

Research Article

Evaluation of Hypertension, Proteinuria, and Abnormalities of Body Weight in Italian Adolescents Participating in the World Kidney Days

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Keywords

Anthropometric indicators · BMI · Proteinuria · Hypertension · Obesity · Adolescents

Abstract

Introduction: World Kidney Day (WKD) was promoted by the Italian Kidney Foundation and the Italian Society of Nephrology for raising awareness, detection, prevention, and treatment of kidney diseases. The Italian WKD focused on the "School Project" by screening students attending the fifth year of high school. The main goal of the "School Project" was to assess in healthy adolescents the presence of hypertension (HTN) and proteinuria; as well as to evaluate potential interrelations between overweight, obesity (both measured with different anthropometric methods), blood pressure (BP) levels, and proteinuria. The ancillary goal was to have an estimate of awareness on some nephrology topics. **Methods:** The study population consisted of 17- to 19-year-old students. HTN was defined as systolic BP (SBP) ≥ 140 mm Hg and/or diastolic BP (DBP) ≥ 90 mm Hg. Isolated systolic hypertension (ISH) was defined as SBP ≥ 140 mm Hg and DBP < 90 mm Hg; isolated diastolic hypertension as SBP < 140 mm Hg and DBP ≥ 90 mm Hg; systolic and diastolic hypertension as SBP ≥ 140 mm Hg and DBP ≥ 90 mm Hg; pre-hypertension as SBP > 120 mm Hg but < 140 mm Hg or DBP > 80 mm Hg but < 90 mm Hg; and optimal BP as SBP ≤ 120 mm Hg and DBP ≤ 80 mm Hg. Urine tests were performed with a dipstick; the subjects were regarded as proteinuric when the urine dipstick was positive (proteinuria ≥ 30 mg/dL). Body weight, height, and waist circumference (WC) were measured; body mass index (BMI), waist-to-height ratio (WHtR), and conicity index (Ci) were calculated. According to the BMI, the

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following classifications were adopted: underweight ($< 18.5 \text{ kg/m}^2$), normal weight ($18.5\text{--}24.9 \text{ kg/m}^2$), overweight ($25\text{--}29.9 \text{ kg/m}^2$), class-I obesity ($30\text{--}34.9 \text{ kg/m}^2$), class-II obesity ($35\text{--}39.9 \text{ kg/m}^2$), class-III obesity ($\geq 40 \text{ kg/m}^2$). **Results:** Data from 12,125 students (45.6% males) were evaluated. HTN was found in 1,349 participants (11.1%; 61.1% male), and ISH was present in 7.4%. Overweight (24.1%) and class-I (6%), -II (3.6%), and -III (1%) obesity were present in hypertensive participants. Compared to participants with normal BP, hypertensive participants had a higher BMI ($p < 0.001$), WC ($p < 0.001$), and WHtR ($p < 0.001$); whereas the Ci was not different ($p = 0.527$). Multivariate linear regression analysis showed that both WC and BMI were predictors of abnormal SBP and DBP ($p < 0.001$) both in males and females. Proteinuria was present in 14.8, 13.8, 14.7, and 14.7% of all normal weight, overweight, obese, and all subjects, respectively. In addition, no association was found between body weight, proteinuria, and BP. **Conclusion:** This study shows that overweight and obesity were significantly associated to HTN in Italian adolescents. BMI and WC were predictors of SBP and DBP. The occurrence of proteinuria was quite similar to that of HTN, but it was not associated with anthropometric indicators or HTN.

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Introduction

World Kidney Day (WKD) is a global campaign, promoted by the International Federation of Kidney Foundations (IFKF) and the International Society of Nephrology (ISN) aimed at raising awareness, detection, prevention, and treatment of kidney diseases [1]. In Italy, the WKD is planned and conducted by the Fondazione Italiana del Rene (FIR; National Kidney Foundation of Italy), in collaboration with the Italian Society of Nephrology (SIN) and the Red Cross of Italy [2]. The Italian WKD focused on 2 projects: “Square Project” and “School Project” [3]. In the “Square Project,” adults of the general population were screened [4]. The “School Project” was a school-based epidemiological survey including students attending the fifth year of high school. This project is exclusively carried out by Italian nephrologists participating in the WKD.

