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Original Article

Increased waist circumference is associated with subclinical atherosclerosis in schoolchildren

Hayder Al-Domi, Alaa Al-Shorman*

Department of Nutrition and Food Science, School of Agriculture, The University of Jordan, Amman, 11942, Jordan

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ABSTRACT

Background: Waist circumference (WC) is an indicator of adiposity; particularly visceral fat, cardiometabolic risk factors and related morbidity. The aim of this study was to determine the attribution of WC to increased carotid intima-media thickness (cIMT) and circulating levels of inflammation and endothelial dysfunction in schoolchildren.

Methods: A total of 122 children (61 boys and 61 girls) aged 10–15 years were distributed into three groups: (i) the lower smoothed sex- and age-specific WC (LWC) group (ii) the middle smoothed sex- and age-specific WC (MWC) group, and (iii) the higher smoothed sex- and age-specific WC (HWC) group. Measurements of cIMT using high-resolution B-mode ultrasound, lipemic profile, blood pressure, serum proinflammatory cytokines and soluble adhesion molecules were performed.

Results: Mean measured values in the HWC and/or MWC groups showed significantly higher values ($p \leq 0.05$) of cIMT (mm), total cholesterol, triglycerides, low-density lipoprotein (LDL), blood pressure, interlukien-6 (IL-6), and interlukien-1 beta (IL-1β), vascular cell adhesion molecule-1 (VCAM-1), intercellular adhesion molecule-1(ICAM-1) and E-selectin, and significantly lower values of high-density lipoprotein (HDL) as compared to the LWC group. Using multiple linear regression analysis of WC-SDS adjusted for BMI-SDS with the studied subclinical atherosclerosis risk, WC-SDS was significantly ($p \leq 0.05$) associated with the variation in HDL ($R^2 = -0.12$), LDL ($R^2 = 0.36$), IL-6 ($R^2 = 0.26$), and VCAM-1 ($R^2 = 0.26$).

Conclusions: Higher WC is positively associated with atherosclerosis risk factors including increased cIMT, a state of dyslipidemia, higher blood pressure and circulating levels of inflammation and adhesion molecules among schoolchildren. Waist circumference seems to be useful for the prediction of subclinical atherosclerosis in schoolchildren.

1. Introduction

Cardiovascular diseases (CVD) are the leading cause of death and disability-adjusted life years (DALY) lost worldwide [1]. Both CVD and cardiometabolic disorders (CMD) are expected to impose a more critical public health burden since the prevalence of obesity is increasing steadily worldwide, provided that obesity is considered the most serious cardiometabolic risk factor [2,3]. The prevalence of obesity among children and adolescents has reached pandemic proportions in developed and developing countries alike [3]. Estimates revealed that 23.8% of boys and 22.6% of girls in developed countries were overweight or obese in 2013, compared to 12.9% of boys and 13.4% of girls in developing countries [3]. Childhood obesity is considered an important predictor for adulthood obesity; overweight and obese children and adolescents are more likely to become overweight and obese adults [4].

Increased intima-media thickness of the common carotid artery (cIMT) is an indicator of preclinical atherosclerosis, which could start during childhood and progress through life [5]. Modifiable risk factors for CVD in adults are observed in children [6]. Childhood obesity is strongly involved in the clustering of cardiovascular risk factors and associated with increased mortality rate from CVD during adulthood [6].

Evidence indicated that inflammatory mechanisms are highly associated with the development and the progression of atherosclerosis and other chronic non-communicable diseases [8]. Obesity is a state of systemic low grade inflammation [7]:

* Corresponding author.
E-mail addresses: h.aldomi@ju.edu.jo (H. Al-Domi), alaa.a.shorman@hotmail.com (A. Al-Shorman).

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interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and interleukin-1β (IL-1β) are biomarkers of inflammation, which are strongly implicated in the pathogenesis of atherosclerosis and other CVD [8–10]. Circulating levels of adhesion molecules such as E-selectin, vascular cell adhesion molecule-1 (VCAM-1), and intercellular adhesion molecule-1 (ICAM-1) are molecular markers for endothelial dysfunction [11], which have been linked to obesity and suggested to play a major role in atherogenicity [12,13].

The pattern of body fat distribution is more important than total fat mass in the determination of obesity-associated morbidities [14]. Fat mass accumulation in the abdominal area increases the risk of metabolic complications such as atherogenic dyslipidemia and diabetes mellitus [14]. Waist circumference (WC) has been reported as a marker of adiposity-related morbidity [15], provided that WC is becoming more popular since it is considered an indicator of visceral fat and cardiometabolic risk factors [16]. Recent studies reported that WC is more sensitive than other anthropometric measurements in predicting obesity-related atherogenicity in children [17,18].

