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Prevalence of High Blood Pressure in 122,053 Adolescents: A Systematic Review and Meta-Regression

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Abstract: Several studies have reported high prevalence of risk factors for cardiovascular disease in adolescents.

To perform: i) systematically review the literature on the prevalence of high blood pressure (HBP) in adolescents; ii) analyze the possible methodological factors associated with HBP; and iii) compare the prevalence between developed and developing countries.

We revised 10 electronic databases up to August 11, 2013.

Only original articles using international diagnosis of HBP were considered. The pooled prevalence's of HBP were estimated by random effects. Meta-regression analysis was used to identify the sources of heterogeneity across studies.

Fifty-five studies met the inclusion criteria and total of 122,053 adolescents included. The pooled-prevalence of HBP was 11.2%, 13% for boys, and 9.6% for girls ($P < 0.01$). Method of measurement of BP and year in which the survey was conducted were associated with heterogeneity in the estimates of HBP among boys.

The data indicate that HBP is higher among boys than girls, and that the method of measurement plays an important role in the overall heterogeneity of HBP value distributions, particularly in boys.

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Abbreviations: 95% CI = confidence interval, BPb = lood pressure, CVD = cardiovascular diseases, HBPh = igh blood pressure, PRISMAp = referred reporting items for systematic reviews and meta-analyses.

INTRODUCTION

Cardiovascular diseases (CVD) are the main sources of disease burden worldwide, and constitute a major public health problem in many countries.[1] High blood pressure (HBP) is an established major risk factor for stroke and coronary heart disease.[2] Studies have shown that blood pressure (BP) in childhood and adolescence are crucial factors in developing hypertension in adulthood.[3]

Several studies have reported high prevalence of factors such as abdominal obesity,[4] inflammation markers,[5] metabolic syndrome,[6] and clustered metabolic risk,[7] among the risk factors for CVD. Between the cardiovascular risk factors, some article highlights increased BP values among adolescents as being particularly noteworthy.[8,9] Because the prevalence of obesity has been increasing,[4] we would expect to observe an increase in the prevalence of HBP, since there is a strong association between obesity and hypertension. Freedman et al[10] also found that the prevalence of obesity increased but no increase in BP was observed.

Because of these major discrepancies in the literature and there has not been any systematic review verifying either the prevalence of HBP among adolescents or the for identifying the factors associated with this important aspect of adolescent health, we systematically reviewed the literature to collate the prevalence data of HBP among adolescents. Thus, we hypothesized the: i) the prevalence of HBP is high in adolescents and has increased over the past years; ii) the characteristics of the study are associated with HBP variation; iii) and the prevalence of HBP is different between developed and developing countries.

METHODS

Identification of Studies

This study followed the systematic review methodology proposed in the Preferred Reporting Items for Systematic

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[a] ''Probability sampling relies on the principle of randomization to ensure that all individuals have a known chance of selection; it requires that members of the target population be identified through a sampling frame or listing of potential respondents. They may all have an equal chance of being selected or, if a stratified sampling method is used, the rate at which individuals from several subsets are sampled can be varied so as to produce greater representation of some classes than of others.'' Porta M. A dictionary of epidemiology. Oxford: Oxford University Press, 6th edition. 2014.
Augusto César Ferreira de Moraes and Maria Beatriz Lacerda contributed equally to this work.
Author Contributions: **Augusto César F. de Moraes:** Dr. de Moraes designed the data collection instruments, coordinated and supervised data collection, carried out the initial analyses and the interpreted the data critically, drafted the initial manuscript and reviewed the manuscript, and approved the final manuscript as submitted. **Maria Beatriz Lacerda: Miss. Lacerda** conceptualized and designed the study, drafted the initial manuscript, data collection, carried out the initial analyses and the interpreted the data critically and approved the final manuscript as submitted. **Luis Alberto Moreno: Dr. Moreno** drafted the initial manuscript and reviewed the manuscript, and approved the final manuscript as submitted. **Bernardo L Horta: Dr. Horta** carried out the initial, final analyses and the interpreted the data critically and approved the final manuscript as submitted. **Heráclito Barbosa Carvalho**: **Dr. Carvalho** designed the data collection instruments, coordinated and supervised data collection, critically reviewed the manuscript, and approved the final manuscript as submitted.
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Reviews and Meta-Analyses (PRISMA) statement.[11] This is a systematic review article and as no data were collected on humans or animals, there was no need to be submitted to ethics committee. The study is registered in the PROSPERO database (CRD42011001422). Searches involved 10 electronic databases: BioMed Central, Cinahl, Embase, ERIC, Medline/PubMed, PsyINFO, Scielo, Scopus, SportDiscus, and Web of Science. Articles listed in the databases through August 11, 2013 were evaluated for inclusion in the analysis. This extended number of databases was used in order to minimize selection bias. The articles identified in the search were reviewed and contact made with the corresponding authors to solicit other relevant details, and studies that may have been missed in our search.

