Blood Pressure in Schoolchildren and Adolescents and its Variation according to Nutritional Status Evaluation: An Early Preventive Key for Obesity Comorbidities

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Received: : July 02, 2015; Accepted: August 29, 2015; Published: September 18, 2015

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Abstract

Background: Cardiovascular diseases (CVD) already exist in pediatric ages although their progress and major clinical burden occur in adulthood. Wide international studies have shown their tracking from early ages. Elevated blood pressure (EBP) is more frequent in overweight and obese children and adolescents (C&A), although this is often overlooked, particularly in slightly overweight children. The aim of this study is to screen the asymptomatic C&A in order to stress the importance of it.

Methods: 1347 C&A (45% girls) regularly attending urban and suburban state schools with ages between 6-18 years were enrolled after having relevant inclusion criteria. Gender, age, height, weight and circumferences were obtained with a specified precision limits for each one. The nutritional status was after BMI-Z score. Blood pressure measurements were also taken with the same strict patterns using mercury column devices. Prehypertension was considered when systolic or diastolic blood pressure (SBP, DBP) were higher than 90th centile and below the 95th centile.

Results: SBP > 90th centile was founded in 25.7% of the whole sample and in 31.9% of the overweight and obese subgroups. Overweight C&A were 24%, and obese 8% of the total populations, these ratios unfortunately are concordant to the skewed national pediatric population. Significant differences occur when subgroups were analyzed by nutritional status, gender and age. The multiple regression analysis shows a clear association of SBP (dependent variable) with age, waist circumference and gender.

After the evaluation of these data it would be of great interest to standardize as much as possible the anthropometric indexes in order to properly assess the nutritional status, even using the Z score methods can over or underestimate the overweight situation, delaying preventive actions. This has been evident when applying them to this same population, with such high prevalence of overweight and subsequent pre hypertension, which in most cases was unknown by parents. For the correct identification of pre hypertension the auscultatory methods are not the ideal ones due to the inherent subjectivity they imply particularly when assessing DBP, which is later, affected but having an important pathogenetic role in CVD.

Background

Cardiovascular diseases and pediatric obesity should be considered as a risk situation for adult life [1] but also for the present alterations already in the pediatric patient. Blood

pressure elevations are certainly the tip of the iceberg that should lead us to assess and act on this initial condition. This is perhaps different from primary hypertension which is normally treated in the hypertension units. In previous publications [2,3] we analyzed the tracking of cardiovascular diseases (CVD) from pediatric ages, therefore, we now add two new epidemiological aspects. The first is related to the data that forecast that overweight children are at increased risk of becoming obese adults which may lead to shorter life expectancies in the current generation of children compared to their parents [4]. The second comes after well-designed studies in different parts [5,6] in which overweight adolescents have risks of 2.7 or greater for suffering from Elevated Blood Pressure (EBP). Once at this point it is worth adding how this problem will become greater [7] as the increasing prevalence of obesity is not being curved in the next decade.

To the well-known silent cardiovascular alterations in pediatric ages [3], it is important to consider the Iceland-study [8] on target-organ damage when estimated at a mean of 58 years of age. There is a significant correlation between both coronary disease and adult hypertension with adolescents' blood pressures $\geq 95^{\text{th}}$ centile.

EBP in children & adolescents is of concern not only because of its association with even subtle overweight but also for the involved mechanisms. The role of sympathetic nervous system in the modulation of sympathetic cardiovascular system is evident and although requiring a highly specific technique, it is a field to be worked on [9]. In the last decade [10], a relationship between cardiovascular phenotypes with healthy and overweight youths was established. This could mark the starting point of epigenetic studies on this particular problem of EBP, because not all the obese children & adolescents develop hypertension or CVD. Epigenetic marks are tissue specific and basically comprise DNA-methylation and histone modifications that in turn will modulate the gene expression. The obesity appearing in Albright hereditary osteodystrophy is the classic example and it is now known that the cause is the disruption of the imprinting GNAS gene [11], but in common obesity, these types of alterations are

not yet described. Obese mothers tend to have obese children [12] and the interventions to cause maternal weight loss can reverse this effect [13]. Possible disturbances of methylation may arise during fetal development due to the lack of bioavailable methyl donors [14]. However from these hypotheses, the way to ascertain the involved mechanisms exists due to the Human Epigenome Project (www.epigenome.org). This is a part of the future for improving knowledge on hypertension genesis.

