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Editorial

At what level of blood pressure should hypertension be defined in children?

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In a recent issue of the journal, Marras et al[1] described the prevalence of hypertension in a school-based cohort in southern Italy. They observed that, by using the most recent criterions of the National High Blood Pressure Education Program Working Group in the United States of America, the so-called Fourth report,[2] just over one-third of children had systolic, one sixth had diastolic, and one-eighth had both systolic and diastolic hypertension. The prevalence of hypertension was significantly lower when they used previously published normal standards established in Italy,[3] at 8.4% systolic, 5.4% diastolic, and 2.0% for both systolic and diastolic hypertension. The prevalence rates remained at similar low levels when they used a statistical definition, as any blood pressure value above the 95th percentile, to define hypertension in their own population. On repeated measurement of blood pressure at 6-monthly intervals over the following 2 years, they observed reduction in the values for blood pressure, with consequent falls in the prevalence rates of hypertension. Using the criterions established in the fourth report, the prevalence of hypertension was 17.3% for systolic, 8.4% for diastolic, and 4.1% for both systolic and diastolic hypertension. Using more local standards of normality, the prevalence of hypertension remained significantly lower, at 4.9% for systolic values, 4.6% for diastolic measurements, and 0.5% for both systolic and diastolic hypertension. In their second report they observed that up to one-quarter of children were overweight or obese, with excessive weight strongly correlated with systolic hypertension in particular.[4]

Their reports raise some important issues for professionals managing children with elevated levels of blood pressure as measured in the clinic. Although significant gains have been made in our understanding and management of arterial hypertension in children over the past couple of decades some fundamental questions remain unanswered.

At what blood pressure level should hypertension be defined in children? The precise level of blood pressure taken to define hypertension during childhood has been debated for some time. Population-based studies have provided some understanding of the physiological changes in blood pressure during childhood. The major determinants of blood pressure in this population are race, gender, height, weight, and age. The predominant influence of height over age on variability in blood pressure, up to nearly 40%, has been well demonstrated by the Bogalusa Heart Study.[5] Moreover, at a given age, taller children have higher levels of blood pressure, and this relationship of increasing blood pressure with body size is physiological.

In adults, normal values for blood pressure have been established based on clinical evidence of end-organ damage, and/or reduction of cerebrovascular and cardiovascular morbidity.[6] No such data exists for children, and the definition of hypertension

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remains purely statistical. Abnormal blood pressure is defined as a value above the 95th percentile for the population. The use of a statistical definition to define hypertension based on population percentiles has some disadvantages.

First, different populations would have different values for their blood pressure percentiles. This would occur even if the technique remained uniform, as other major determinants of blood pressure, such as race, gender, height, and weight will vary between populations. Data from two large population-based studies from Europe shows a difference in the values for the 95th percentile when compared with the values obtained from the Fourth report.[2] There is an increase of 6 mmHg for systolic and a reduction of 3 mmHg for diastolic blood pressures at the 95th percentile for a Northern European cohort,[7] and an increase from 3 and 8 mmHg for systolic levels, and 2 and 3 mmHg for diastolic levels, in the 90th and 95th percentiles for an Italian cohort.[3]

Second, the major determinants of blood pressure could change with time within the same population from whom the population percentiles were determined in the first instance. In the United States of America, for example, there has been an increase in height, weight and body mass index of children over the past 25 years,[8] with a marked increase in both the prevalence and severity of overweight and obese children.[9] An increase in the blood pressure of children in the United States of America has also been observed, at least partly attributable to the increased prevalence of overweight status.[10,11] As discussed eloquently by Lurbe and colleagues,[12] this change in the demographics of children living in the United States of America will result in overall higher values of blood pressure, and consequent higher values of population-based 95th percentiles. Similar trends of increasing prevalence of overweight status have been reported from other parts of the world.[13,14]

Third, a further problem with the percentiles appearing in the Fourth report is related to the fact that the data from studies pooled to develop these percentiles includes one or more blood pressure measurements at a single time point only. It is well recognised that values for blood pressure reduce when repeated measurements are made over a period of time. This is because of a combination of tolerance of the measurement by the individual, and the statistical phenomenon of regression towards the mean. Using the present statistical definition of hypertension, 5% of children would be classified as being hypertensive, although on repeated measurement this figure is thought to be nearer 1%.[2] As in the study by Marras et al,[1] other reports have observed a reduction of at least half in the number of subjects having elevated blood pressure measurements beyond the 95th percentile when measured repeatedly.[15,16] It is interesting to note that, in the study by Marras et al, the prevalence rates of hypertension remained persistently elevated at nearly one-quarter using the criterions of the Fourth report, but only one-tenth using Italian standards.[1] This would suggest a true increase in prevalence rates of hypertension in keeping with reports from other parts of the world.[15,17,18]

For a given population of children, do percentiles for values of blood pressure need updating with new data at regular intervals? Rather than moving the goal posts in increasingly unhealthy populations, it is more important to develop clinically useful definitions of hypertension in children based on clinical evidence of end-organ damage that reduce some of the shortcomings of present definitions.

The major limitation of blood pressure as assessed in the clinic is the marked variability of measurements. This will largely be addressed by the introduction of 24-hour ambulatory monitoring in the evaluation of a child with elevated measurements in the clinic.[19] Ambulatory monitoring of blood pressure, however, has its own limitations, with absence of any normal standards for young children, and with the available standards developed from a relatively small number of children. It is worth remembering that hypertension based on ambulatory criterions is currently also defined on values above the population-based 95th percentile. The additional advantage of ambulatory monitoring will be in identifying children who have so called white-coat hypertension. This is defined as high values measured in the clinic, but normal daytime measurements as obtained using ambulatory monitoring.

There is a striking lack of population-based data on the relationship between blood pressure measured in the clinic and the effects on end-organs or long-term outcomes in children. Given the phenomenons of marked blood pressure variability, and white-coat hypertension, a strong association of elevated measurements in the clinic with end-organ damage is unlikely, but this remains to be clarified in children. Studies in children that have assessed the association of hypertension with left ventricular hypertrophy as a marker of end-organ damage have found up to two-fifths of hypertensive patients to have left ventricular hypertrophy,[20,21] with better correlation of elevated measurements with left ventricular hypertrophy when using ambulatory monitoring.[22]

As detection of left ventricular hypertrophy in children with hypertension by measuring blood pressure in the clinic is found in less than half of

patients, there is a need to evaluate other intermediate markers of the effect of hypertension.[19] These could include changes in the peripheral arterial beds by measuring retinal vascular narrowing, looking for changes in arterial structure and function in large vessels by measuring carotid intimal medial thickness and measures of arterial stiffness, examining left ventricular function, and assessing cardiovascular biomarkers such as inactive amino terminal Pro-B-type-natriuretic peptide. These alone, or in combination, may prove to be more sensitive markers of the effect of elevated levels of blood pressure.

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