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Three command groups (according to key words) were used for the database search. Within each group, we used the Boolean operator "OR" and between groups we used the Boolean operator "AND." In the first group we included terms related to BP: *high blood pressure, blood pressure,* and *hypertension*. In the second group we included terms related to age: *adolescent, adolescence, young, youth, teenager,* and *teenage*. Given that the aim of the present review was to verify the prevalence of HBP, in the third group we added a set of commands to restrict study design to cross-sectional studies, because this type of epidemiological study is the most appropriate for studies that attempt to estimate the prevalence. These terms were: *prevalence studies, cross-sectional studies,* and *survey.*

Inclusion of Studies

We included studies that published original data, in cases of duplicated data, the studies presenting outcomes related to our systematic review were retained and the articles that did not meet the inclusion criteria were excluded. The duplicates were removed using EndNote Web® reference management software, Thomson Reuters, Carlsbad, CA.

Potentially relevant articles were selected by: i) screening the titles; ii) screening the abstracts; iii) and if abstracts were not available or did not provide sufficient data, the entire article was retrieved and screened to determine whether it met the inclusion criteria. Abstracts were reviewed independently by 2 authors (ACdeM and MBL) and were selected based on their consensus according to the same criteria used described bellow. If consensus was not reached, the abstract was set aside for further evaluation. Full-text articles of abstracts selected were retrieved and reviewed. Inclusion was based on consensus between 2 investigators (ACdeM and MBL). To be included the study the article needed to: 1) have a representative population-based sample that included adolescents (aged between 10 and 19 years old; eg: if some studies had prevalence data of 10–15 yo or 15–19 yo, they were included); 2) be a cross-sectional design (because we are interested in verifying the prevalence of HBP, cross-sectional studies are the kind of epidemiological study more appropriate to check the prevalence, however we know the limitations and were considered); 3) have employed a probabilistic method to sample the population[a]; 4) present the HBP prevalence; 5) be an original study presenting the prevalence of HBP for both genders; 6) and have diagnosed HBP according to international guidelines: SBP and/or DBP $\geq$95th percentile for gender, age, and height (currently just there are 2 guidelines; one of the American Academy of Pediatrics[12] and other European Society of Hypertension[13]). We also included those articles that did not present the prevalence per se, but contained an estimation of prevalence by gender. Also included were those articles that contained the confidence interval (95% CI) according to gender. The STROBE checklist for cross-sectional studies was applied by 2 members of the research team in assessing the percentage of items correctly related to the individual articles[14,15] and, in case of disagreement between the assessors, the article was evaluated by a 3rd member of the team (see Figure 1). We not used the STROBE for to available the quality of the studies, just check the important methodological aspects this type of study.

Assessment, Data Extraction, and Analysis

The evaluation and data extraction were performed independently by 2 members of the research team (ACdeM and MBL). Disagreements were resolved by consultation within the team until consensus was reached.