The identification of obesity risk factors at early age could help to prevent obesity-related diseases or at least ameliorating their prevalence. Additionally, the association of WC with atherogenicity and inflammatory state among healthy schoolchildren has not been thoroughly investigated yet, no data are available about Jordanian or Middle Eastern schoolchildren. Hence, the objectives of this study were to examine the association between WC and cIMT, inflammation, endothelial dysfunction, dyslipedimia and blood pressure; and to examine the attribution of increased WC in subclinical atherosclerosis in three WC percentiles among a group of schoolchildren.

2. Methods

2.1. Study population

The recruitment of this study was carried out between March 2016 and June 2016. A total of 146 normal bodyweight and obese schoolchildren (10–15 years) were recruited from four public schools which enroll pupils from the 5th to the 9th grades. These schools were selected from a list of 20 public schools in four districts of Amman, as provided by the Jordanian Ministry of Education. Eighteen pupils were excluded because they did not meet the inclusion criteria; 6 pupils were excluded because their parents withdrew from the agreement. We collected the data from a total of 122 participants who were included in the study: 61 boys (32 obese and 29 normal bodyweight), and 61 girls (30 obese and 31 normal bodyweight).

Inclusion criteria was for apparently healthy of normal bodyweight or obese schoolchildren according to the World Health Organization (WHO) BMI-z score adjusted for age and gender criteria [19]. Exclusion criteria were as follows: schoolchildren with chronic diseases other than the state of obesity (e.g. renal, cardiac or hepatic diseases), schoolchildren with reported chronic use of medications, or schoolchildren with a history of first-hand smoking. Parents of the participating students gave written consent before inclusion and were given brief guidance to explain the objective and the procedures of the study to their children. Verbal assent was obtained from children after explaining the study objective and procedures upon the examination.

Weight, height, WC, hip circumference (HC), systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured using standard procedure [20]. Body mass index (BMI) and waist-to-hip ratio (WHR) were calculated. Bodyweight status was classified according to the World Health Organization (WHO) BMI-z score adjusted for age and gender [19].

The study population was divided into three groups according to WC percentiles reported by the National Health and Nutrition Examination Survey (NHANES) for children and adults [21] as follows: (i) the lower smoothed sex- and age-specific waist circumference (LWC) group for schoolchildren who reported ≤50th percentile; (ii) the middle smoothed sex- and age-specific waist circumference (MWC) group for schoolchildren who reported >50th percentile and >85th percentile; and (iii) the higher smoothed sex- and age-specific waist circumference (HWC) group for schoolchildren who reported ≥ 85th percentiles.

The protocol of the present study was approved by the Deanship of Academic Research at the University of Jordan, The Jordanian Ministry of Education and Abdul Hameed Shoman Foundation Research Committee, Jordan.

2.2. Body composition analysis

Body composition measurements of fat mass (FM), fat mass percentage (FM%), fat free mass (FFM), dry FFM, water volume and basal metabolic rate (BMR) were estimated using bioelectrical impedance (BIA) (Bodystat®1500, body stat, Ltd., UK). Students were asked to fast overnight except for water, refrain from exercise for at least 12 h before the test and to urinate within 30 min before starting the examination. At the time of the test, participants were placed in supine position, with legs and arms abducted around 45°. Two sets of electrodes were attached to the dorsal surface of the wrist and the dorsal surface of the ankle on the right side of the body.

2.3. Carotid intima-media thickness measurement

Intima-media thickness of the common carotid artery was measured using B-mode ultrasound with a linear probe at 7.5 MHz frequency. Measurements were performed by a single-blinded sonographer at the King Hussein Medical City, Jordan. Images of the right common carotid artery were taken as longitudinal ultrasonographic scan as single measurement session for each participant, 1 cm below the carotid bulb while participants lay in supine position, head turned 45–50° rotation of the neck to the contralateral side; images were taken at the lateral angle. Mean cIMT values were taken for the far wall, while participants were in the supine position for at least 5 min before starting the examination [22]. The intra-observer reliability, analyzed with coefficient of variation (CV) in 20 participants, was 5.3%.

2.4. Biochemical analysis

In a follow-up visit, blood samples were drawn after 10–12 h overnight fasting and serum aliquots were stored at −20 °C until analyzed. Total cholesterol (TC), high density lipoprotein cholesterol (HDL), low density lipoprotein cholesterol (LDL) and triglycerides (TG) concentrations were determined by a colorimetric direct method. The reproducibility of the intra- and inter-assay CV were <9% and <13%, respectively, for all lipid profile measurements. IL-6, TNF-α, IL-1β, sVCAM-1, sICAM-1 and E-selectin levels were measured by high-sensitivity sandwich enzyme-linked immunosorbent assay (ELISA) kits, using plate reader (ELX808, BioTek Instruments, Winooski, USA) at 450 nm. The reproducibility of the intra- and inter-assay CV were <10% and <14%, respectively, for all ELISA measurements.

