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Prevalence of High Blood Pressure and Association With Obesity in Macedonian Children Aged 6 Years Old

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Abstract: *The prevalence of high blood pressure in children is increasing worldwide, largely but not entirely, determined by the concurrent epidemic of childhood obesity. The objectives of this study were to determine the prevalence of prehypertension and hypertension in Macedonian children of 6 years of age and to determine the relationship between the different components of blood pressure (BP) with different adiposity indicators. Cross-sectional study including a sample of 1200 children aged up to 6 years, drawn randomly from several schools from three regions in the Republic of North Macedonia. To achieve the goals of the research, weight, height, the body mass index (BMI), tri-ponderal mass index (TMI), percentage of fat tissue (%FM), systolic and diastolic BP, mean arterial pressure and pulse pressure were measured. The prevalence estimates for prehypertension and hypertension were 6.8% and 13.2%, respectively. In both sexes, adiposity indicators were positively and significantly related to systolic and diastolic BP ($p<0.001$), so students from higher categories of adiposity had significantly higher BP levels ($p<0.001$). Our results show a high prevalence of high blood pressure in Macedonian children. Moreover, high levels of adiposity are associated with high blood pressure in early childhood, confirming that this may be associated with cardiovascular risk later in life. Taking into account also lack of exercise and pathologies that may develop also in physiotherapeutic aspect due to this issue.*
Keywords: *Blood pressure, Obesity, Weight status, Children, Physical activity, BMI, Kinesiology.*

Introduction

Over the last decade, epidemiological studies have reported an increase in blood pressure (BP) levels in children (Xi et al., 2016), as well as the prevalence of prehypertension and hypertension (Sorof et al, 2006; McNiece et al., 2007).; Ostrowska-Nawarycz, & Nawarycz, 2007; Raj et al., 2007; Kelishadi et al., 2006) largely, but not entirely, driven by a concurrent increase in childhood obesity. This fact is accompanied by a growing recognition of the importance of blood pressure measurements in children. However, the importance of monitoring blood pressure (BP) levels in the pediatric age goes beyond its association with obesity because it has been consistently reported that, independent of body mass index (BMI), BP levels track from childhood to adulthood (Bao et al., 1995; Chen & Wang, 2008), and that BP levels in childhood predict young adult cardiovascular risk (Rademacher et al., 2009). Despite the widely reported increase in the prevalence of high BP in the pediatric population worldwide, only a few studies have investigated blood pressure in Macedonian children, reporting the prevalence to be around 21% (Stankovska et al., 2021).

The prevalence of overweight/obesity among Macedonian children is around 37% (Gontarev et al., 2018; Gontarev & Ruzdija., 2014; Myrtaj et al., 2018). A recent study conducted in 6-year-old children from the Skopje region (Macedonia) reported an overweight/obesity prevalence of 34% (Emini et al., 2022). Increased BP levels should be associated with the high prevalence of obesity, but studies analyzing the association between adiposity indicators and BP are rare in Macedonian children (Stankovska et al., 2021), and none have been conducted in children ≤ 6 years.

Traditionally, BP measurements include only systolic blood pressure (SBP) and diastolic blood pressure (DBP) values, but other indices such as mean arterial blood pressure (MAP) or pulse pressure (PP) have also been shown to be independent predictors of cardiovascular events in both normotensive and hypertensive adults (Franklin et al., 2009; Safar et al. 2001).

In contrast, recent studies have suggested that tri-ponderal mass index (TMI) could be a better prognosticator of health in children than BMI (Khoshhali et al. 2020; De Lorenzo et al., 2019; Peterson et al., 2017). Despite its usefulness in body conformation research, the connection between TMI and blood pressure in children has not been conclusively elucidated.