The data extracted from each study were: author, country, publication year, year of survey, journal in which the article was published, total study sample size, sample size of adolescents, age of subjects in years, proportion of girls, prevalence of HBP, and risk factors associated with HBP. The 95% CI was obtained from the articles[16–28] whenever possible, or was calculated using Stata 12.0 "cii" command (95% CI exact for binomial distribution).[29–62]

The outcome of this review is the HPB prevalence's, diagnosed in the articles included in accordance with international guidelines. The pooled prevalence's of HBP (total sample and for each gender) were estimated by random effects (estimated pooled-prevalence adjusting variation between levels and the variation within each level). Test of heterogeneity (Q test) was used to evaluate whether the differences in prevalence estimates across studies were higher than expected by chance. Meta-regression analysis was used to identify the sources of heterogeneity across studies by I^2, initially to assess the contribution of each variable (year of survey; geographic location; characteristic of countries; study population; method of BP measurement) to the overall heterogeneity.[63] Those variables that were significantly associated with the heterogeneity ($P < 0.20$) were included in a multivariate hierarchical model.[64] At the first level, year of survey (1988–1998, 1999–2004, and 2005–2009) was introduced, at the second level were geographic location (North America, Europe, Asia, Latin America, Oceania, Middle East, and Africa), characteristic of countries according International Monetary Fund classification (developed or developing), and study population (community or school); at the third level were the devices used to measure BP (sphygmomanometer or automatic digital monitor). This hierarchical model was constructed following the methodology proposed by Victora et al[64] where the effect of variables increases as the level increases, approaching the outcome, for example: the year of research theoretically has less influence on the HBP prevalence, the geographic location, and this has less effect that the measuring method of BP. A P value of <0.05 was considered statistically significant in all the analyses. The Stata 12 (Stata Corp., College Station, TX) was used for all statistical calculations.

RESULTS

Literature Search

The literature search yielded 727 titles of potentially relevant articles (see Figure 1 for selection procedure flow diagram). Of