The study of EBP as a comorbidity of pediatric overweight is now more common but it has not got the clinical consideration that it deserves particularly when in front of us are a so-called healthy population of children and adolescents. Therefore, the aim of the present study is to adequately screen asymptomatic children and adolescents and evaluate the influence of the spreading overweight when it is evaluated with different anthropometric indices.

Methods

Subjects

1347 (out of 48641) children and adolescents, 45% girls, regularly attending state schools were enrolled in the study. Inclusion criteria were: absence of acute or chronic disease including abnormal puberty stages, providing informed consent signed by parent(s) and required dietary and physical activity questionnaires. Their age ranged between 6–19 years, but they were allocated into two groups: 1 (6-10 years) and 2 (11-18 years) due to puberty onset, growth acceleration and subsequent BMI change.

Data from the sample

Gender and age (present date-birth date) was primarily obtained. Anthropometrics include: height (precision of 1 mm), weight (precision of 100 g), and waist circumference (precision of 1 mm) [Table 1]. All measurements were taken in the school, in

an appropriate room and by the same team. The anthropometric used index was the Body Mass Index–Z score obtained from the CDC standards [15]. Other anthropometric indexes CDC- LMS Zs [15] and International Obesity Task Force Cole curves [16] were used but only for inter comparison on the same population.

Blood pressure measurements

On the non-dominant arm only auscultatory technique with a mercury column device (Nova Presameter precision of 2 mm Hg) was used, the cuffs were of two sizes (9 cm and 12 cm wide). The room was quiet, more than 30' after the last food intake or moderate physical activity and the void bladder. Measurement of BP [17] was on the right arm preceded by the measure of heart rate through the radial pulse, then fixing of the pulse abolishing point, maximum inflate (20 mm Hg above pulse abolishing point) and determine as Systolic Blood Pressure (SBP) when the first sound was heard (Korotkoff phase I) and Diastolic (DBP) coincidental with the last audible sound (Korotkoff phase V). This procedure was repeated 2-3 times and results were averaged. The cases with audible sounds down to zero mm Hg were discarded from the blood pressure study. For the study group, the 90th centile was obtained through the methods of computation of blood pressure percentiles for arbitrary sex, age and height given by the Working Group on High blood Pressure that allows the Z score of blood pressure of each individual and 90th centile is considered when the Z score is greater than 1.282.

Multiple regression analysis, Enter method, estimated the effect of the independent variables on SBP and DBP.

Results

In Table 2, the BP data (mean $\pm$ SD) of the whole sample appear but also the percentiles 90 according to gender and age. These percentiles can act as a threshold [18] for further evaluation through the Working Group on High Blood Pressure in children

Table 1: Anthropometric data from 1347 children and adolescents according to age and gender (m $\pm$ SD).