2.5. Statistical analysis

Statistical analysis was performed using SPSS software (SPSS Inc. Released 2008. SPSS Statistics for Windows, Version 17.0. Chicago:

Table 1
Anthropometrics, clinical and body composition characteristics of study groups according to waist circumference percentile.

	LWC n = 54	MWC n = 42	HWC n = 26	*p* value[†]
Females, n (%)	31 (57%)	20 (48%)	10 (38%)	
Obese participants, n (%)	8 (14.8%)	28 (66.7%)	26 (100%)	
Age, years	12.96 ± 1.15[a]	12.74 ± 1.36[a]	13.00 ± 1.06[a]	0.6
Weight, kg	42.11 ± 11.52[a]	62.43 ± 10.98[b]	80.18 ± 16.34[c]	0.001
Height, m	1.50 ± 0.11[a]	1.59 ± 0.092[b]	1.61 ± 0.09[c]	0.001
BMI, kg/m^2	18.48 ± 3.24[a]	24.51 ± 3.27[b]	30.78 ± 4.16[c]	0.001
BMI-SDS	0.11 ± 0.85[a]	2.29 ± 1.27[b]	4.68 ± 1.49[c]	0.001
WC, cm	63.42 ± 7.21[a]	79.64 ± 6.25[b]	99.11 ± 9.80[c]	0.001
WC-SDS	−0.78 ± 0.28[a]	0.21 ± 0.39[b]	1.41 ± 0.55[c]	0.001
HC, cm	82.02 ± 9.75[a]	95.51 ± 10.05[b]	107.60 ± 8.66[c]	0.001
WHR	0.78 ± 0.06[a]	0.84 ± 0.11[b]	0.92 ± 0.08[c]	0.001
SPB, mm Hg	111.24 ± 12.93[a]	120.56 ± 12.88[b]	124.71 ± 12.65[b]	0.001
DBP, mm Hg	64.88 ± 11.69[a]	68.45 ± 10.16[a,b]	74.64 ± 9.49[b]	0.004
Fat, %	19.65 ± 7.03a	27.57 ± 7.01b	33.35 ± 5.16c	0.001
FM, kg	8.42 ± 4.95[a]	17.29 ± 5.77[b]	26.92 ± 7.60[c]	0.001
FFM, kg	31.62 ± 6.98[a]	44.59 ± 10.01[b]	53.58 ± 10.39[c]	0.001
Dry FFM, kg	7.82 ± 1.70[a]	11.23 ± 2.63[b]	13.49 ± 3.02[c]	0.001
Water, L	24.62 ± 4.61[a]	33.83 ± 6.50[b]	39.96 ± 8.03[c]	0.001
BMR, kcal/day	1272.96 ± 139.86[a]	1645.58 ± 218.09[b]	2020.40 ± 314.67[c]	0.001
cIMT, mm	0.38 ± 0.09[a]	0.42 ± 0.10[a,b]	0.47 ± 0.08[b]	0.013

Data are means ± SD or number (%).
[†]P value is significant for values equal or less than 0.05, which represents the difference between the three groups. Different superscript letters within the same raw (a,b,c) indicate statically significant differences ($P \leq 0.05$).
LWC, lower smoothed sex- and age-specific waist circumference group; MWC, middle smoothed sex- and age-specific waist circumference group; HWC, higher smoothed sex- and age-specific waist circumference group; BMI, body mass index; BMI-SDS, body mass index-standard deviation score; WC, waist circumference; WC, waist circumference -standard deviation score; HC, hip circumference; WHR, waist-to-hip ratio; SPB, systolic blood pressure; DPB, diastolic blood pressure; FM, fat mass; FFM, fat-free mass; BMR, basal metabolic rate; cIMT, carotid intima-media thickness.

SPSS Inc.). Data is expressed as mean ± standard deviation. Correlation analysis was performed using crude partial Spearman correlation analysis, adjusted for age and sex. Multiple linear regression analysis were performed using WC-SDS as dependent variable, adjusted for BMI-SDS and cIMT, SBP, DBP,TC, TG, LDL, HDL,IL-6, TNF-α, IL-1β, VCAM-1, ICAM-1 and E-selectin as the independent variables. Mean difference of continuous variables were examined using one way ANOVA. Comparisons of means were performed by post hoc Tukey HSD (honest significant difference) test, P value less than or equal 0.05 was considered statistically significant.

3. Results

Table (1) presents general, anthropometric, clinical and body composition characteristics of the participating schoolchildren. Weight, height, BMI, HC, WHR, SPB, DBP, FM, FM%, FFM, dry FFM, water volume, BMR and cIMT were significantly higher ($p \leq 0.05$) in HWC group as compared to MWC and LWC groups. No significant difference ($p = 0.6$) was found in age between the three groups.