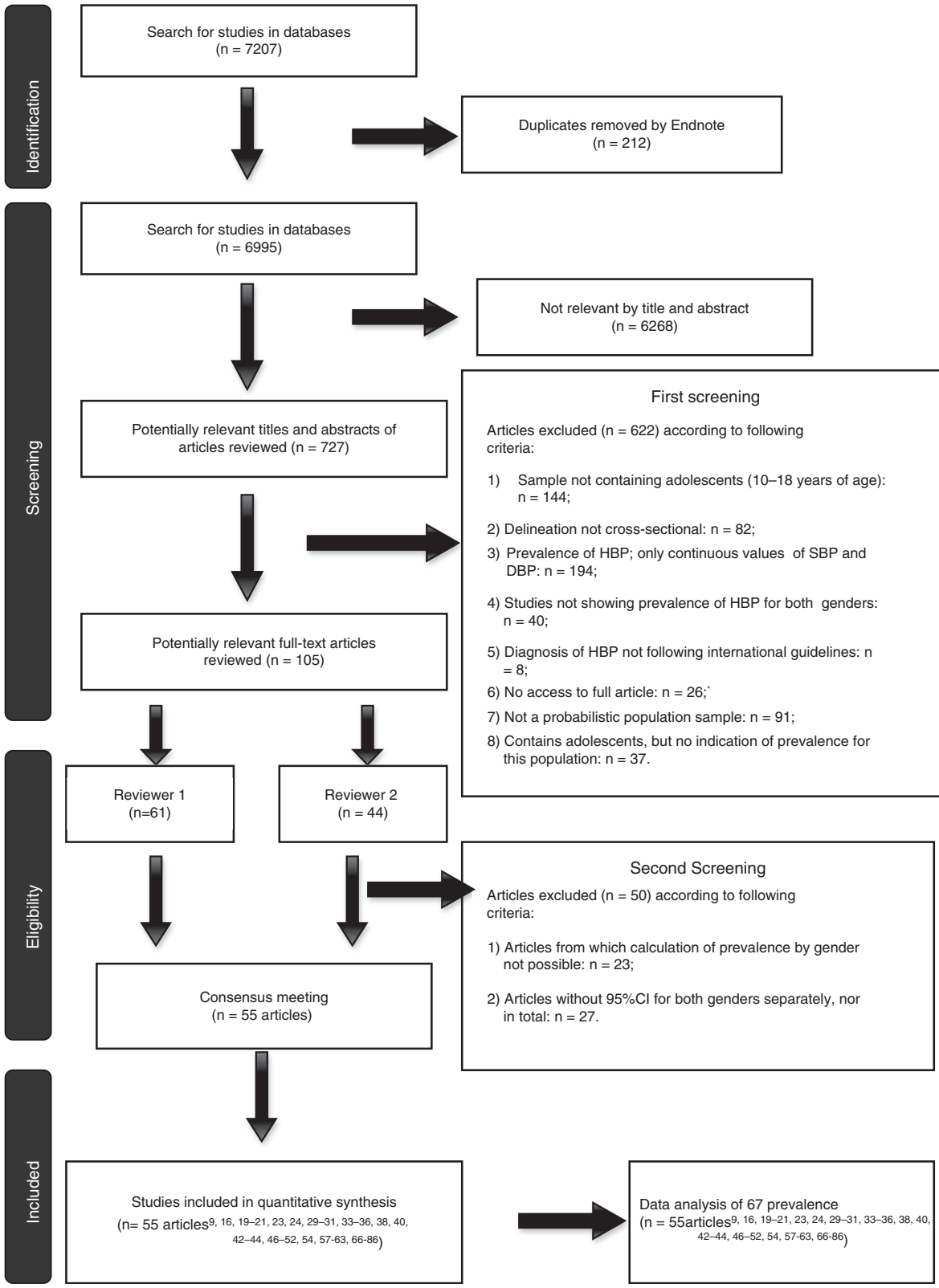

FIGURE 1. Flowchart of search strategy and results. DBP = diastolic blood pressure, HBP = high blood pressure, SBP = systolic blood pressure.

these, 55 articles were eligible according to the inclusion criteria established for this review.[9,16,19–21,23,24,29–31,33–36,38,40,42–44,46–52,54,56–62,65–85] The supplement file presents a description of the 55 articles with the relevant inclusion criteria including: lead author, year of publication, country where the study was performed, year of survey, total number of participants in the study, number of adolescents, proportion of girls, age range, study population, method of measurement, overall and gender-based prevalence, and the respective 95% CI.

Among the study that used automatic digital monitors for measuring BP, 77% used Omron BP device (Omron Healthcare Inc., Tokyo, Japan); 22.3% did not describe which model and 0.7% used the Space Labs device.

Five articles evaluated the secular trend of prevalence, 2 of which were from USA. The continents with the highest numbers of studies included in this review were Asia and Latin America (n = 18 in each), and only 1 study from Oceania was identified. Of the populations studied, 55.6% were from high-school samples; 75.5% of studies used sphygmomanometer to measure BP; 63.5% of surveys were conducted in low- and middle-income countries (supplementary file, http://links.lww.com/MD/A83). Total of 122,053 adolescents included in this review (61,049 girls).

Prevalence

In the overall sample, the pooled-prevalence estimated by random effects was of HBP was 11.2% (Table 1), 13% for boys, and 9.6% for girls ($P < 0.01$). The analyses revealed significant heterogeneity across studies for all analyses ($P < 0.001$): the overall sample (Table 1), girls (Table 2) and boys (Table 3), rejecting the hypothesis of homogeneity of results.

Table 1 summarizes the associations between HBP prevalence and characteristics of the study in the overall sample. In the overall sample, the significant association of geographical location lost significance in the adjusted model. The year of survey was not significantly associated with the prevalence of HBP while, conversely, the characteristic of countries and method of measuring BP retained their significant associations.

Table 2 depicts the HBP prevalence in the girls in relation to the methodological characteristics. Those studies from Africa showed higher prevalence while the lowest were those studies from Latin America. We found no significant associations

TABLE 1. Association Between Prevalence of High Blood Pressure With Methodological Covariates for Total (n = 122,053) of Sample of the Studies