The relevance of screening healthy adolescents relies on the fact that this population is seldom evaluated by pediatricians or general practitioners unless there is an overt disease. In addition, adolescents have a longer life expectancy than adults; consequently, they are exposed to risk factors for a longer time [5]. Therefore, the early detection of biochemical and clinical abnormalities may prevent or reduce the risk of irreversible diseases that can appear some years later. This is the case for diseases that are characterized by the absence of relevant symptoms such as hypertension (HTN) and proteinuria. High blood pressure (BP) progresses to HTN in adulthood, especially in adolescents with a tendency to have excess weight [6, 7]. The presence of proteinuria is an established early marker of kidney disease and independent risk factor for cardiovascular events.

The main goal of the “School Project” was to assess, in healthy adolescents, the presence of HTN and proteinuria; as well as to evaluate potential interrelations between overweight, obesity (both measured with different anthropometric methods), BP levels, and proteinuria. The ancillary goal was to have an estimate of awareness on kidney function, kidney transplantation, proteinuria, dialysis, and BP.

Materials and Methods

This is a report on data collected from students, attending Italian high schools (range of age: 17–19 years), who participated in the Italian Kidney Day from 2008 to 2016. Written consent was obtained from all participants as well as from the parents for under-age students.

Data on age and gender were recorded. BP was recorded by auscultation, using a sphygmomanometer with appropriate cuff for the arm circumference, after the student had remained seated and at rest for 5 minutes. The measurement was performed on the right arm at heart level. Systolic BP (SBP) was determined at the onset of Korotkoff sounds (phase I), and diastolic BP (DBP) at the disappearance of Korotkoff sounds (phase V). Hypertensive participants (HP) were considered those with SBP ≥ 140 mm Hg and/or DBP ≥ 90 mm Hg.

Isolated systolic hypertension (ISH), isolated diastolic hypertension, systolic and diastolic hypertension, pre-HTN, and optimal BP were defined as SBP ≥ 140 mm Hg and DBP < 90 mm Hg; SBP < 140 mm Hg and DBP ≥ 90 mm Hg; SBP ≥ 140 mm Hg and DBP ≥ 90 mm Hg; SBP > 120 mm Hg but < 140 mm Hg or DBP > 80 mm Hg but < 90 mm Hg; and SBP ≤ 120 mm Hg and DBP ≤ 80 mm Hg, respectively. The heart rate was measured using the palpation method at the wrist (radial artery) and counting the number of beats within 1 minute.

A urine test was performed using a urine dipstick for assessing the presence of proteinuria. Positive reactions were based on color change corresponding to the color chart provided by the test strip's manufacturer. Subjects were considered proteinuric when the urine dipstick was positive for proteinuria ≥ 30 mg/dL.

Body weight and height were measured. The body mass index (BMI) was calculated as weight (kg)/height² (m²). According to the BMI, normal weight was from 18.5 to 24.9 kg/m², underweight < 18.5 kg/m², overweight from 25 to 29.9 kg/m², class-I obesity from 30 to 34.9 kg/m², class-II obesity from 35 to 39.9 kg/m², and class-III obesity ≥ 40 kg/m². Waist circumference (WC) was measured with an anthropometric fiberglass tape at the midpoint between the last rib and the iliac crest. Normal WC was considered < 88 cm in females and < 102 cm in males. The waist-to-height ratio (WHtR) was calculated by dividing WC (cm) by height (cm). The conicity index (Ci) was determined using the following mathematical equation [8]:

$$Ci = \frac{\text{waist circumference (m)}}{\sqrt{\frac{\text{body weight (kg)}}{\text{height (m)}}}}$$

Coffee consumption and current tobacco smoking were self-reported as the number of cups and cigarette consumed daily, respectively.

