

Prehypertension and Cardiovascular Risk Factors in Children and Adolescents Participating in the Community-Based Prevention Education Program Family Heart Study

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ABSTRACT

Background: Because prehypertension identifies children most at risk for the development of future hypertensive disease, the purpose of this study was, to examine the association of prehypertension with risk factors for cardiovascular disease (CVD) in a large sample of youths participating in the community-based prevention education program family heart study.

Methods: We estimated blood pressure and body mass index (BMI) for age and the lipid profile in terms of total cholesterol (TC), low-density-lipoprotein-cholesterol (LDL-C), high-density-lipoprotein-cholesterol (HDL-C), non-HDL-C, triglycerides (TG) and the LDL-C to HDL-C ratio.

Results: Among 10,841 (5,628 males) children and adolescents 1,587 (14.6%) had prehypertension (85th to <95th percentile). This was strongly affected by weight, resulting in 19.7% in overweight (BMI \geq 85th percentile) and 23.7% in obese (>95th percentile) youth. The prevalence of dyslipidemia was similar in prehypertensive boys and girls in terms of LDL-C 11.2% versus 11.8%, non HDL-C 11.9% versus 14.3%, TG 2.4% versus 2.7% and for low HDL-C 2.1% versus 2.3%. The prevalence of low HDL-C increased from 2.1% in non-overweight, through 3.9% in overweight to 5.2% in obese youth and of elevated TG from 1.2% via 4.5% to 6.5% respectively. The number of risk factors is affected by BMI. Significant associations between prehypertension and CVD risk factors were observed in boys and girls for overweight/obesity odds ratios (OR 2.0/2.4), for hypertriglyceridemia (OR 1.9/2.0), for high non HDL-C (OR 1.4/1.4) and for elevated LDL-C (OR 1.3/1.1).

Conclusions: Prehypertension was significantly associated with overweight, obesity and dyslipidemia in 10,841 children and adolescents.

Keywords: Cardiovascular risk factors, prehypertension, urban children and adolescents

INTRODUCTION

Prehypertension in children and adolescents is defined as average levels of age, gender and height adjusted systolic blood

pressure (SBP) or diastolic blood pressure (DBP) of $\geq 90^{\text{th}}$ to $< 95^{\text{th}}$ percentile.^[11] Data on the prevalence of childhood prehypertension are heterogeneous mainly depending on measurements, age, gender and region.^[2-9] Thus, prevalence of prehypertension at the initial screen was 9.5% and 15.7% after three screenings using four oscillometric blood pressure (BP) readings in 11-17 years old US adolescents. Prehypertension increased with increasing body mass index (BMI) and almost 20% of the prehypertensive adolescents were at risk of future cardiovascular disease (CVD).^[10] Children with prehypertension are at significant risk for development of hypertension within 2-4 years with a progression rate of about 7%/year.^[11] Substantially lower rates of progression (0.5% to 0.8%/year) are described and adolescents with abnormal BP had an >4-fold increased rate for the development of hypertension than their normotensive counterparts.^[12]

Among 2-18-year-old overweight youths the prevalence of prehypertension was 27.9%,^[13] whereas 17.7% of obese children had prehypertension.^[14] Prehypertension defined as BP 120 to 139/80 to 89 mm Hg is very common in 16.5-19-year-old Israeli adolescents in terms of 56.8% of male and 35.8% of female subjects increasing with overweight and obesity.^[15]

The purpose of the present study was to establish the prevalence of prehypertension and to assess its associations with CVD risk factors in a large sample of children and adolescents aged 3-18 years participating in the community-based prevention education program (PEP) family heart study in the city of Nuremberg (Germany).

METHODS

Study population

We selected 10,841 youths with complete data sets out of 22,051 children and adolescents, participating in yearly cross-sectional surveys of the PEP family heart study Nuremberg from 1993/1994 to 2007/2008.^[16,17] At the beginning of each school year, we informed first graders and their parents/guardians about the PEP. Families deciding to participate voluntarily and free of charge in this community-wide project for detection and improvement of cardiovascular risk factors in terms

of family-based life-style modifications contacted the PEP office in the Sanitary Board of the City of Nuremberg for more detailed information and written consent. Nearly 94% of all 53 elementary schools participated in this long-term project. Self-reported cardiovascular, metabolic, endocrine and malignant disorders and specific medication were exclusion criteria. The ethical committee of the medical faculty of the Ludwig Maximilian University of Munich (Germany), the Bavarian Ministry of Science and Education and the local school authorities approved PEP, which fulfilled the criteria of the Declaration of Helsinki.