				Total of Sample	
				Univariate Model	Metaregression (Multivariate Model)*
Level**	Independent Variables	Number of Studies	Pooled Prevalence of HBP (95% CI)	*P*-Value	*P*-Value
1	Year of survey			0.138	
	1988–1998	9	11.8 (7.7–12.4)		Referent
	1999–2004	26	8.3 (5.7–18.7)		0.098
	2005–2009	20	8.5 (5.3–16.4)		0.050
2	Geographic location			**0.001**	
	North America	14	7.3 (2.8–8.8)		Referent
	Europe	4	16.2 (10.3–27.1)		0.222
	Asia	15	12.4 (7.7–19.6)		0.177
	Latin America	14	6.2 (3.1–10.6)		0.720
	Oceania	1	24.6 (23.2–26.0)		0.692
	Middle East	4	5.3 (4–16.5)		0.971
	Africa	3	25.5 (10.1–39.1)		0.479
	Characteristic of countries			**0.001**	
	Higher income	19	8.3 (3.2–13.8)		Referent
	Low- and middle-income	36	9.8 (5.7–17.8)		0.646
	Study population			**0.004**	
	School	26	9.3 (4.7–17.5)		Referent
	Community	29	8.3 (6.9–13.8)		0.942
3	Method of measured BP‡			**0.041**	
	Sphygmomanometer	34	8.9 (5.7–16.2)		Referent
	Automatic digital monitor	13	12.2 (5.3–21.5)		**0.015**
	Between-study variance assessed by moment-based estimate ($tau^2 = 5.307$)				

95% CI = confidence interval of 95%, HBP = high blood pressure.

* The adjusted analysis was conducted following a theoretical conceptual model that had been previously formulated in three levels: 1) year of survey (1988–1998, 1999–2004, and 2005–2009); 2) geographic location (North America, Europe, Asia, Latin America, Oceania, Middle East, and Africa); characteristic of countries (higher or low- and middle-income); and study population (community or school); 3) method of measured BP (sphygmomanometer or automatic digital monitor).

** The effect of each variable on the outcome was adjusted for other variables in the same model or above in the hierarchical model. Variables with $P > 0.2$ were not included in the subsequent adjusted models. Statistically significant associations are in **bold** type.

‡ Eight articles are not described the method of measured blood pressure.

TABLE 2. Association Between Prevalence of High Blood Pressure With Methodological Covariates for Girls (n = 61,049) of the Studies

				Girls	
				Univariate Model	Metaregression (Multivariate Model)*
Level**	Independent Variables	Number of Studies	Pooled Prevalence of HBP (95% CI)	*P*-Value	*P*-Value
1	**Year of survey**			0.972	
	1988–1998	9	9.0 (5.9–11.5)		Referent
	1999–2004	26	7.8 (3.4–13.8)		0.111
	2005–2009	20	7 (3.1–14.1)		0.450
2	**Geographic location**			0.214	
	North America	14	5.85 (2.9–8.7)		Referent
	Europe	4	11.2 (7.8–15.2)		0.484
	Asia	15	11.5 (6.7–18.7)		0.536
	Latin America	14	4.8 (2.8–9.2)		0.913
	Oceania	1	24.7 (22.7–26.8)		0.717
	Middle East	4	5.0 (2.3–13.6)		0.751
	Africa	3	29.0 (23.8–33.3)		0.552
	Characteristic of countries			0.679	
	Higher income	19	7.8 (3.4–10.5)		Referent
	Low- and middle-income	36	9.1 (3.3–13.7)		0.755
	Study population			0.746	
	School	26	8.6 (3.4–12.5)		Referent
	Community	29	7.8 (3.4–13.8)		0.995
3	**Method of measured BP**‡			0.897	
	Sphygmomanometer	34	8.6 (3.7–13)		Referent
	Automatic digital monitor	13	10 (5.5–23.8)		0.894
	Between-study variance assessed by moment-based estimate ($tau^2 = 2.349$)				

HBP = high blood pressure.

* The adjusted analysis was conducted following a theoretical conceptual model that had been previously formulated in three levels: 1) year of survey (1988–1998, 1999–2004, and 2005–2009); 2) geographic location (North America, Europe, Asia, Latin America, Oceania, Middle East, and Africa); characteristic of countries (higher or low- and middle-income); and study population (community or school); 3) method of measured BP (sphygmomanometer or automatic digital monitor).

** The effect of each variable on the outcome was adjusted for other variables in the same model or above in the hierarchical model. Variables with $P > 0.2$ were not included in the subsequent adjusted models. Statistically significant associations are in **bold** type.

‡ Eight articles are not described the method of measured blood pressure.

between prevalence of HBP in girls and methodological characteristics.

Table 3 shows the prevalence in the boys in relation to methodological characteristics. The highest prevalence was observed in Oceania and the lowest in the studies conducted in Middle East/Latin America, and North America.