Questions asked concerned the following topics: awareness of kidney function, kidney disease, dialysis, kidney transplantation, meaning of the word proteinuria, relevance of measuring BP, and the information source.

Statistical analysis was performed using the SPSS-22 package. Descriptive statistics included frequencies and percentages or means with standard deviation errors (SD) for demographic, health characteristics, and urinalysis results. Analysis of variance or χ^2 tests were used to assess differences in baseline characteristics. Linear regression was used to evaluate the association of BMI categories, Ci, WC, and WHtR with proteinuria and BP after adjusting for potential confounders, respectively.

Results

From 2008 to 2016, 12,125 participants (45.6% males) took part in the "School Project" of the WKDs. Pertinent data were evaluated both in aggregate and divided either on the basis of sex or on 4 areas of Italy – i.e., Northern, Central, Southern, and Islands. Some participant characteristics, level of BP, and anthropometrics are reported in Table 1. HTN was found in 1,349 (11.1%) participants (61.1% males), more specifically ISH in 7.4%, isolated diastolic hypertension in 1.6%, and systolic and diastolic hypertension in 2.1% of all

Table 1. Participant characteristics

	Total (n = 12,125)	Optimal BP (n = 9,055)	Pre-HTN (n = 1,721)	ISH (n = 903)	IDH (n = 182)	SDH (n = 264)	p value
Men, %	45.6	39.2	59	76.4	46.8	60.2	<0.001
Age, years	18.5 (18.4–18.5)	18.4 (18.4–18.5)	18.5 (18.4–18.6)	18.5 (18.4–18.6)	18.8 (18.5–19.1)	18.8 (18.6–19)	<0.001
BMI, kg/m ²	22.4 (22.3–22.5)	22 (21.9–22.1)	23.1 (22.91–23.3)	24 (23.7–24.3)	22.7 (21.9–23.5)	25.7 (24.8–26.5)	<0.001
Current smokers, %	26.9	27.7	27	22.7	30.6	17.4	0.005
SBP, mm Hg	117.3 (117–117.7)	111 (110.7–111.2)	130.4 (130.2–130.7)	145.4 (144.7–146.1)	125.9 (124.4–127.4)	148.1 (146.3–149.9)	<0.001
DBP, mm Hg	70.2 (70–70.4)	67.8 (67.6–68.0)	74.2 (73.7–74.7)	75.3 (74.7–76)	91.6 (90.9–92.2)	92.9 (92–93.8)	<0.001
Region of origin, %							<0.001
North	16	74.2	13.5	8.8	1.7	1.7	
Center	12.4	65.5	19.9	10.5	2.3	1.8	
South	63.3	79.9	11.7	5.5	1.2	1.7	
Isles	8.2	78.6	15.1	5.1	0.3	0.8	
Pulse pressure, mm Hg	47.1 (46.8–47.4)	43.1 (42.9–43.4)	56.3 (55.7–56.8)	70.1 (69.2–70.9)	34.3 (32.8–35.8)	55.1 (53.6–56.7)	<0.001
Heart rate, beats/min	74.7 (74.4–74.9)	73.7 (73.4–73.9)	76.5 (75.7–77.3)	78.9 (77.8–80.0)	77.8 (74.9–80.6)	80.9 (78.6–83.2)	<0.001
Waist circumference, cm	82.3 (82–82.5)	81.2 (80.9–81.5)	84.3 (83.5–85.1)	87.8 (86.6–88.9)	83.9 (81.1–86.6)	91.7 (89.0–94.4)	<0.001
Men	85.1	83.7	86.6	88.9	86.5	93.6	
Women	80.1	79.7	81.1	84.5	81.6	88.9	
WHR	0.4 (0.4–0.5)	0.4 (0.4–0.5)	0.4 (0.4–0.5)	0.5 (0.4–0.6)	0.5 (0.4–0.6)	0.5 (0.4–0.6)	<0.001
Conicity index	1.2 (1.1–1.3)	1.2 (1.1–1.3)	1.2 (1.1–1.3)	1.2 (1.1–1.3)	1.2 (1.1–1.3)	1.2 (1.1–1.3)	ns
Normal weight, %	72.9	75.1	68.7	65.3	66	55	<0.001
Underweight, %	8.4	9.7	5.8	2.4	8.3	1.9	<0.001
Overweight, %	15.6	13.1	21.5	24.6	22.9	25	<0.001
Obesity class I, %	2.4	1.8	2.9	5.7	1.8	10.6	<0.001
Obesity class II, %	0.6	0.3	0.9	1.8	0	5.6	<0.001
Obesity class III, %	0.1	0	0.2	0.2	0.9	1.9	<0.001
Proteinuria, %	14.7	14.5	14.4	14.8	14.7	14.9	ns