Measurements

Continuously trained medical research assistants estimated BMI, WC and %BF as previously described, SBP and DBP twice on both arms using non-mercury aneroid ERKA sphygmomanometers (MTM Munich, Germany), which were recalibrated as needed by bioengineering services with an appropriate cuff size as previously described.^[16-18] Based on the first index visit, age-, gender- and height-adjusted SBP and DBP $< 90^{\text{th}}$ percentile were classified as normal, 90^{th} to 95^{th} percentile as prehypertensive and $\geq 95^{\text{th}}$ percentile as hypertensive beginning at age 3-years.^[1,19] CVD risk factors were defined as overweight obesity and fasting values of total cholesterol ≥ 200 mg/dL, low-density-lipoprotein-cholesterol (LDL-C) ≥ 130 mg/dL, high-density-lipoprotein-cholesterol (HDL-C) ≤ 35 mg/dL, triglycerides (TG) ≥ 150 mg/dL, non-HDL-C ≥ 145 mg/dL and fasting plasma glucose ≥ 100 mg/dL.^[16-18,20,21] Body weight was categorized as normal (BMI for age $< 85^{\text{th}}$ percentile), overweight (BMI for age 85^{th} to $< 95^{\text{th}}$ percentile) and obese (BMI for age $> 95^{\text{th}}$ percentile).^[22]

Statistical analysis

Using IBM SPSS 18.0 (statistical package for social sciences, IBM Deutschland GmbH, IBM Allee 1, 71139 Ehingen, Deutschland) we assessed the distribution of continuous variables and conducted log transformation for TG, which were not normal distributed. Differences between subgroups were compared by using χ^2 test. Point estimates and 95% of the confidence intervals were calculated for the prevalence of all CVD risk factors. A 2-tailed α of $P < 0.05$ was chosen of the criterion of significance.

We used linear regression analysis to evaluate the associations among CVD risk factors. We constructed multivariate logistic models to estimate associations between prehypertension and CVD risk factors. Significance for odds ratios (OR) was standardized as $P < 0.001$. We derived age- and gender-specific values from percentiles of 22,843 youths aged 3-18 years using the LMS Chartmaker Pro, version 2.3, estimating the skewness parameter L, the median M and a measure of variation S.^[23] Analyses were restricted to participants with complete data sets.

RESULTS

Among the 10,841 children and adolescents presenting complete data sets the 5,628 males (mean age 10.2 ± 3.4 years) were taller and heavier and had significantly ($P < 0.05$) higher BMI, SBP and DBP values than the 5,213 females aged 10.0 ± 3.4 years [Table 1]. The prevalence of prehypertension (BP 90th to 95th percentile) was 14.9% in boys and 14.3% in girls, 8.5% of boys and 9.2% of girls were overweight (85th to <95th percentile) and 5.1% of boys and 4.5% of girls had obesity (BMI >95th percentile). Girls had significantly higher mean lipid values except lower HDL-C than boys.

Table 1: Characteristics of 10,841 children and adolescents

CVD risk variables	Boys	Girls
N	5628	5213
Mean age, years	10.2 (3.4)*	10.0 (3.4)
Median age, years	10.0	10.0
Weight, kg	40.0 (16.9)*	37.4 (14.8)
Height, cm	145.3 (20.2)*	141.8 (17.9)
BMI, kg/m ²	18.0 (3.2)*	17.8 (3.4)
BMI >85 th -95 th percentile (%)	8.5	9.2
BMI >95 th percentile (%)	5.1	4.5
SBP, mm Hg	107.9 (10.9)*	105.5 (9.7)
DBP, mm Hg	69.0 (8.2)*	67.9 (8.2)
BP 90 th -95 th percentile (%)	14.9	14.3
TC, mg/dL	164.8 (29.6)	170.2 (29.8)*
TC >200 mg/dL (%)	10.3	13.4
LDL-C, mg/dL	95.2 (26.2)	99.7 (27.1)*
LDL-C >130 mg/dL (%)	8.3	11.1
Non-HDL-C, mg/dL	108.3 (27.2)	114.2 (28.0)*
Non-HDL-C >145 mg/dL (%)	9.1	13.0
HDL-C, mg/dL	56.5 (12.4)*	55.8 (12.2)
HDL-C <40 mg/dL (%)	2.1	2.7
TG, mg/dL	63.9 (26.8)	70.5 (29.8)*
TG >150 mg/dL (%)	1.3	2.1