Table (2) shows that there were significant differences ($p \leq 0.05$) between the three WC groups observed in the mean values of TC, TG, HDL, LDL, IL-6 and E-selectin. Using the Tukey HSD Post-hoc Test, significantly higher ($p \leq 0.05$) mean values of TC, TG, LDL and IL-6 were observed in MWC and HWC groups than in the LWC group. Also, there were significantly higher values ($p \leq 0.05$) of IL-1β and VCAM-1 in the HWC in comparison to the LWC groups. Mean serum levels of ICAM-1 and E-selectin were significantly higher ($p \leq 0.05$) among the MWC group compared to the LWC group. Furthermore, significantly lower mean values ($p \leq 0.05$) of HDL were observed in the LWC group compared to the MWC and HWC groups. However, no significant differences ($p > 0.05$) were observed in TNF-α between all groups.

Table (3) displays the relationship between WC and selected cardiovascular risk factors in the study population, using crude and adjusted for age and sex partial Spearman's correlation. Waist

Table 2
Biochemical markers of the study population.

	LWC n = 54	MWC n = 42	HWC n = 26	*p* value[†]
TC, mg/dL	124.63 ± 40.35[a]	153.81 ± 24.93[b]	170.41 ± 14.36[b]	0.001
TG, mg/dL	111.15 ± 30.58[a]	139.43 ± 34.23[b]	132.77 ± 41.36[b]	0.002
HDL, mg/dL	54.65 ± 17.01[b]	46.63 ± 7.98[a]	45.21 ± 6.69[a]	0.02
LDL, mg/dL	78.10 ± 15.52[a]	76.94 ± 8.82[a]	90.84 ± 13.45[b]	0.02
IL-6 pg/ml	1.39 ± 0.39[a]	2.29 ± 0.95[b]	2.10 ± 0.94[b]	0.002
TNF-α pg/ml	3.07 ± 0.99[a]	3.30 ± 1.194[a]	3.27 ± 1.01[a]	0.77
IL-1 β pg/ml	2.54 ± 1.75[a]	3.23 ± 2.15[a,b]	3.93 ± 1.58[b]	0.21
VCAM-1 ng/ml	230.94 ± 44.48[a]	239.54 ± 65.63[a,b]	280.18 ± 81.92[b]	0.14
ICAM-1 ng/ml	153.45 ± 29.81[a]	171.87 ± 33.61[b]	167.37 ± 38.06[a,b]	0.17
E-selectin ng/ml	25.10 ± 8.72[a]	35.47 ± 12.78[b]	30.38 ± 11.79[a,b]	0.05

Data are means ± SD.
[†]P value is significant for values equal or less than 0.05, which represents the difference between the three groups. Different superscript letters within the same raw (a,b,c) indicate statically significant differences ($P \leq 0.05$).
LWC, lower smoothed sex- and age-specific waist circumference group; MWC, middle smoothed sex- and age-specific waist circumference group; HWC, higher smoothed sex- and age-specific waist circumference group; TC, total cholesterol; TG, triglyceride; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; IL-6, Interleukin 6; TNF-α, Tumor necrosis factor −alpha; IL-1β, Interleukin-1 beta; VCAM-1, vascular cell adhesion molecule −1; ICAM-1; intercellular adhesion molecule −1.

Table 3
Crude and adjusted for age and sex partial spearman correlation analysis between waist circumference and selected cardiovascular risk factors.

	Not adjusted WC[a]		Adjusted WC[b]	
	r_s	*P*	r_s	*P*
cIMT	0.417	0.001	0.440	0.001
SBP	0.538	0.001	0.380	0.001
DBP	0.483	0.001	0.504	0.001
TC	0.446	0.001	0.398	0.001
TG	0.281	0.005	0.344	0.001
HDL	−0.266	0.02	−0.299	0.006
LDL	0.442	0.006	0.440	0.004
IL-6	0.377	0.002	0.191	0.07
TNF-α	0.064	0.63	0.126	0.17
IL-1β	0.343	0.01	0.259	0.04
VCAM-1	0.191	0.2	0.309	0.01
ICAM-1	0.269	0.05	0.302	0.02
E-selectin	0.436	0.005	0.356	0.01

$p \leq 0.05$ is considered statistically significant.
cIMT, carotid intima-media thickness; SPB, systolic blood pressure; DPB, diastolic blood pressure; TC, total cholesterol; TG, triglyceride; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; IL-6, Interleukin 6; TNF-α, Tumor necrosis factor −alpha; IL-1β, Interleukin-1 beta; VCAM-1, vascular cell adhesion molecule −1; ICAM-1; intercellular adhesion molecule −1.
[a] Partial Spearman correlation coefficient.
[b] Partial spearman correlation coefficient adjusted for age and sex.

