60	60	60	60	60	61	60	61	60	61	60
	DBP90	70	67	70	68	71	69	72	70	73	71	73	71	73	72
	Height	122		125		127		130		131		133		133	
10.0	SBP50	88	91	89	92	91	94	93	94	94	95	94	95	94	95
	SBP90	102	101	103	103	105	108	106	109	107	110	108	110	108	110
	DBP50	58	60	59	60	60	60	61	60	61	60	62	60	62	60
	DBP90	70	71	71	72	72	74	72	75	73	75	73	75	73	75
	Height	126		128		132		135		137		138		139	
11.0	SBP50	91	92	91	92	93	92	94	93	95	94	96	95	96	95
	SBP90	104	105	105	106	107	108	108	110	109	111	109	112	110	113
	DBP50	60	60	60	60	61	60	62	60	62	61	63	61	63	61
	DBP90	72	75	72	75	73	77	74	77	74	78	75	79	75	79
	Height	131		133		136		139		141		142		143	
Total	SBP50	87	89	88	90	89	90	91	92	92	92	92	93	92	93
	SBP90	101	99	101	100	103	103	104	106	105	107	106	108	106	108
	DBP50	57	59	58	60	59	60	59	60	60	60	60	60	60	60
	DBP90	69	68	70	70	70	69	71	71	72	71	72	72	72	72
	Height	121		122		125		128		129		130		131	

Abbreviation: QR = Quantile Regression; PR = Polynomial Regression; BP = Blood Pressure; SBP50 = 50th Systolic Blood Pressure; SBP90 = 90th Systolic Blood Pressure; DBP50 = 50th Diastolic Blood pressure; DBP90 = 950th Diastolic Blood Pressure

Second, we constructed the QR model, separately by sex for the 5th, 10th, 25th, 50th, 75th, 90th, and 95th percentiles of blood pressure. For illustration of the relations, plots of the pre-hypertensive level of systolic and diastolic BP by age and percentiles models. Table 5 displays the observed number of height presented in Figure 2. The predicted 90th percentile of blood pressure showed a curve-linear increase in age, with the highest slope appearing in pre-hypertensive level between the 10th and 90th percentiles of height in girls and a more moderate rate of increase evident in boys.

The 50th and 90th percentiles of systolic and diastolic BP levels for the boys and girls in relation

Table5. Goodness of fit of polynomial Regression (PR) and Quantile Regression (QR) models for systolic BP measurements by sex in children.

		Percentile Group		<5	5.0-9.9	10.0-24.9	25.0-49.9	50.0-74.9	75.0-89.9	90.0-94.9	>=95	Total	Chi-square	P value
		Expected percent		5	5	15	25	25	15	5	5	100		
Sex	**BP**	method	Age											
Boys	**SBP**	QR	6-7	19	14	41	76	76	43	15	12	296	2.180	0.949
			8-9	20	25	65	110	106	67	22	19	434	1.109	0.993
			10-11	19	15	56	85	84	54	20	17	350	1.345	0.987
		PR	6-7	11	8	57	70	77	50	16	7	296	12.928	0.074
			8-9	18	27	61	116	111	62	20	19	434	3.376	0.848
			10-11	18	23	52	96	71	40	17	33	350	22.404	0.002
	DBP	QR	6-7	16	18	41	83	62	48	12	16	296	5.009	0.659
			8-9	23	16	71	104	113	66	21	20	434	2.651	0.915
			10-11	19	14	57	82	91	54	16	17	350	1.886	0.966
		PR	6-7	21	10	38	69	100	37	7	14	296	19.937	0.006
			8-9	21	11	62	96	151	53	22	18	434	26.418	0.000
			10-11	28	15	44	98	63	66	13	23	350	22.510	0.002
Girls	**SBP**	QR	6-7	13	12	43	68	73	46	11	17	283	2.178	0.949
			8-9	24	21	56	100	95	49	14	20	379	4.307	0.744
			10-11	17	16	55	89	83	36	9	17	322	8.269	0.309
		PR	6-7	12	9	39	76	68	54	19	6	283	12.477	0.086
			8-9	16	17	66	98	104	36	16	26	379	13.876	0.053
			10-11	18	19	46	81	82	34	18	24	322	9.222	0.237
	DBP	QR	6-7	12	14	39	67	72	51	14	14	283	2.555	0.923
			8-9	21	17	67	93	99	46	18	18	379	4.624	0.706
			10-11	21	13	56	85	79	39	14	15	322	5.735	0.571
		PR	6-7	17	6	40	48	107	40	19	6	283	37.796	0.000
			8-9	15	14	60	108	101	51	11	19	379	8.493	0.291
			10-11	28	13	36	106	48	46	12	33	322	52.617	0.000

Abbreviation: QR = Quantile Regression; PR = Polynomial Regression; BP = Blood Pressure; SBP = Systolic Blood Pressure; DBP = Diastolic Blood pressure

to age and height percentiles by polynomial and QR models were reported in Table 3 and Table 4 respectively.