BMI=Body mass index, TC=Total cholesterol, SBP=Systolic blood pressure, DBP=Diastolic blood pressure, BP=Blood pressure, LDL-C=Low-density-lipoprotein-cholesterol, HDL-C=High-density-lipoprotein-cholesterol, TG=Triglycerides

of girls were overweight (85th to <95th percentile) and 5.1% of boys and 4.5% of girls had obesity (BMI >95th percentile). Girls had significantly higher mean lipid values except lower HDL-C than boys.

Figure 1 displays a decreasing proportion of non-overweight between normotensive and prehypertensive children from 61.3% to 68.0% and simultaneously an increasing likelihood of overweight and obesity. Thus, in normotensive children and adolescents the prevalence of overweight (13.6%) and obesity (5.1%) was lower than in youths with prehypertension (19.7% respectively 12.3%).

Table 2 demonstrates that prehypertensive youth have a more adverse CVD risk profile than normotensive youth have. Among prehypertensive children, the prevalence of increased BMI was two times higher (31.3%) in girls than in boys (18.4%). The lipid levels were also higher in prehypertensive than in normotensive youth girls having more adverse lipid profiles. Among non-overweight girls the prevalence of ≥ 3 CVD risk factors (out of seven including hypertension) was 9.5% increasing to 20% in overweight and obese girls. As can be seen in Figure 2, the prevalence of prehypertension and of four lipids is strongly affected by BMI resulting in substantial increases of prehypertension from 13.6% in non-overweight through 19.7% in overweight and 23.7% in obese youth.

The significant associations between prehypertension and CVD risk factors in children and adolescents are presented in Table 3 and in Figure 3. Hypertriglyceridemia was most strongly associated with prehypertension in boys (OR 2.5; 95% CI 1.5-4.2) closely followed by combined

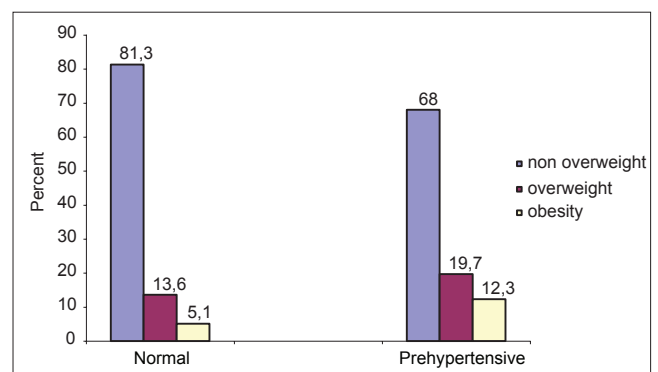
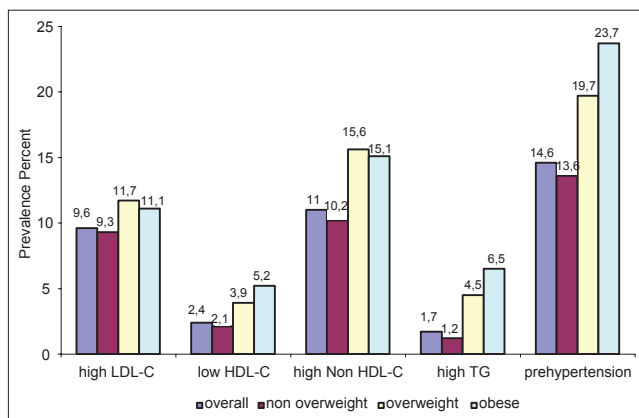


Figure 1: Prevalence of non-overweight, overweight and obesity in normotensive and hypertensive youth