circumference showed significant positive correlation with cIMT ($r = 0.538$, $p = 0.001$), SPB ($r = 0.538$, $p = 0.001$), DBP($r = 0.483$, $p = 0.001$), TC ($r = 0.446$, $p = 0.001$), TG ($r = 0.281$, $p = 0.005$), LDL ($r = 0.442$, $p = 0.006$), IL-6 ($r = 0.377$, $p = 0.002$), IL-1β ($r = 0.343$, $p = 0.01$), ICAM-1 ($r = 0.269$, $p = 0.050$) and E-selectin ($r = 0.436$, $p = 0.005$). It also showed significant negative correlation with HDL ($r = -0.266$, $p = 0.02$) using crude partial Spearman's correlation. Furthermore, after adjusting for age and sex, there were significant positive correlations between WC with cIMT($r = 0.44$, $p = 0.001$), SBP ($r = 0.380$, $p = 0.001$), DPB ($r = 0.50$, $p = 0.001$), TC ($r = 0.398$, $p = 0.001$), TG ($r = 0.344$, $p = 0.001$), LDL (0.44, $p = 0.004$), IL-1β ($r = 0.259$, $p = 0.04$), ICAM-1 ($r = 0.302$, $p = 0.02$), and E-selectin ($r = 0.356$, $p = 0.02$), whereas there was significant negative correlation with HDL ($r = -0.299$, $p = 0.006$).

Table (4) shows the multiple linear analysis using WC-SDS as the dependent variable adjusted for BMI-SDS, and cIMT, SBP, DBP,TC,TG, HDL, LDL, IL-6, TNF-α, IL-1β, VCAM-1, ICAM-1, and E-selectin as the independent variables. WC-SDS showed significant ($p \leq 0.05$) associations with the variation in HDL ($R2 = -0.12$), LDL ($R2 = 0.36$), IL-6 ($R2 = 0.26$), and VCAM-1 ($R2 = 0.26$). However, no significant associations ($p > 0.05$) were found between WC-SDS and cIMT, SBP, DBP, TC,TG, TNF-α, IL-1β, ICAM-1 and E-selectin.

Table 4
Multiple linear regression analysis for selected cardiovascular risk factors; where WC-SDS is the dependent variable, adjusted for BMI-SDS.

	B	S.E	β	T	*p*-value	$R^{2*}100\%$
cIMT	−0.004	0.028	−0.049	−0.149	0.882	%6.8
SBP	−2.799	1.651	−0.231	−1.695	0.093	%25.3
DBP	−1.451	1.193	−0.166	−1.217	0.227	%19.8
TC	−2.323	4.650	−0.081	−0.500	0.619	%26.1
TG	0.073	4.532	0.002	0.016	0.987	%13.7
HDL	**−8.995**	**4.019**	**−0.662**	**−2.238**	**0.028**	**%12.3**
LDL	**−7.376**	**2.451**	**−0.632**	**−3.010**	**0.005**	**%35.7**
IL-6	**0.961**	**0.249**	**1.007**	**3.867**	**0.001**	**%25.7**
TNF-α	−0.662	0.373	−0.537	−1.777	0.081	%8.5
IL-1 β	0.093	0.673	0.041	0.138	0.891	%9.2
VCAM-1	**72.479**	**19.200**	**1.025**	**3.775**	**0.001**	**%26.0**
ICAM-1	−4.028	11.333	−0.105	-.355	0.724	%9.6
E-selectin	3.722	4.715	0.267	0.789	0.435	%12.0

cIMT, carotid intima-media thickness; SPB, systolic blood pressure; DPB, diastolic blood pressure; TC, total cholesterol; TG, triglyceride; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; IL-6, Interleukin 6; TNF-α, Tumor necrosis factor −alpha; IL-1β, Interleukin-1 beta; VCAM-1, vascular cell adhesion molecule −1; ICAM-1; intercellular adhesion molecule −1. $p \leq 0.05$ is considered statistically significant between WC-SDS adjusted for BMI-SDS and selected cardiovascular risk factors.

4. Discussion

A degree of subclinical atherosclerosis in children and adolescents is related to obesity assessed by BMI [23]. We previously reported that increased BMI is associated with increased cIMT, circulating levels of inflammation, and endothelial dysfunction and other CVD risk factors among schoolchildren aged 10–15 years [24]. The relationship between abdominal obesity and atherosclerosis development has been established among adults [14]. As such, atherosclerotic events could be avoided by preventing abdominal obesity [25]. Given that increased WC has been linked to an increased risk of cardiovascular events in children and in adults, WC has been used as surrogate marker to evaluate abdominal obesity [17,26]. Hence, the objective of the current study was to examine the attribution of increased WC to cIMT, endothelial dysfunction, and inflammatory biomarkers in a group of healthy schoolchildren.