Data are reported as mean (95% confidence interval) unless indicated otherwise. The p values were obtained by analysis of variance or χ^2 tests among hypertension subtypes. BP, blood pressure; DBP, diastolic blood pressure; IDH, isolated diastolic hypertension; ISH, isolated systolic hypertension; pre-HTN, pre-hypertension; SBP, systolic blood pressure; SDH, systolic and diastolic hypertension; WHtR, waist-to-height ratio.

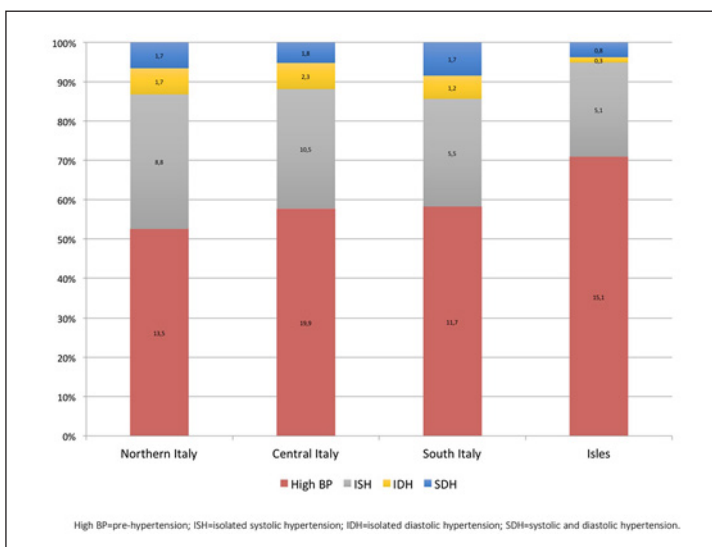


Fig. 1. Blood pressure divided on the basis of 4 areas of Italy – i.e., Northern, Central, Southern, and Isles.

students. No differences in BP were found among the 4 areas of Italy (Fig. 1). Overweight, class-I, -II, and -III obesity in HP were found in 24.1, 6, 3.6, and 1%, respectively. Compared to participants with normal levels of BP, HP had higher BMI ($p < 0.001$), WC ($p < 0.001$), and WHtR ($p < 0.001$); whereas Ci was not different ($p = 0.527$). Multivariate linear regression analysis showed that WC was a predictor of SBP, DBP, high heart rate ($p < 0.001$) in males and females (Fig. 2–4), while BMI was a predictor of SBP and DBP in the whole cohort (fig. 5). 74.2 and 62.2% of all students had undergone urinalysis and had a measurement of their BP before the WKDs as part of their routine examination planned by their clinicians, respectively.

Urine dipstick was not performed in 10% of the cohort because of either refusal or concomitant menstruation. At urine dipstick, proteinuria was present in 14.7% of the entire cohort compared to 14.8, 13.8, and 14.7% in the normal weight, overweight, and obese subjects, respectively. In multivariate linear regression analysis, no association was found between proteinuria, anthropometric indicators, and BP levels.

Most students were conscious of the role and function of the kidneys (89%), of the meaning of chronic kidney disease (70%), dialysis (65.3%), and transplantation (75.2%); few students were aware of the meaning of the word proteinuria (6.6%). Almost all students were conscious of the importance of HTN control. Information sources were the parents (31%) and teachers (38%) but not general practitioners (6.9%), media (4.9%), and the internet (2.2%).