Since the current prevalence estimates of overweight/obesity among Macedonian children is one of the highest in Europe (Ortega et al., 2023), the prevalence estimates of high blood pressure among Macedonian children may represent an indirect indicator of the impact of the obesity epidemic on the BP level. Thus, the objectives of this study were to determine in Macedonian children aged 6 years: 1) the prevalence of prehypertension and hypertension and 2) the association between indicators of adiposity (BMI, %FM and TMI) with traditional ones (SBP, DBP) and alternative (MAP, PP) blood pressure components.

METHODS

Sample of respondents

The research was carried out on a sample of 1200 children randomly selected from several schools from three regions (Skopje, South-Eastern and Pologsk) in the Republic of North Macedonia. The sample is divided into two subsamples according to gender, namely 557 respondents are boys and 643 respondents are girls. The average age of respondents of both sexes was 6.3±0.3 years.

The study included all students whose parents consented to their children's participation in the research, who were psychophysically healthy, and who regularly attended Physical and Health Education classes. The respondents were treated in accordance with the Helsinki Declaration.

The measurements were performed in the months: March, April and May 2019, in standard school conditions during the regular classes in Physical and Health Education. The measurements were performed by experts in the field of kinesiology and medicine, previously trained to perform functional tests and to take anthropometric measurements.

Anthropometric measures and body composition

The measurement of anthropometric measures was carried out according to the recommendations of the IBP-International Biological Program. The height of the subjects (without shoes) was measured to the nearest 0.1 cm with a portable stadiometer. BMI was calculated as weight divided by height squared. TMI was calculated as weight divided by height cubed. The percentage of adipose tissue % FM was determined by the bioelectrical impedance (BIA) method. The measurement is realized by Body Composition Monitor, model "OMRON - BF51. Before starting the measurement in the Body Composition Monitor, the parameters of gender, age and body height of the respondent were entered. In order to ensure better accuracy of the results obtained from the assessment of body composition, before each measurement were fulfilled, prerequisites recommended by ACSM.

Blood pressure

The blood pressure measurement (systolic and diastolic) is performed by experts from the medicine, doctor-specialist's pediatrician fields. Blood pressure measurements were performed using the oscillometric method through a calibrated Omron (Kyoto, Japan) electronic and digital device model HEM 742, with cuffs of appropriate size to fit the arms of adolescents. This device has been validated for use with adolescents (Christofaro et al. 2009). Participants were informed about the procedures and were instructed to remain at quiet rest for at least five minutes in a quiet environment and without noise, with emptied bladder, not having performed exercise 90 min before the tests or smoked or ingested food, coffee, alcoholic drinks or mate at least 30 min before data collection. The atmosphere was quiet and with no noise. Blood pressure was measured three times at intervals of 60 seconds, and the result was the median value of the three measurements. NBP was defined as BP < 90th percentile; prehypertension was defined as BP between the ≥90th percentile and the <95th percentile; and hypertension was defined as BP ≥ 95th percentile. The mean arterial pressure (MAP) was calculated using the traditional formula. The pulse pressure (PP) was calculated as SBP minus DBP. We adopted the methodological recommendations of the Update on the Task Force Report on High Blood Pressure in Children and Adolescents.

Statistical analysis

The normal distribution of the continuous variables was checked graphically (normal probability plot) and statistically (Kolmogorov - Smirnov test) procedures. All variables had a normal distribution, which is why we used parametric statistics in the analyses. Anthropometric and blood pressure (BP) measures were presented as arithmetic mean and standard deviation (SD). Gender differences on quantitative variables were tested using the Student T-test.

Partial correlation coefficients were applied in order to determine the relationship between each component of BP (SBP, DBP, MAP and PP) and indicators of adiposity (BMI, %FM, TMI), controlling for age, according to sex.

We categorized %FM low (first quartile), medium (second and third quartiles) and high (fourth quartile). Children were classified as underweight, normal weight, overweight and obese according to the BMI cut-offs proposed by Cole and Lobstein (2012).