The findings of the current study show that mean cIMT levels were significantly ($p \leq 0.05$) higher among HWC schoolchildren as compared to LWC counterparts. cIMT was significantly correlated with WC after adjusting for age and sex. Findings demonstrated that WC is an independent predictive risk factor for increased vascular structure measured in children and young adolescents [27]. Waist circumference was more sensitive than other anthropometric measurements in predicting increased cIMT [17]. Our results were in line with the findings of Melo and colleagues [28] who reported that mean cIMT was significantly higher among schoolchildren aged 11–13 years in HWC group as compared to LWC group. Melo et al.'s study [18], which included 385 children (11–13 years), reported that cIMT was positively correlated with BMI, FM, WC and trunk FM; additionally, by using multiple regression, WC was the only predictor for cIMT ($\beta = 0.22$, $p < 0.001$). Although the correlation analysis showed positive values of cIMT and WC even after adjusting for age and sex, the multiple linear regression of the current study showed no significant correlation between cIMT and WC-SDS after adjusting for BMI-SDS. This can be explained by the high correlation between BMI and WC; therefore, it is difficult to separate them as independent risk factors in epidemiological studies [29].

The findings of this study show an increase in both SBP and DBP among the HWC group as compared to the MWC and LWC groups. Increased blood pressure (BP) is common among obese children in comparison to non-obese children of all ages [30]. Higher BP during childhood can be predictive of sustained hypertension in adulthood [30]. Waist circumference was more positively associated with blood pressure than other anthropometric measures among children [31]. The findings of the present study demonstrate that an increase in WC is correlated with an increase in BP. Similar observations have been observed in other reports. Duncan et al. [32] reported that WC was associated with hypertension in their cross-sectional study which included 445 children and adolescents (10–17 years). In addition, Flores-Huerta and colleagues [33] indicated that the prevalence of increased blood pressure and the risk of it occurring were significantly higher when using WC than BMI in a sample of 2029 children and adolescents.

Our findings revealed that higher WC is significantly correlated with higher levels of TC, TG, LDL and lower levels of HDL. We found a significant correlation between dyslipidemia, and WC after adjusting for age and sex. Moreover, significant associations

between WC-SDS and HDL and LDL were reported using multiple linear regression analysis after adjusting for BMI-SDS. Parallel to this, Ling-Hui and colleagues' [34] large scale cross-sectional study, which included 1452 school-age children (7–17 years), revealed that the levels of dyslipidemia increased by increasing the degree of obesity, while WC had a stronger relationship with dyslipidemia than BMI. Therefore, the findings of the current study support the hypothesis that WC is associated with atherogenic dyslipedimia.

Obesity is a state of low-grade chronic inflammation [7]. It has been suggested that the adverse effects of abdominal obesity on the cardiovascular system are mediated by chronic inflammation [35,36]. Findings demonstrated that low-grade inflammatory mechanisms play a significant part in the onset, development, and settlement of atherosclerotic lesions [35]. The current results show an increase in IL-6 and IL-1β in the HWC group as compared to LWC. Moreover, we demonstrate associations between WC and IL-6 and VCAM-1 using multiple linear regression, suggesting that the increase of WC might be associated with a degree of inflammation and early endothelial damage. Other reports have demonstrated that abdominal obesity is associated with enhanced low-grade systemic inflammation and increased adhesion molecules serum levels [36,37]. The TNF-α did not increase in the HWC group as compared to the LWC group, and no significant associations were observed in most of the inflammatory and increased adhesion molecules markers studied. This could be partially explained by the young age of the study participants, the sample size and the interference of other factors such as free fatty acid and growth factors (including vascular endothelial growth factors), which were not examined in this study [13] and necessitate further investigation.

This study has both strengths and limitations. To our knowledge, this is the first study to evaluate the risk factors of subclinical atherosclerosis in apparently healthy schoolchildren with high WC in low income countries. Also, this study investigated larger number of variables than in other investigations. The study participants are young, do not consume medications and are non-smokers, which could have helped strengthen our results. A few limitations are worth mentioning: as a cross-sectional study, no cause-effect nor conformation of the speculation can be made. The study sample size may also reduce the statistical power of our findings. Finally, in spite of the rising interest in measuring fat distribution, a major limitation in measuring WC is the inexistence of commonly accepted cut-off points among children and adolescents, as different ethnicities may interfere with these cut-off points which may be interfered with different ethnicities [18]. Therefore, multi-ethnic research is needed to identify the cutoff points for cardiometabolic risk factors among young populations, which may provide useful information for risk assessment and possible interventions regarding abdominal obesity.

5. Conclusion

The findings of the present study indicate that higher waist circumference is associated with atherosclerosis risk factors including increased cIMT, a state of dyslipidemia, higher blood pressure, inflammation and endothelial dysfunction. Waist circumference seems to be useful for the prediction of subclinical atherosclerosis stage. However, this study highlights the need for reevaluating the appropriate of waist circumference cut-off points of increased cardiovascular risk among schoolchildren.

Compliance with ethical standards

The protocol and all procedures of the present study were approved by the Deanship of Academic Research at the University of Jordan, The Jordanian Ministry of Education and Abdul Hameed Shoman Foundation Research Committee, Jordan.