The mean number of coffees per day was 1.82 ± 1.04 , and males were heavier smokers (8.17 ± 4.8 cigarettes per day) than females (6.4 ± 4.3). No differences in clinical characteristics and habits were found among the 4 areas of Italy.

Discussion

The data of this study are of some clinical interest. Abnormal SBP and/or DBP levels were found in 11.1% of the screened population; more than half of all HP (61.1%) were male. The percentage of HTN, observed during the “School Project,” is similar to that reported by others (10.2%) in first school students [9]. An interesting finding in the present study is the percentage of students with ISH (66.9% of all HP with a high prevalence in males). ISH seems to be frequent in adolescents and young adults [9, 10]. The clinical significance of ISH in adoles-

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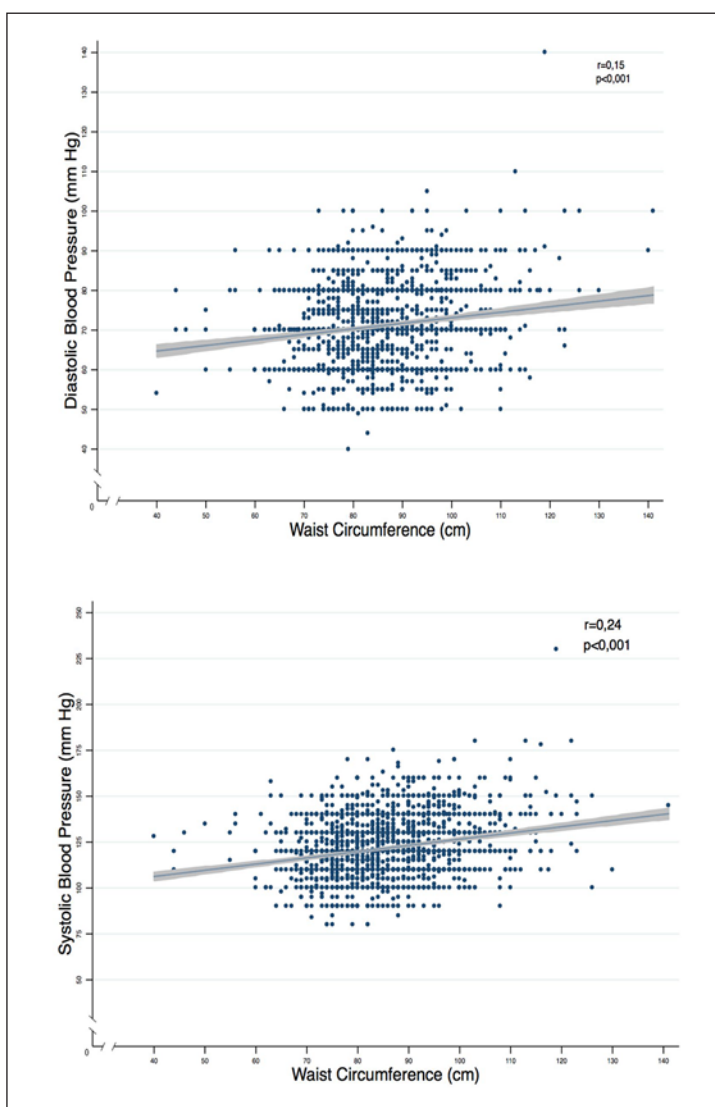


Fig. 2. Multivariate linear regression analysis: DBP/SBP and waist circumference in men.

cents and young adults is still debated [11]; however, ISH is associated with a higher risk of cardiovascular disease and coronary heart mortality [12].