ANCOVA models were used to determine mean differences in each BP component (SBP, DBP, MAP and PP) between BMI and %FM categories, controlling for age in the total sample and also separately by sex. Pairwise post hoc hypotheses were tested using the Bonferroni correction for multiple comparisons. All, analyzes were performed using the Statistical Package for Social Sciences software (SPSS, v. 22.0 for WINDOWS; SPSS Inc., Chicago, IL, USA), and values of $p < 0.05$ were considered statistically significant.

Results

The research was carried out on a sample of 1200 respondents, of which 557 (46.4%) were boys and 643 (56.6%) were girls. The average age of the respondents was 6.3±0.3 years. No significant differences were observed between the mean age of the girls and boys.

Table 1. *Characteristics of the study sample.*

	Total (n=1200)		Boys (n=557)		Girls (n=643)		F	Sig.
	Mean	SD	Mean	SD	Mean	SD		
Age (years)	6.30	0.26	6.30	0.27	6.30	0.26	0.17	0.681
Weight (Kg)	121.49	5.69	121.89	5.94	121.15	5.45	5.11	0.024
Height (cm)	25.66	5.59	26.01	5.70	25.35	5.48	4.12	0.043
BMI (kg/m2)	17.26	2.77	17.38	2.73	17.14	2.80	2.21	0.137
TMI (kg/m3)	14.09	2.46	13.89	2.31	14.26	2.57	6.69	0.010
% FM	22.51	7.65	23.87	7.07	21.35	7.93	30.76	0.000
SBP (mm Hg)	101.01	11.18	101.72	10.55	100.40	11.67	4.15	0.042
DBP (mm Hg)	63.81	10.93	63.95	10.88	63.69	10.98	0.17	0.681
MAP (mm Hg)	36.99	10.28	36.02	9.25	37.83	11.03	9.29	0.002
PP (mm Hg)	75.97	10.48	77.03	7.96	75.06	12.18	10.68	0.001

Abbreviations: *BMI = body mass index; FM = fat mass; TMI = Tri-Ponderal Mass Index; SBP = systolic blood pressure; DBP = diastolic blood pressure; MAP = mean arterial pressure (DBP + {0.333 x (SBP—DBP)}); PP = pulse pressure (SBP-DBP). In bold when p value ≤ 0.05*

Table 1 shows the characteristics of the sample. From the review of the table showing the values of arithmetic means. standard deviations and the level of statistical significance. it can be seen that no statistically significant differences were determined between boys and girls in the variables weight. height. BMI (body mass index) and DBP (diastolic blood pressure). Mean values of height. weight. percentage of body fat. SBP (systolic blood pressure) and PP (pulse pressure) were higher in boys compared to girls. Girls showed higher mean values of Tri-Ponderal Mass Index and MAP (mean arterial pressure). The prevalence of prehypertension was 6.8% in boys and 6.7% in girls. while the prevalence of hypertension was 10.9% in boys and 15.3% in girls. No statistically significant differences were found between the estimates of prehypertension prevalence by sex groups. but girls had a significantly higher prevalence of hypertension than boys ($p<0.05$).

Table 2. *Partial correlations coefficients (r) of systolic blood pressure. diastolic blood pressure. mean arterial pressure and pulse pressure with BMI. %fat mass and TMI controlling for age.*

		BMI	%FM	TMI
SBP	Total	0.206	0.192	0.080
	Boys	0.153	0.101	0.106
	Girls	0.244	0.247	0.068
DBP	Total	0.143	0.119	0.055
	Boys	0.107	0.038	0.054
	Girls	0.173	0.182	0.056
MAP	Total	0.073	0.071	0.108
	Boys	0.083	0.065	0.115
	Girls	0.063	0.056	0.120
PP	Total	0.071	0.049	0.028
	Boys	0.123	0.094	0.025
	Girls	0.043	0.046	0.015

Abbreviations: *BMI = body mass index; FM = fat mass; TMI = Tri-Ponderal Mass Index; SBP = systolic blood pressure; DBP = diastolic blood pressure; MAP = mean arterial pressure (DBP + {0.333 x (SBP—DBP)}); PP = pulse pressure (SBP-DBP). In bold when p value ≤ 0.05*