Conflicts of interest

The authors declare no conflict of interest.

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Informed consent

Parents of the participating students gave a written consent before inclusion.

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References

[1] Smith SC. Screening for high-risk cardiovascular disease: a challenge for the guidelines: comment on “systematic review of guidelines on cardiovascular risk assessment: which recommendations should clinicians follow for a cardiovascular health check?”. Arch Intern Med 2010;170(1):40–2.
[2] Yusuf S, Reddy S, Ôunpuu S, Anand S. Global burden of cardiovascular diseases part I: general considerations, the epidemiologic transition, risk factors, and impact of urbanization. Circulation 2001;104(22):2746–53.
[3] Ng M, Fleming T, Robinson M, Thomson B, Graetz N, Margono C, Abraham JP. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet 2014;384(9945):766–81.
[4] Guo SS, Wu W, Chumlea WC, Roche AF. Predicting overweight and obesity in adulthood from body mass index values in childhood and adolescence. Am J Clin Nutr 2002;76(3):653–8.
[5] de Groot E, Hovingh GK, Wiegman A, Duriez P, Smit AJ, Fruchart JC, Kastelein JJ. Measurement of arterial wall thickness as a surrogate marker for atherosclerosis. Circulation 2004;109(23 suppl 1). III-33.
[6] Ribeiro JC, Guerra S, Oliveira J, Andersen LB, Duarte JA, Mota J. Body fatness and clustering of cardiovascular disease risk factors in Portuguese children and adolescents. Am J Hum Biol 2004;16(5):556–62.
[7] Montero D, Walther G, Perez-Martin A, Roche E, Vinet A. Endothelial dysfunction, inflammation, and oxidative stress in obese children and adolescents: markers and effect of lifestyle intervention. Obes Rev 2012;13(5):441–55.
[8] Okazaki S, Sakaguchi M, Miwa K, Furukado S, Yamagami H, Kitagawa K. Association of interleukin-6 with the progression of carotid atherosclerosis a 9-year follow-up study. Stroke 2014;45(10):2924–9.
[9] Tsimikas S, Duff GW, Berger PB, Rogus J, Huttner K, Clopton P, Witztum JL. Pro-inflammatory interleukin-1 genotypes potentiate the risk of coronary artery disease and cardiovascular events mediated by oxidized phospholipids and lipoprotein (a). J Am Coll Cardiol 2014;63(17):1724–34.
[10] Zhang J, Chen L, Delzell E, Muntner P, Hillegass WB, Safford MM, Curtis JR. Republished: the association between inflammatory markers, serum lipids and the risk of cardiovascular events in patients with rheumatoid arthritis. Postgrad Med 2014;J 90(1070):722–9.
[11] Desideri G, De Simone M, Iughetti L, Rosato T, Iezzi ML, Ferri C. Early activation of vascular endothelial cells and platelets in obese children. J Clin Endocrinol Metab 2005;90:3145–52.
[12] Hughan KS, Tfayli H, Warren-Ulanch JG, Barinas-Mitchell E, Arslanian SA. Early biomarkers of subclinical atherosclerosis in obese adolescent girls with polycystic ovary syndrome. J Pediatr 2016;168:104–11.
[13] Dalmas E, Kahn JF, Giral P, Abdennour M, Bouillot JL, Fellahi S, Poitou C. Intima-Media Thickness in Severe Obesity Links with BMI and metabolic status but not with systemic or adipose tissue inflammation. Diabetes Care 2013;36(11):3793–802.
[14] Lam BC, Koh GH, Chen C, Wong MK, Fallows SJ. Comparison of body mass index (BMI), body adiposity index (Bai), waist circumference (WC), waist-to-