Table 2: Prevalence (%) of CVD risk factors by blood pressure groups in normotensive and prehypertensive children and adolescents

Risk factors	Boys		Girls	
	Normal BP n=4,416	Prehypertension n=839	Normal BP n=4,116	Prehypertension n=748
BMI \geq 85 th percentile	11.5	18.4	10.1	31.3
TC \geq 200 mg/dL	9.6	13.6	12.5	16.3
LDL-C \geq 130 mg/dL	8.2	11.2	10.7	11.8
HDL-C \leq 35 mg/dL	2.1	2.1	2.7	2.3
Non-HDL-C \geq 145 mg/dL	8.3	11.9	12.4	14.3
TG \geq 150 mg/dL	1.1	2.4	1.7	2.7

CVD=Cardiovascular disease, BMI=Body mass index, HDL-C=High-density-lipoprotein-cholesterol, LDL-C=Low-density-lipoprotein-cholesterol, TC=Total cholesterol, TG=Triglycerides, BP=Blood pressure

**Figure 2:** Prevalence of risk factors by body mass index groups

overweight/obesity (BMI \geq 85th percentile) in girls (OR 2.4; 95% CI 2.1-2.8). Associations of all the four lipid fractions were lower in girls than in boys, whereas the associations for HDL-C were not significant.

DISCUSSION

This community-based observational study providing a family environment unlike school-based studies was performed from 1993 to 2008 and describes the prevalence of prehypertension and its associations with CVD risk factors in 10,841 children and adolescents aged 3-18 years. BP prevalence data are based on the first index measurement resulting in 14.6% prehypertensive and 6.7% hypertensive children. This is consistent with 12.7% prehypertension and 5.4% hypertension in the community-based pediatric practices and with 16.7% in a multiracial school district both studies using a single BP

measurement, too.^[3,4] In the National Health and Nutrition Survey (NHANES) 13.6% of boys and 5.7% of girls were prehypertensive^[5] and 15% of boys and 20.2% of girls in rural northeast China had prehypertension.^[9] After three screenings, the prevalence was 81.1% of normal BP, 15.7% of prehypertension and of 3.2% hypertension among adolescents in the Houston area.^[10] Among adolescents, 21% boys and 13% girls at the initial examination met BP criteria for prehypertension.^[11] In the present study, the above seven studies were describe mean prevalence of 14.9% for prehypertensive youth, which is consistent with 14.6%. However, disparate findings are reported from China describing prevalence of 7.2% for prehypertension in urban adolescents,^[8] which is consistent with 7.6% in rural Canadian community.^[6] Even lower prevalences of prehypertension of 2.7% are described in urban Italian^[7] and 3.4% of youth within a large urban medical system in northeast Ohio.^[2] Differences in age, ethnicity, rural and urban environment, period of assessment, methods of ascertainment and especially body weight are among the set of explanations for these disparities. Among 1020 students in a Houston area, only 4% had persistent prehypertension after repeated measurements, but an additional 7.5% had a mean BP fluctuating between ranges of prehypertension and hypertension on all 3 visits. Almost 30% of the students had at least one elevated BP measurement significantly influenced by obesity.^[24]

Data on the relationship between prehypertension and weight are sparse and inconsistent. Therefore, we assessed the distribution of non-overweight, overweight and obesity in a large sample of normotensive,