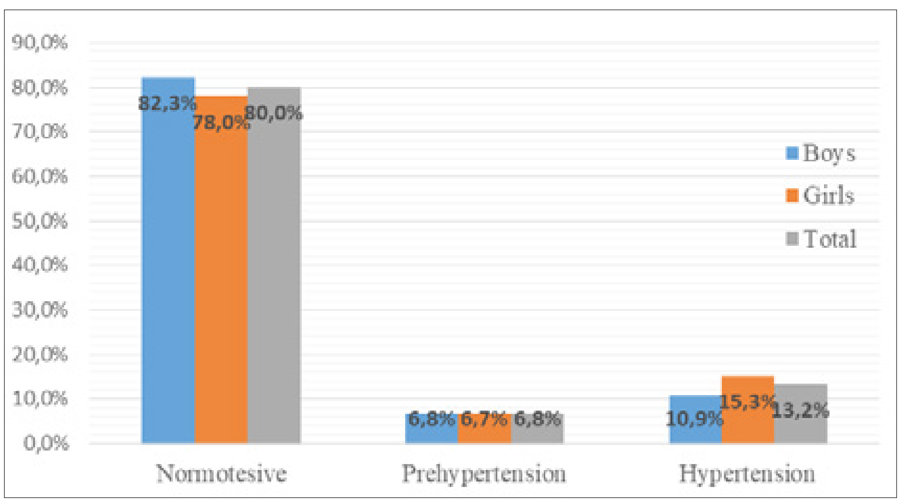

Figure 1. *Prevalence of normotensive. prehypertension and hypertension includes stages 1 and 2 in children. by sex and in the total sample.*

The partial correlation coefficients between blood pressure and adiposity indicators. controlling for age. are shown in Table 2. The Body mass index (BMI) is in a low statistically significant positive correlation with SBP and DBP in the entire sample of subjects and individually in subjects from male and female. Also. body mass index has a low and statistically significant correlation with pulse pressure (PP) in male respondents. Percentage of adipose tissue (%FM) has a low statistically significant positive correlation with SBP in the overall sample of subjects and individually in male and female subjects. Percentage of adipose tissue (%FM) had a low statistically significant positive correlation with DBP in the overall sample of subjects and in female subjects. Tri-Ponderal Mass Index (TMI) was in a low and statistically significant correlation with SBP in the overall sample and male respondents. Also. Tri-Ponderal Mass Index (TMI) is in a low and statistically significant correlation with mean arterial pressure (MAP) in the entire sample of respondents and individually in male and female respondents.

Mean differences in all BP components (SBP. DBP. MAP. PP) by categories of BMI and %FM. controlling for age and sex. are shown in Table 3. In the total sample. children categorized as obese according to body mass index and with high percentage of body fat showed higher mean values of systolic and diastolic blood pressure. Similar results were found when data were analyzed separately by gender ($p<0.001$) (data not shown).

Table 3. *Mean differences in blood pressure parameters according to adiposity categories in total sample controlling for age.*

BODY MASS INDEX										
	UW		NW		OV		OB		p	Post-hoc
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		
SBP	100.83	11.88	99.16	10.12	101.68	10.82	105.55	11.14	0.000	1<4; 2<3; 2<4
DBP	62.95	11.14	62.57	9.92	64.65	10.59	67.27	13.47	0.000	1<4; 2<4
PP	35.43	13.08	36.47	10.42	38.33	9.57	38.10	8.93	0.032	1<3; 2<3
MAP	75.87	10.50	75.70	9.73	75.70	9.14	77.96	11.51	0.023	2<4

% FAT MASS								
	Low		Medium		High		p	Post-hoc
	Mean	SD	Mean	SD	Mean	SD		
SBP	99.87	10.80	99.87	10.01	104.56	11.01	0.000	1<3; 2<3
DBP	62.48	10.44	63.28	10.00	66.05	12.63	0.000	1<3; 2<3
PP	36.58	11.19	36.98	9.88	38.42	9.22	0.070	ns
MAP	75.25	10.25	76.18	9.36	77.25	11.12	0.062	ns