Although almost all participants of the “School Project” were aware of the importance of measuring BP, only slightly more than half (62.2%) had had their BP measured occasionally. This finding is in agreement with the data reported by da Silva et al. [13] in a smaller survey in which only 28.6% of the 1,215 Brazilian students had had their BP measured but not during a medical consultation. These data indicate that BP measurement is not a procedure incorporated into the clinical practice despite guidelines suggesting that BP should be measured at least annually in health adolescents and more frequently in those who have risk factors such as abnormal body weight or proteinuria [6]. The most likely explanation for this inertia is that adolescents, as it is the case with adults, do not have their BP measured unless they become symptomatic [14]. Early detection and normalization of abnormal BP levels in adolescents may prevent the occurrence of subsequent stable HTN, especially among subjects with unknown proteinuria or with a tendency to add excess weight [11, 14, 15].

Overweight and obesity were present in 15.6 and 3.1% of all students, respectively. These results are consistent with the percentages of overweight (15.6%) and obesity (2.3%)

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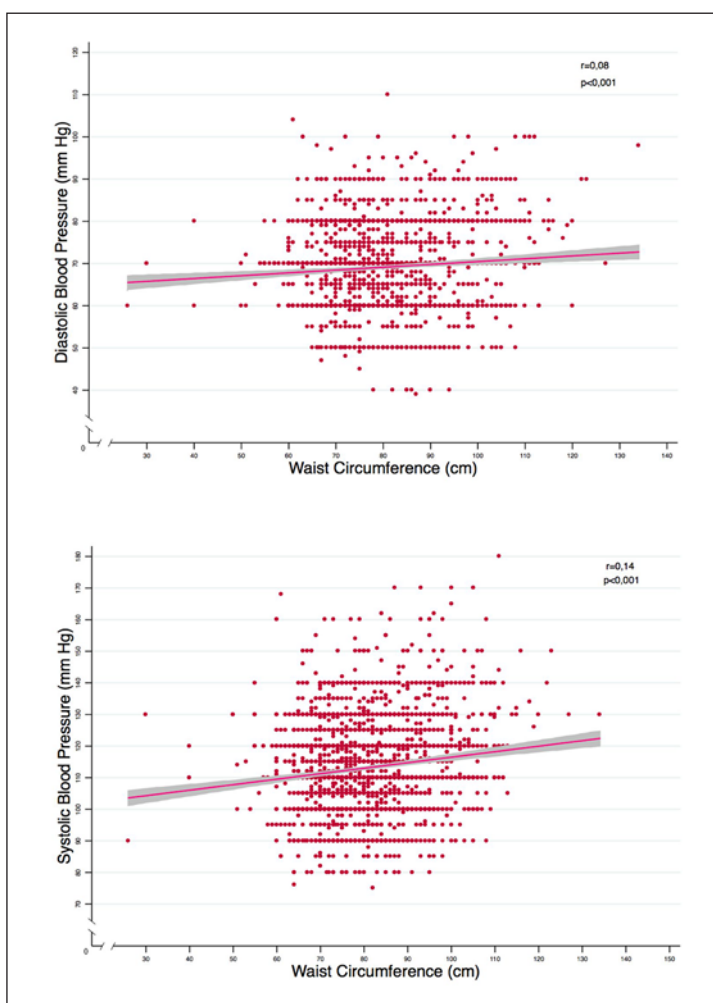


Fig. 3. Multivariate linear regression analysis: SBP/DBP and waist circumference in women.

observed in Italian adolescents in general [16]. The association between BP and abnormal body weight is well established even in young subjects. Obesity has been identified as an important risk factor for the development of cardiovascular diseases. Indeed, overweight adolescents have a high likelihood of remaining overweight or developing obesity and HTN as adults [17]. In these cases, an appropriate healthy lifestyle, attentive search for causes of proteinuria, proper medications, and regular follow-up may normalize BP and/or prevent overt renal disease with a consequent reduction of kidney function.