Among boys, all the variables were associated with heterogeneity in the distributions of HBP in the univariate model, but only the year in which the survey was conducted, the geographical location, and the method of measuring BP maintain the significance in the adjusted model.

DISCUSSION

We conducted a comprehensive systematic review of studies addressing the prevalence of HBP in adolescents, and we used meta-regression to examine the possible sources of heterogeneity in the data presented in the articles. The prevalence of HBP was higher among boys, and the heterogeneity across studies was due to methodological differences, especially method of measuring BP. Further, the prevalence of HBP was higher among studies from low- and middle-income countries in boys. To the best of our knowledge, this is the first systematic review article analysing the associations between HBP prevalence and studies characteristic's in adolescents, and is the most extensive systematic review on this subject, to date.

Contrary to expectations, the prevalence of HBP was inversely related to the year of the survey. Because the prevalence of obesity has been increasing[4] we would expect to observe an increase in the prevalence of HBP, since there is a strong association between obesity and hypertension.[10] Freedman et al[10] also found that the prevalence of obesity increased but no increase in BP was observed. The authors emphasized that a possible explanation is the improvement of maternal and child health[86,87] and increased prevalence of breastfeeding alone[88] observed over the past 2 decades. These factors, which are inversely associated with adolescent BP levels,[89] can be responsible for the decrease in HBP prevalence.

Boys had higher pooled prevalence than girls. There are 2 possible explanations for our finding: 1) studies showed that boys has a higher accumulation of visceral fat[90] and intra-abdominal fat[91] than girls, and visceral fat has been associated

TABLE 3. Association Between Prevalence of High Blood Pressure With Methodological Covariates for Boys (n = 61,004) of the Studies

				Boys	
				Univariate Model	Metaregression (Multivariate Model)*
Level**	Independent Variables	Number of Studies	Pooled Prevalence of HBP (95% CI)	*P*-Value	*P*-Value
1	**Year of survey**			**<0.001**	
	1988–1998	9	13.3 (8.7–14.6)		Referent
	1999–2004	26	10.3 (6.3–18.8)		**0.011**
	2005–2009	20	9.4 (5.3–25.1)		**0.004**
2	**Geographic location**			**0.004**	
	North America	14	7.1 (3.3–10.8)		Referent
	Europe	4	17.5 (12.6–26.8)		0.334
	Asia	15	13.9 (10.4–22.8)		0.664
	Latin America	14	7.4 (4.4–13.5)		0.891
	Oceania	1	24.7 (22.8–26.7)		0.607
	Middle East	4	6.4 (3.4–20.0)		0.551
	Africa	3	24.0 (9–46.1)		0.617
	Characteristic of countries			**0.003**	
	Higher income	19	9.0 (4–18.0)		Referent
	Low- and middle-income	36	11.5 (6.4–22.7)		**0.007**
	Study population			**0.001**	
	School	26	9.4 (5.1–22.8)		Referent
	Community	29	10.8 (6.9–16.2)		0.557
3	**Method of measured BP‡**			**<0.001**	
	Sphygmomanometer	34	9.7 (6.1–19.4)		Referent
	Automatic digital monitor	13	14.4 (5.1–24.7)		**<0.001**
	Between-study variance assessed by moment-based estimate ($tau^2 = 1.305$)				

HBP = high blood pressure.

* The adjusted analysis was conducted following a theoretical conceptual model that had been previously formulated in three levels: 1) year of survey (1988–1998, 1999–2004, and 2005–2009); 2) geographic location (North America, Europe, Asia, Latin America, Oceania, Middle East, and Africa); characteristic of countries (higher or low- and middle-income); and study population (community or school); 3) method of measured BP (sphygmomanometer or automatic digital monitor).

** The effect of each variable on the outcome was adjusted for other variables in the same model or above in the hierarchical model. Variables with $P > 0.2$ were not included in the subsequent adjusted models. Statistically significant associations are in **bold** type.