Abbreviations: *SBP = systolic blood pressure; DBP = diastolic blood pressure; MAP = mean arterial pressure (DBP + {0.333 x (SBP—DBP)}); PP = pulse pressure (SBP-DBP). Categories of BMI are Underweight (UW). Normal Weight (NW). Overweight (OV) and Obesity (OB) according to gender-and-age-specific cut-offs defined by Cole and Lobstein. Categories of fat mass are Low. Medium. and High. representing the 1st. 2nd and 3rd and 4th quartiles.*

Discussion

Studies that assess the prevalence of high blood pressure in children ≤ 6 years old are rare worldwide. and none have been conducted in Macedonia. This study shows that the prevalence of high blood pressure (prehypertension and hypertension) in children aged 6 years from three regions in Macedonia was 17.7% and 22.0% in boys and girls. respectively. Furthermore. the prevalence of prehypertension and hypertension in the total sample was 6.8% and 13.2%. respectively. Also. a positive relationship between adiposity categories and BP levels was established.

Considerable variability in the prevalence of hypertension (≥95th percentile) has been reported in different population studies in the same age groups of children worldwide; some of them were similar to our results: 23% in China (Chen & Li. 2011) and 19.9% in Brazilian children (Crispim et al. 2014). Lower percentages are reported in Sydney. 13.7% (Gopinath et al.. 2011). Seychelles. 12% (Chiolero et al.. 2007) and 6.4% in Minnesota and California (Lo et al.. 2013).

Potential reasons that could explain this variability in blood pressure levels across countries include differences in the procedures used to measure BP in these studies and differences in obesity trends and samples that included children of different ethnicities.

In Macedonia. so far no special studies have been conducted on the prevalence of hypertension in children under the age of 7. using the classification of BP established by the 4th report have been conducted so far. In the research carried out by Stankovska et al. (2021) year of a sample of children from 6 to 10 years. prehypertension was determined in 8.4% and hypertension in 21.3% of Macedonian children. Other studies were conducted in older children (Pireva et al. 2018; Gontarev et al.. 2017).

The relationship between adipose tissue and various components of BP in children has been shown in several studies. Eisenmann et al. found that BMI. WC. skinfold sum and %FM (measured via dual energy X-ray absorptiometry) were moderately and positively correlated with SBP. DBP and MAP (Eisenmann et al.. 2005). as also determined in other studies in which BMI (Aguirre et al.. 2012; Martín. García-Aranda & Almendro. 2005) and triceps skin fold thicknesses (Freedman et al.. 2009) were associated with SBP and DBP.

Our results are partially consistent with other studies. which indicated that. overall. the intensity of association of various indicators of adiposity was similar with SBP and physiological components of BP (MAP. PP) (Drozdz et al.. 2009; Plachta-Danielzik et al.. 2008). supporting that children with greater obesity are more likely to be at risk of hypertension.

Our findings also suggest that children in the higher BMI and %FM categories have higher levels of SBP and DBP in both boys and girls. as found in other studies in the same age group and different ethnicity (Falkner et al.. 2006; Salvadori et al.. 2008; Flores-Huerta et al.. 2009; Almas & Jafar. 2011; LA de Hoog et al.. 2012). However. the results of longitudinal studies are inconsistent because while some authors have concluded that the increase in obesity rates partly explains the rise in high blood pressure (Peters et al.. 2012; Din-Dzietham et al.. 2007). Other authors have determined that the prevalence of elevated blood pressure decreases while the prevalence of obesity increases (Chiolero et al.. 2009; Freedman et al.. 2012). supporting the notion that children with high levels of BMI at such an early age are less likely to become hypertensive or have high blood pressure during adolescence (Din-Dzietham et al.. 2007). Therefore. other factors. such as physical fitness or dietary changes (Aburto et al.. 2013) may be influencing this longitudinal relationship.