According to urine dipstick, proteinuria was present in 14.7% of our students, and the percentage was similar in normal weight (14.8%), overweight (13.8%), and obese subjects (14.7%). In addition, no association was found between alterations of body weight, proteinuria, and BP. There are conflicting results about the association between alterations of body weight and proteinuria. Rutkowski et al. [18] found albuminuria in 16% of Polish adolescents; the occurrence of albuminuria was more frequent in those with normal weight but not associated with any of the cardio-metabolic risk factors taken into account. The National Health and Nutrition Examination Survey (NHANES) [19], a population-based study including 2,515 adolescents, reported a lower prevalence of albuminuria (0.3%) in overweight adolescents compared to non-overweight ones (8.7%). A proposed possible explanation for this finding is that normal-weight subjects more likely do exercise 24 h prior to urine collection, leading to physiological microalbuminuria [20]. Despite the conflicting

Fig. 4. Multivariate linear regression analysis: heart rate and waist circumference in women (red) and men (blue).

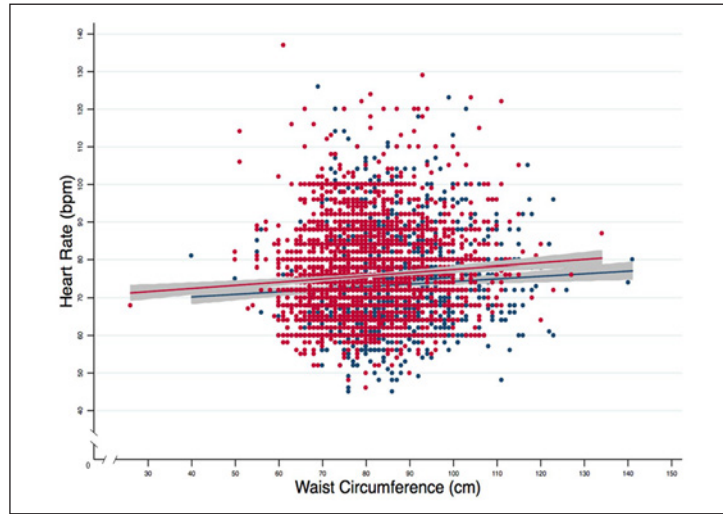
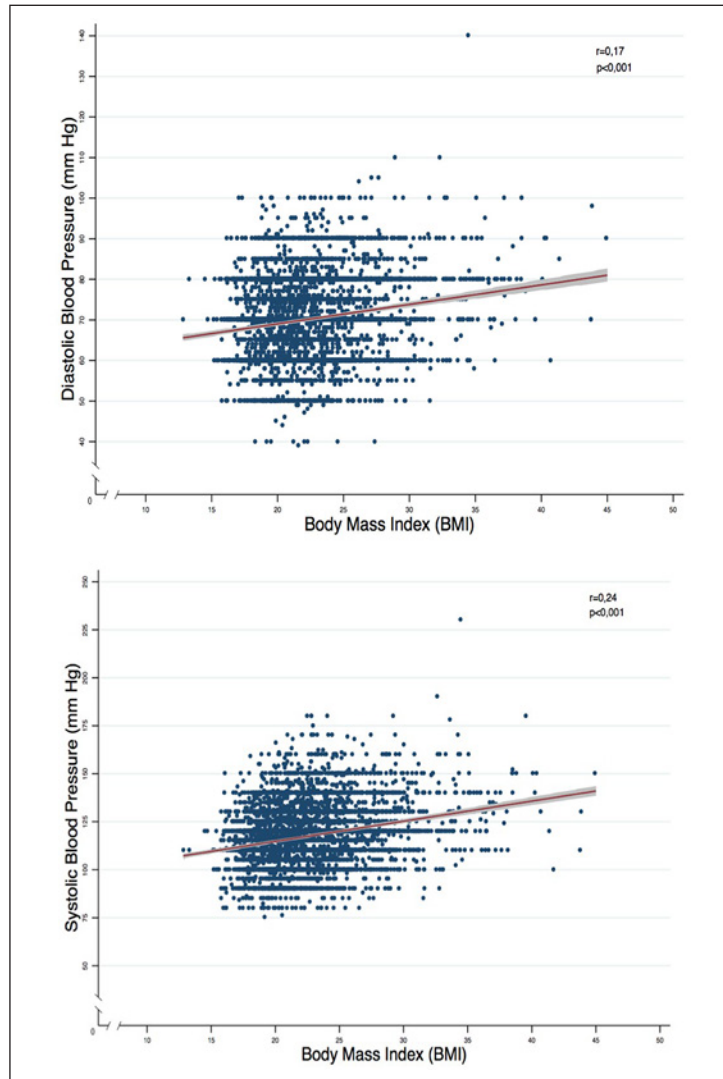