hip ratio (WHR) and waist-to-height ratio (WHtR) as predictors of cardiovascular disease risk factors in an adult population in Singapore. PLoS One 2015;10(4), e0122985.
[15] Cerhan JR, Moore SC, Jacobs EJ, Kitahara CM, Rosenberg PS, Adami HO, Horn-Ross PL. A pooled analysis of waist circumference and mortality in 650,000 adults. Mayo Clin Proc 2014;89(3):335–345.
[16] Crawford M, Chataut C, Avery EF, Janssen I, Powell LH, Kravitz HM, Kazlauskaite R. Waist-to-Height ratio performs as well as waist circumference as the principal adiposity indicator of cardiometabolic risk across five ethnic groups of midlife women. In: Clinical studies in obesityvol. 12; 2014 (1): SAT-0906-SAT-0906.
[17] Elkiran O, Yilmaz E, Koc M, Kamanli A, Ustundag B, Ilhan N. The association between intima media thickness, central obesity and diastolic blood pressure in obese and owerweight children: a cross-sectional school-based study. Int J Cardiol 2013;165(3):528–532.
[18] Melo X, Santa-Clara H, Pimenta NM, Carrolo M, Martins SS, Minderico CS, Sardinha LB. Body composition phenotypes and carotid intima-media thickness in 11–13-year-old children. Eur J Pediatr 2014;173(3):345–52.
[19] World health organization (WHO). Growth reference 5-19 years. http://www.who.int/growthref/who2007_bmi_for_age/en/. [Accessed 26 August 2015].
[20] Center for disease control and prevention (CDC). National health and nutrition examination Survey (NHANES): anthropometry procedures manual. http://www.cdc.gov/nchs/data/nhanes/nhanes_07_08/manual_an.pdf. [Accessed 30 January 2013].
[21] Fryar CD, Gu Q, Ogden CL. Anthropometric reference data for children and adults: United States, 2007-2010. Vital and health statistics. Series 11, vol. 252; 2012. p. 1–48. Data from the national health survey.
[22] Pozza R, Ehringer-Schetitska D, Fritsch P, Jokinen E, Petropoulos A, Oberhoffer R. Intima media thickness measurement in children: a statement from the association for European paediatric cardiology (AEPC) working group on cardiovascular prevention endorsed by the association for European paediatric cardiology. Atherosclerosis 2015;238:380–7.
[23] Reinehr T, Wunsch R. Intima media thickness-related risk factors in childhood obesity. Pediatr Obes 2011;6(S1):46–52.
[24] Al-Shorman A, Al-Domi H, Faqih A. Markers of subclinical atherosclerosis in schoolchildren with obesity and metabolic syndrome. Swiss Med Wkly 2017;147:w14446.
[25] Silaghi CA, Silaghi H, Craciun AE, Farcas A, Colosi HA, Cosma DT, Georgescu CE. Age, abdominal obesity, and glycated hemoglobin are associated with carotid atherosclerosis in type 2 diabetes patients with nonalcoholic fatty liver disease. Med Ultrason 2015;17(3):300.
[26] Ackermann D, Jones J, Barona J, Calle MC, Kim JE, LaPia B, Lerman RH. Waist circumference is positively correlated with markers of inflammation and negatively with adiponectin in women with metabolic syndrome. Nutr Res 2011;31(3):197–204.
[27] Alpsoy S, Akyuz A, Akkoyun DC, Nalbantoglu B, Topcu B, Tulubas F, Donma MM. Is overweight a risk of early atherosclerosis in childhood? Angiology 2013. 0003319713476134.
[28] Melo X, Santa-Clara H, Pimenta NM, Martins SS, Minderico CS, Fernhall B, Sardinha LB. Intima-media thickness in 11–13 years-old children: variation attributed to sedentary behavior, physical activity, cardiorespiratory fitness and waist circumference. J Phys Activ Health 2015;12(5):610–7.
[29] Moore SC. Waist versus weight—which matters more for mortality? Am J Clin Nutr 2009;89(4):1003–4.
[30] Morrison JA, Friedman LA, Gray-McGuire C. Metabolic syndrome in childhood predicts adult cardiovascular disease 25 years later: the Princeton Lipid Research Clinics Follow-up Study. Pediatrics 2007;120(2):340–5.
[31] Nowson CA, Crozier SR, Robinson SM, Godfrey KM, Lawrence WT, Law CM, Hammond J. Association of early childhood abdominal circumference and weight gain with blood pressure at 36 months of age: secondary analysis of data from a prospective cohort study. BMJ open 2014;4(7). e005412.
[32] Duncan MJ, Mota J, Vale S, Santos MP, Ribeiro JC. Associations between body mass index, waist circumference and body shape index with resting blood pressure in Portuguese adolescents. Ann Hum Biol 2013;40(2):163–7.
[33] Flores-Huerta S, Klünder-Klünder M, de la Cruz LR, Santos JI. Increase in body mass index and waist circumference is associated with high blood pressure in children and adolescents in Mexico City. Arch Med Res 2009;40(3):208–15.
[34] Ling-Hui MG, Na L, Jie MI. Impacts of types and degree of obesity on non-alcoholic fatty liver disease and related dyslipidemia in Chinese school-age children? Biomed Environ Sci 2011;24(1):22–30.
[35] Després JP. Abdominal obesity and cardiovascular disease: is inflammation the missing link? Can J Cardiol 2012;28(6):642–652.
[36] Harada K, Amano T, Kataoka T, Takeshita M, Harada K, Kunimura A, Kato M. Impact of abdominal and epicardial fat on the association between plasma adipocytokine levels and coronary atherosclerosis in non-obese patients. Atherosclerosis 2014;237(2):671–6.
[37] Couillard C, Ruel G, Archer WR, Pomerleau S, Bergeron J, Couture P, Bergeron N. Circulating levels of oxidative stress markers and endothelial adhesion molecules in men with abdominal obesity. J Clin Endocrinol Metab 2005;90(12):6454–9.