A number of studies investigating the relationship between tri-ponderal mass index (TMI) and blood pressure indicate that children classified as underweight are less likely to be hypertensive. Overweight/obese individuals tend to be more hypertensive than those with a normal weight classification. Shim (Shim. 2019; Onagbiye & Toriola. 2022). who evaluated the allocation of tri-ponderal mass index under age and sex. and the association of excessive fatness groups in according to sex- and age-specific tri-ponderal mass index with MetS and its components. found that children in the overweight and obese groups had a higher propensity for increased BP compared with individuals having normal weight. In this study tri-ponderal mass index (TMI) was shown to be a weaker predictor of blood pressure than the body mass index and percentage of fat tissue. Perhaps the tri-ponderal mass index has a greater predictive power in older children.

The mechanisms of the association between obesity and hypertension can be explained by adipose tissue dysfunction characterized by decreased levels of adiponectin. hyperleptinemia. increased infiltration of macrophages. increased level of free fatty acid and elevated resistin levels. leading to activation of the sympathetic nervous system and the renin-angiotensin-aldosterone system. increased systemic inflammation and oxidative stress. and chronic vascular inflammation. leading to hypertension (Dorresteijn et al.. 2012).

However. epidemiological data suggest that BP is an important and common health problem in children. Therefore. it is essential to develop and implement effective public health strategies to prevent and control prehypertension and hypertension. Early identification. control and treatment of risk factors and healthy lifestyles (especially in children and adolescents) can reduce the risk of cardiovascular disease and other chronic non-communicable diseases and can reduce the public health burden in the future. It is also important to focus attention on subjects with established prehypertension or hypertension - at high risk or very high risk of cardio metabolic comorbidities. However. given the recommendations and guidelines used for the evaluation and treatment of HBP in children and adolescents. it may often go undiagnosed. For example. in a large cohort study of a pediatric population. a high frequency of undiagnosed prehypertension and hypertension was found (Hansen et al.. 2007). There is evidence that both prehypertension and hypertension in adolescents and children are significant determinants of cardiovascular target organ damage (Urbina. et. al.. 2011). and these adverse changes are strongly associated with an increased risk of cardiovascular problems in adulthood. A meta-analysis of analyzed studies showed that prehypertension and hypertension were associated with a higher risk of stroke. myocardial infarction. and total cardiovascular outcomes (Guo et al.. 2013).

This study has some limitations that should be mentioned. First. because this was a cross-sectional study. it does not allow us to draw causal conclusions. Second. potential overestimation of the prevalence of high BP due to the determination of BP in a single occasion. compared to other studies that reported two more screenings of BP in those individuals classified as pre-hypertensive and hypertensive (Crispim et al.. 2014; Chandramohan et al.. 2012). According to the Fourth Report. the recommended measurement of BP should be performed by auscultatory method (Fourth Report. 2004). but in this study. BP measurements were obtained using an automatic oscillometric monitor validated for children. Unfortunately. we could not do that in the current study. since the measurements were performed in school conditions in one day. so we chose an automatic oscillometric monitor to avoid inter-observer variability. since it is usually difficult to distinguish between 4th and 5th Korotkoff sound in young children. even for trained nurses. Biochemical parameters. socioeconomic factors. family history and dietary factors were not taken into account in the research. Finally. measurements in school settings may also affect BP values. due to the difficulties that sometimes exist in maintaining a quiet and peaceful environment.

Conclusion

Our data show a high prevalence of prehypertension and hypertension in Macedonian children from 6 years old. These findings are important from a clinical and public health point of view. as they support the idea that early detection of pre-hypertensive and hypertensive status in young children can help prevent cardiovascular disease in adulthood in the Macedonian population. Healthy lifestyle changes and correction of unfavorable lifestyle habits (through increasing physical activity. kinesiology exercises. maintaining an appropriate body weight and healthy eating habits. reducing sodium intake. increasing dietary potassium intake) are essential to prevent HBP.

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