AGE (Y)	BOYS				GIRLS			
	N	Weight (kg)	Height (cm)	BMI-Zs	N	Weight (Kg)	Height (cm)	BMI-Zs
6	48	26 $\pm$ 4.8	121.1 $\pm$ 5.1	0.959 $\pm$ 0.884	39	23.2 $\pm$ 4.1	118.1 $\pm$ 7.1	0.481 $\pm$ 0.970
7	74	29 $\pm$ 6.2	126.8 $\pm$ 5.2	0.874 $\pm$ 0.830	57	27.4 $\pm$ 6.2	123.4 $\pm$ 5.7	0.770 $\pm$ 0.865
8	67	32.6 $\pm$ 6.8	132.5 $\pm$ 6.5	0.860 $\pm$ 0.866	39	30.8 $\pm$ 6.2	130.6 $\pm$ 6.6	0.455 $\pm$ 1.56
9	51	34.5 $\pm$ 7.2	136.6 $\pm$ 6.7	0.590 $\pm$ 0.940	51	33 $\pm$ 7.2	133.8 $\pm$ 6.9	0.905 $\pm$ 0.905
10	61	40.7 $\pm$ 9	141.5 $\pm$ 6.8	0.864 $\pm$ 0.998	53	39 $\pm$ 9.6	141.4 $\pm$ 7.4	0.447 $\pm$ 1.22
11	62	45.7 $\pm$ 10.8	146.9 $\pm$ 7.6	0.901 $\pm$ 0.870	48	45.9 $\pm$ 9.7	148.5 $\pm$ 7.8	0.694 $\pm$ 0.994
12	57	49.4 $\pm$ 11.4	151 $\pm$ 7.4	0.778 $\pm$ 0.967	47	49.6 $\pm$ 10.3	152.5 $\pm$ 5.9	0.618 $\pm$ 0.931
13	62	56.9 $\pm$ 11	160.7 $\pm$ 8.6	0.771 $\pm$ 0.766	52	53.7 $\pm$ 9.8	156.2 $\pm$ 6.7	0.647 $\pm$ 0.862
14	79	59.6 $\pm$ 11.4	167 $\pm$ 6.6	0.375 $\pm$ 0.933	41	54.7 $\pm$ 6.6	159.3 $\pm$ 5.6	0.474 $\pm$ 0.547
15	58	63.7 $\pm$ 11.5	169.2 $\pm$ 6.7	0.447 $\pm$ 0.797	45	56.4 $\pm$ 9	159.6 $\pm$ 5.7	0.395 $\pm$ 0.769
16	33	67.2 $\pm$ 11.3	172.9 $\pm$ 6.8	0.322 $\pm$ 0.874	44	58 $\pm$ 7.1	161.8 $\pm$ 6.2	0.332 $\pm$ 0.637
17	55	69.4 $\pm$ 10.7	173.9 $\pm$ 6.2	0.282 $\pm$ 0.899	59	59 $\pm$ 110.6	161.6 $\pm$ 6.5	0.273 $\pm$ 0.701
18	26	71.9 $\pm$ 11.4	175.7 $\pm$ 8.3	0.193 $\pm$ 0.841	39	58.9 $\pm$ 8.5	161.7 $\pm$ 5.6	0.139 $\pm$ 0.868

Table 2: Systolic (SBP) and Diastolic Blood Pressure (DBP) of the whole sample (n= 1347) according to gender (m ± SD). The last two columns in each subgroup refer to the blood pressure values > 90th centile in children and adolescents whose height was on the 5th centile, I e the worst condition thus indicating further evaluation.

AGE (Y)	BOYS				GIRLS			
	SBP mmHg	DBP mmHg	SBP(P90)* mmHg	DBP(P90)* mmHg	SBP mmHg	DBP mmHg	SBP(P90)* mmHg	DBP(P90)* mmHg
6	104 ± 10	55 ± 14	105	68	102 ± 10	50 ± 14	104	68
7	104 ± 9	53 ± 16	106	70	105 ± 9	52 ± 16	106	59
8	104 ± 10	54 ± 14	107	71	103 ± 9	54 ± 15	108	71
9	109 ± 10	62 ± 14	109	72	101 ± 10	61 ± 9	110	72
10	111 ± 10	59 ± 12	111	73	112 ± 11	62 ± 10	112	73
11	113 ± 11	62 ± 10	113	74	114 ± 11	62 ± 11	114	74
12	114 ± 10	62 ± 10	115	74	114 ± 12	63 ± 12	116	75
13	123 ± 11	58 ± 13	117	75	117 ± 11	63 ± 9	117	76
14	123 ± 10	56 ± 12	120	75	118 ± 11	64 ± 12	119	77
15	125 ± 12	61 ± 13	120	76	116 ± 12	64 ± 10	120	78
16	125 ± 11	61 ± 14	120	78	113 ± 8	63 ± 12	120	78
17	128 ± 12	62 ± 13	120	80	118 ± 9	64 ± 12	120	78
18	131 ± 13	67 ± 13	120	80	119 ± 11	68 ± 11	120	80

* Kaelber, Pickett [24]

Table 3: Nutritional status of the whole sample according to the BMI- Z score [15] with the absolute number and percentage for underweight, normal weight, overweight and obese.