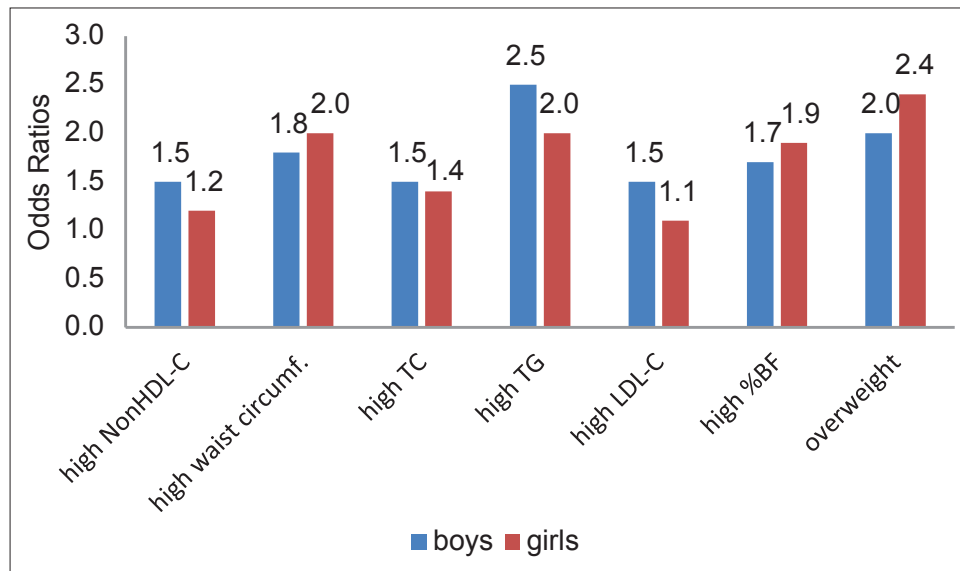


Figure 3: Associations of prehypertension with risk factors in prehypertensive boys and girls

prehypertensive and hypertensive youths [Figure 1]. We found that 19.7% of prehypertensive children had overweight which is consistent with 19.4% overweight in prehypertensive children who participated in a large community-based study in pediatric practices.^[4] We found a significant association of combined overweight/obesity (BMI $\geq 85^{\text{th}}$ percentile) with prehypertension (OR 2.0), which is lower than in the Canadian Walkerton Health Study describing OR of 4.5 for prehypertension.^[6]

NHANES data describe a strong, positive and independent association of overweight and obesity with elevated BP classifying overweight boys (OR 1.5) as well as obese boys (OR 2.8) and obese girls (OR 2.6) being significantly more likely to have prehypertension.^[5] This is consistent with our findings of a significant association of combined overweight/obesity (BMI $\geq 85^{\text{th}}$ percentile) with prehypertension in boys (OR 2.0) and girls (OR 2.4). Among obese children and adolescents prevalence of prehypertension was described as 27.9% and 17.7%.^[13,14]

These associations between elevated BP and overweight/obesity in children and adolescents are of concern.^[25] Obesity increase partially explained the rise in hypertension and prehypertension from 1988 to 1999.^[26] In South Korean youth, prehypertension and hypertension decreased by 52% from 1998 to 2008, which is not explained by secular changes in childhood obesity.^[27] From 1980 to 2008, SBP levels have increased with time,

but increased BMI explained only 15% of SBP increases among UK children.^[28]

In the Bogalusa Heart Study, the levels of SBP and DBP among children did not increase despite the large increase in obesity from 6% to 17% during the 1974 to 1993.^[29]

Especially overweight/obese US adolescents carry a substantial burden of CVD risk factors in terms of overall prevalence of 14% for prehypertension/hypertension, 22% for borderline high/high LDL-C and 6% low HDL-C.^[30] This is consistent with our findings in terms of prevalence of 14.6% prehypertensive and 6.7% hypertensive, for high LDL-C of 11.5% in prehypertension and 12.5% in hypertension and for low HDL-C of 2.2% respectively 2.8%.

One limitation is the cross-sectional design of the current study. Furthermore, Tanner stage and life-style data are not available from all cross-sectional surveys. Because elevated BP must be confirmed on repeated visits on ≥ 3 occasions^[1] we report data from index measurements though BP measurements were performed every year. Strength is that BP measurements were performed at home during interviews thus avoiding white-coat effects, which is particularly problematic in children and complicates the assessment of outcomes.^[31] Furthermore, the setting was homogeneous in terms of sustained staff, methods and equipment, one city, one ethnic group and representative recruitment from 94% of the elementary schools in Nuremberg.

CONCLUSIONS

A prevalence of 14.6% prehypertension among 10,841 children and adolescents deserves attention because of the close associations with unhealthy fat patterning and adverse lipid profile. The strong effect of overweight and obesity on this risk constellation demand intensive family-based efforts to improve healthy life-style behavior beginning in childhood. However, “simply focusing on obesity lacks credibility in a population where nearly 1 in 20 children have elevated BP, nearly 1 in 5 has elevated cholesterol and close to 50% have normal weight.”

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