Fig. 5. Multivariate linear regression analysis: SBP/DBP and BMI in the whole cohort.



results, obesity in adolescents has been associated with albuminuria, insulin resistance, HTN, and dyslipidemia which are all factors contributing to an elevated risk for future cardiovascular events [21, 22].

The pathophysiological mechanisms underlying the potential association between proteinuria and obesity are not fully understood. Insulin likely interferes at several points in the renin-angiotensin-aldosterone system, increasing its activity despite a state of sodium retention and volume expansion. Reduced insulin sensitivity (leading to higher plasma insulin levels) may lead to vascular damage and renal injury [23]. Therefore, prolonged obesity-dependent insulin resistance from adolescence predisposes to either cardiovascular events and impairment of renal function in adulthood.

In clinical practice, abnormalities in body weight are commonly reported as values of BMI. For the assessment of the amount of body fat and its distribution, the gold standard is computed tomography or magnetic resonance, but high costs of these methods limit their feasibility in clinical practice [24]. The propensity of many authors is to take into account anthropometric indicators other than the BMI, especially in assessing an association with levels of BP, prevalence of HTN and ISH, cardiovascular risk, metabolic syndrome, and chronic kidney disease [25–28]. Controversial opinions exist about the optimal anthropometric indicator to discriminate the amount of body fat and its distribution, and to assess the relationship between BP and distribution of body fat [28, 29]. There is evidence suggesting that it is more important to measure abdominal obesity than general obesity for the evaluation of health risks in the first decades of life.

The BMI predicts the overall fat but tends to overestimate the amount of body fat in subjects with high muscle mass; WC and Ci identify the fat located in the central region of the body; the Ci is more widely used in research with adult populations; the WHtR considers the proportion of central fat to the individual's height [30, 31]. In this study, WC and BMI but not Ci were reliable predictors of SBP and DBP suggesting that not only weight and height should be recorded in young people during medical consultation.

There are several limitations to our study. A single urine specimen may be subject to random variation and transient proteinuria from prolonged standing or exercise [32]; however, single-measure proteinuria does reflect a chronic condition in 63% of the general population [33]. Urine was collected at any time during the day, whereas first-morning midstream urine may be preferred for proteinuria assessment and urinalysis [34]. Proteinuria was detected by urine dipstick, while the urine albumin-to-creatinine ratio is commonly considered more appropriate in assessing levels of proteinuria. However, urine dipstick is a simple and less expensive diagnostic tool in public health screenings (as is the case with the “School Project”) compared to the more expensive albumin-to-creatinine ratio [35, 36]. HTN has been diagnosed on the basis of a single measurement of BP, instead of an average of 2 readings on 2 occasions that may better establish the levels of BP [6]. However, this procedure was impossible to apply considering the study-design of the “School Project” lasting half a day.

Conclusion

Overweight and obesity, evaluated through different anthropometric indicators, were present in a significant percentage of HP. BMI and WC were significant anthropometric predictors of SBP and DBP. Proteinuria was found in a percentage similar to HTN, but it was not associated with any anthropometric indicators.

Statement of Ethics

The research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. Written consent was obtained from all participants as well as from the parents for under-age students.

Disclosure Statement

The authors declare that they have no conflicts of interest.

Funding Sources

None.

Author Contributions

Y.B. and P.E. contributed to the conception and design of the study and drafting of the manuscript.

S.C., A.S., and L.R. contributed to the analysis and interpretation of data.

D.R. and A.B. have been involved in revising the manuscript critically for important intellectual content.

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