‡ Eight articles are not described the method of measured blood pressure.

with higher sympathetic activity.[92,93] This activation is a key mechanism underlying the effect of intra-abdominal fat accumulation on the development of hypertension.[94] For example, increased sympathetic flow may increase sodium re-absorption and subsequent increased peripheral vascular resistance resulting in increased BP.[95] Also, this increased sympathetic activation can be caused by increased testosterone concentrations in males. Testosterone, acting as a mediator of the androgen receptor gene function,[96] has been associated not only with increased visceral fat but also with greater vasomotor sympathetic tone and BP in adolescent boys, compared to girls.[96] However, pubertal stage is not included in the diagnostic criteria of HBP, and it can be a limitation, since the analysis cannot adjust for this variable is not included in the articles described. In our review, is not possible to analyze the influence of the obesity on the HBP prevalence, because the cut-off points to diagnosis the obesity in each article is different, and would introduce a classification bias in the analyses if us carried out.

2) The girls have a higher prevalence of healthy behavior patterns (healthy eating habits[97]; avoidance of tobacco smoking[98]; less alcohol abuse[99]; lower levels of sedentary behavior[7]) than boys, and these healthy life-style choices are associated with lower levels of BP and HBP prevalence.[100–102] Additionally, it was not possible to adjust the analysis for other factors potentially associated with BP such as lifestyle, genetic factors, intrauterine development, because theses information's is not provided in the articles included.

Of considerable note is that the type of device used to measure BP was associated with heterogeneity in the prevalence of HBP. The pooled prevalence was higher in articles using the automatic ''digital'' monitors. However, all reported that the monitors used had been validated for measurement of BP in adolescents, according criteria by European Hypertension Society and American Academy of Pediatrics for differences between averages of the measures mercury column and tested monitor for a device to be validated, should be $\leq$5 mmHg and that the standard deviation of the differences of the averages is not larger than 8 mmHg. The differences in the prevalence can introduce differential or non-differential misclassification effects (errors due to disease status or exposure) and may cause underestimation or overestimation of the true prevalence.[103] Our findings suggest that automatic monitors should not be used for diagnosis of hypertension, but may be used only as an initial assessment of current status of cardiovascular health of the

adolescents and, should the teenager present with HBP, additional analysis with more accurate instruments must be performed. The logistics in epidemiological studies often preclude the measurement of BP with the gold standard; for example ambulatory BP monitoring or repeated office BP measurements. The technique is more difficult to master and is not cost-effective on an epidemiological scale. However, cost-effectiveness becomes evident[104] if HBP diagnosis in adults; and the screening of the HBP in the adolescent can lead to better and more prompt treatment and so increase life expectancy of the adolescent, because HBP this age group is asymptomatic.

On the other hand, recently Thompson et al[105] showed that there is no direct evidence that screening for hypertension in children and adolescents reduces adverse cardiovascular outcomes in adults. Are needed new research's to improve diagnosis and risk stratification of children with elevated BP and to quantify risks and benefits of interventions, because on this review we demonstrated higher prevalence of HBP. Secondary hypertension, although it might occasionally appear in our results, it was not described in any article, therefore disregarded in this review, because it is rare in the pediatric population and interfere little in the final result of the HBP prevalence's.

Another important factor could be influence of the classification of the HBP is the race and ethnicity, because the growth speed is influenced by these factors,[106] but the guidelines (American Academy of Pediatrics[12] and European Society of Hypertension[13]) highlights that newly revised CDC growth charts (www.cdc.gov/growthcharts) should be used for the height percentile classification.

We observed higher HBP prevalence in low- and middle-income countries. Previous studies conducted in these countries reported that the hypertension was associated with low socioeconomic status.[83,107] However, the nutritional burden is shifting from deficiency to excess energy imbalance in these countries, while awareness of the problem is increasing in developed countries and, as such, the prevalence in higher income countries is becoming stabilized, albeit not as-yet normalized.[108,109] Hence, strategies for changing lifestyles are necessary; the objectives being to decrease the prevalence and to increase early treatment of HBP.

CONCLUSIONS

Our systematic review indicated that HBP prevalence is high among adolescents; higher in boys and adolescents from low- and middle-income countries. The method of measurement plays an important role in HBP prevalence distribution in the overall sample, and especially in boys, but not in girls. Public health programs that aim to reduce HBP should focus primarily on adolescents from low- and middle-income countries.

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