	GROUP 1 (6-10 Y)		GROUP 2 (11-18 Y)	
	Boys	Girls	Boys	Girls
Underweight < -1 SD	5 (1.7%)	9 (3.9%)	15 (3.5%)	12 (3.2%)
Normal weight -1 SD to +1 SD	177 (58.8%)	150 (63%)	301 (70%)	289 (77.1%)
Overweight +1 SD to +2 SD	54 (17.9%)	47 (19.7%)	70 (16.3%)	56 (14.9%)
Obese >+2SD	65 (21.6%)	32 (13.4%)	44 (10.2%)	18 (4.8%)
ALL	301 (100%)	238 (100%)	430 (100%)	375 (100%)

Table 4: Multiple regression analysis (Enter method) for SBP and DBP as dependent variables.

SBP				DBP			
Model	Beta	t	p	Model	Beta	t	p
(Constant)		26.142	0.000	(Constant)		9.408	0.000
Age	0.409	11.176	0.000	Age	0.189	4.192	0.000
Gender	-0.105	-4.586	0.000	Gender	0.119	4.161	0.000
Waist C.	0.272	6.426	0.000	Waist C.	0.137	2.608	0.009
BMI-Zs	0.000	0.002	0.998	BMI-Zs	0.022	0.480	0.631

Gender: 1-Male; 2-Female; Beta: standardized coefficient; t: Individual regression coefficient

& adolescents 4th Report [19] and clinical study. The proximity of SBP means could give an idea about this sample quality, whereas DBP means were 13 mm Hg lower than Ingelfinger P 90th. The frequency of prehypertension (> 90 centile) in the whole population was 346 (25.7%) for SBP and 88 (6.5 %) for DBP and in the overweight subgroup for SBP, 143 (31.9 %) and for DBP,

35 (8.2 %)

The BMI-Z score data of the two age groups (I and II) are shown in Table 3. The frequency of underweight was scarce. The vast majority corresponds to the normal weights as it was a population normally attending schools and it is worth signaling

Figure 1: Whole sample box plot for SBP and DBP according to the nutritional status: Underweight, normal weight and overweight (comprises overweight and obese).

the important quota of the overweight and obese children and adolescents.

The multiple regression analysis in the whole sample (Table 4) shows the association of SBP and DBP with constant, age, gender, waist circumference and BMI Z score although other related variables were also analyzed. The standardized Beta coefficient was chosen because the independent variables were not in the same kind of units. As regards gender, 1 denotes male and 2 female, therefore it is possible to signal positivity or negativity of Beta coefficient. Individual regression coefficient (t) denotes the significance of the association.

In Figure 1, the box plot of the whole population classified as underweight (UW, n=62), normal weight (NW, n= 834) and overweight including obesity (OW, n = 451) shows a reasonable variation with very little degree of dispersion and of skewness in all three subpopulations. In this, medians for SBP (upper cages) only showed in underweight a lower value than that of normal weight group. The same considerations apply to DBP (lower cages) and only the overweight group showed a little elevation in respect to the reference group. Considering the whole population only in females and for SBP there was a significant difference ($p < .001$) among under and overweight. As regards the influence of age in the group 1 (6-10 years) SBP was significantly ($p < .005$) different between under and overweight in both genders. In the group 2 (11-18 years) the only significant difference ($p < .001$) occurred for SBP between under and overweight females. Later on these differences will be commented on.

In Table 5 in both genders the absolute number and percentage of UW, NW and OW appears. But according to three different classification criteria for nutritional status: CDC BMI-Zs; CDC-LMS and Cole curves widely used as recommended by the International Obesity task Force. Because the anthropometric data belong to the same children and adolescents it is worth

signaling that in underweight the differences of frequency are not striking, but when considering the overweight subpopulation the proportion of subjects being in this category can almost double. This artificial 'different prevalence' can be an obstacle for assessing overweight as a comorbidity risk.

Discussion

The early preventive actions for cardiovascular diseases are justified by the fact of its increased global deaths of 41% between 1990 and 2013 despite a 39% decrease in age-specific death rates, whether in low, middle or high income countries [20]. If hypertension in pediatric ages is associated with heart failure, coronary disease and deaths before 55 years of age [21], the studies about screening for elevated blood pressure in children and adolescents are required at present [22].