As shown in Table 3 and Table 4, generally, predicted BP levels by PR and QR models increased with age and percentiles of height, but with some exceptions. In boys aged 11 (Table 3), frequent measurements of BP by PR and QR and also the systolic BP of 11th year in girls with height between 25th through 75th percentiles by QR (Table 4) were lower than those of previous age groups with corresponding height percentiles.

Finally, to assess goodness of fit, we compared the observed and expected percentages of children in different blood pressure percentile groups by age (6–7, 8–9, and 10–11 years) and sex This was done for both systolic BP and diastolic BP for both the PR and QR children falling into each percentile category, along with the percentage expected in each age group.[2, 33-34]

In the present study, we established and compared sex, age, and height-specific reference values for systolic and diastolic BP levels in a population-based sample of 2064 Iranian school children (52.3% boys and 47.7% girls) aged 6–11 years. For the calculation of the reference values, we used 2 different statistical approaches.

The reference values presented herein by PR and QR models provided generally excellent essential age-height based goodness of fit of the QR model with no significant differences between observed and expected counts. Conversely, the PR models consistently showed a relatively poor goodness of fit (except for systolic BP in boys aged 8-9 and girls aged 10-11 and also diastolic BP in girls aged 8-9).

Discussion

High BP in children is associated with a higher incidence of secondary causes than in adults. Tracking of BP suggests that essential hypertension in adults is the result of a process that begins in childhood.[11, 32] Therefore, monitoring BP of children and adolescents is important for the early detection and prevention of adult hypertensive condition. BP values should be compared with normal curves before deciding on their normality. However, the distribution of BP values varies in different ethnic groups on a large nationally representative sample for use both in the classification of individuals and in the evaluation of BP trends. We found that the use of the QR model based on RCS offered the most flexible and better fitting than PR model. An advantage of the QR was that it was relatively easy to incorporate covariates into the analysis of growth data,[16] which involved estimating BP as a nonlinear function of both age and height.

Both methods reflected the documented increase in BP measurements with age in both sexes based on a nonlinear manner up to 11th year, as observed in other studies.[10, 16] But in both boys and girls aged 11 years old, some of the BP levels were lower than those of previous age groups with corresponding height percentiles. Similar trends were observed in Indian normative Tables.[35] We recommend that the higher values to be used for all the above mentioned age group children to avoid any possibility of mislabeling.

The estimated systolic and diastolic BP for each age and sex ,without taking height of children into account by two approaches in our study, was lower than the similar studies in Iran[13, 22] We think that this result was related to the area of study, and also due to the type of statistical analysis. It is important to appreciate that BP variation in childhood is dependent upon a multitude of factors, both genetic and environmental, but it is difficult to determine which factor is responsible for the difference.[36]

In addition to the well-known differences in age and sex, as indicated in other studies,[10,16, 35, 37] we found 50th and 95th percentile differences by two methods in BP level between the tallest and shortest individuals, ranging from 2-7 mmHg. The difference in the blood pressure values for different height percentiles indicated that the height played substantial role in determining blood pressure value of an individual. Hence the height had to be considered as a factor before classifying a child as hypertensive. This approach of developing BP standards based on height provided a more precise classification of BP according to body size and avoids misclassifying children who were very tall or very short.

In conclusion, the present study established height-age-specific reference ranges for systolic and diastolic BP using the data from apparently healthy children in southern Iran. The advantages of the QR led to a better adaptation of reference limits to the original data. This statistical approach might be preferable for the calculation of reference ranges in particular by non-normal distributed variables. Our results might help clinicians to arrive at a clear definition of hypertension in Iranian children living in Shiraz.

Acknowledgments

This work was financially supported by a grant (87-4373) from Shiraz university of Medical Sciences Research Council. The authors are grateful to Miss M. Zare for her kindly data gathering assistance. The authors declare that they have no conflicts of interest.

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