The occurrence of prehypertension in the whole sample (SBP > 90 centile of the US Preventive Service Task Force [23]) was of 25.7%, higher than that obtained for the US youths, but if we take the DBP cut off limits then the occurrence drops to 6.6%. This difference is hardly acceptable, the high proportion of overweight (19.8%) could be an explanation due to the forwarded action on SBP, but the technique itself despite the measurement policies cannot be ignored. Another more speculative reason could be the predominance of Mediterranean diet in school lunches. It is worth noting that in all these non-false positive cases the elevated blood pressure was unknown by the family, which in turn and in a majority of instances informed that blood pressure had not been measured before.

The multiple regression analysis in the whole sample (Table 4) signals that the greater effect (Beta and individual regression coefficient) in order of importance on SBP of the independent variables were forage (0.41; 11.2), waist circumference (0.27; 6.42) and gender (-0.11; -4.58). For DBP none of them showed significant effect. If in this study waist circumference is removed, then BMI- Z score becomes significant (0.18; 8.48). Due to the cross-sectional character of this study, it is not possible to see the long- term consequences of these moderate elevations of blood pressure, but according to the quoted data [1] after following more than 275000 youths for more than 25 years, the negative issue is evident.

Another aspect of interest is the comparison of SBP and DBP means in the subgroups by gender and the ones by age (6-10 y and 11-18 y) considering the gender also in them. All the significant differences occurred in SBP except in the 6-10 year boys group, in which DBP were between under and overweight ($p = 0.038$). Can this fact be related to: the high proportion of overweight in our sample with a significant higher proportion of prehypertension ($X^2 = 20.3$ $p < 0.000$); to the lesser values for DBP of our whole sample when compared to the 90th centile obtained from Working Group [19] and that of Kaelber et al. (24) was later simplified by Ingelfinger [18], or perhaps due to the variability of the mercury column device and particularly to the subjectivity they imply and the frequent persistence of the 5th Korotkoff sound [25] , but these cases have been eliminated from the study.

Table 5: Different prevalence rates of nutritional status for the same population when evaluated through different methods: CDC- Zs; CDC (LMS) - Zs [15] and IOTF-Cole curves [16].

	BOYS (n = 734)			GIRLS (n= 613)		
	BMI zs CDC	BMI zs LMS CDC	IOTF	BMI zs CDC	BMI zs LMS CDC	IOTF
Under weight	2.9	3.7	1.9	3.4	5.7	3.1
Normal weight	65.1	59.7	63.6	71.7	64.5	67.9
Over weight	17	30.4	24.9	16.8	27.4	22.8
Obese	14.9	6.1	9.5	8.1	2.4	6.2
ALL	100			100		

As seen above pediatric overweight and central obesity are associated with elevated blood pressure, therefore precise evaluation of the individual nutritional status is highly recommendable. The problem is the wide array of anthropometric indexes, most of them developed locally in the past century favoring a certain disparity in this important assessment. Fortunately, the globalization trend has promoted international indexes that can be used all over the world due to their designs. The standards from Cole [16], WHO [26] and in some ways those from CDC [15] have shown that differences in different parts of the world are of not great extent and can be used globally. The last achievement in this trend is the global charts for newborns [27]. This improved methodology will probably give uniformity of data thus avoiding the differences we found in the present study, where the same population can have a double rate of overweight depending on the method used.

Prehypertension or even hypertension cannot be considered alone as precursors of cardiovascular disease with all its later consequences. In normal weight and obese adults [28] and after euglycemic-hyperinsulinemic clamp there was not greater cardiometabolic risk for them insofar as they showed normal insulin sensitivity. This together with the better known experiences about insulin resistance and its associated risks for CVD in adults [29] or pediatric ages [30] should lead to a more efficient search for fasting insulin levels or better for the whole metabolic syndrome factors in all of the overweight people with elevated blood pressure [31], which would imply an earlier preventive intervention. This approach is more practical at the present time, whereas at a more long- term the applied epigenetic studies whether for changes or for variants will be of growing interest. The inherited although not permanent changes (DNA epigenetic markers, mainly 5mC) that could appear in obese families do not have the same degree of development as occurs presently in some type of cancers or immune disorders.

As a summary, it can be said that the risen blood pressure in overweight children and adolescents is probably more frequent than expected with short- and long- term undesirable effects. It is true that in some areas of the world, obesity prevalence is decreasing so is the frequency of hypertension and cardiovascular diseases, but unhappily this situation is far from being generalized.

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