

# Blood pressure, dyslipidemia and inflammatory factors are related to body mass index in scholar adolescents

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## Abstract

**Introduction:** Obesity is associated with increased occurrence of numerous diseases, including hypertension, dyslipidemia, insulin resistance, diabetes, and atherosclerosis. Blood pressure (BP), dyslipidemia, and inflammation markers and their relationships with body mass index (BMI) were determined in scholar adolescents.

**Material and methods:** Adolescents ( $n = 210$ ) (sex ratio G/B = 106/104; 11 to 16 years) were recruited in three colleges of Oran city. Anthropometric parameters were measured to classify adolescents as thin (T), normal weight (NW), overweight (OW), or obese (O). Waist circumference (WC) and BP were measured, and serum glucose, uric acid, urea, lipid parameters, tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), interleukin-1 $\beta$  (IL-1 $\beta$ ), interleukin-6 (IL-6), C-reactive protein (CRP), insulin, leptin, and adiponectin were analyzed.

**Results:** Adolescents were classified according to their BMI as T (15%), NW (63%), OW (13%), and O (9%). Compared to NW, increased values of WC, BP ( $p < 0.001$ ), and glucose ( $p < 0.01$ ) were noted in OW and O groups. Total cholesterol (TC) level was elevated in O adolescents ( $p < 0.01$ ). Increased low-density lipoprotein cholesterol (LDL-C) in OW ( $p < 0.05$ ) and O ( $p < 0.01$ ), and reduced high-density lipoprotein cholesterol (HDL-C) concentrations were noted in both OW and O groups ( $p < 0.05$ ), compared to NW. Elevated triglyceride (TG) values and TG : HDL-C ratio were observed in OW ( $p < 0.05$ ) and O ( $p < 0.01$ ). High values of uric acid were noted in OW and O adolescents ( $p < 0.01$ ). Compared to NW, there was no significant difference in IL-1 $\beta$  whereas IL-6 was elevated in T ( $p < 0.05$ ), OW ( $p < 0.01$ ) and O ( $p < 0.001$ ). Leptin, TNF- $\alpha$ , and CRP concentrations were significantly increased ( $p < 0.001$ ), whereas adiponectin values were decreased in both OW and O groups ( $p < 0.01$ ), compared to NW.

**Conclusions:** Significant associations were noted between WC, BP, dyslipidemia, inflammation markers, and BMI, indicating that both OW and O adolescents have a tendency to present metabolic syndrome risk factors.

**Key words:** adolescent, body mass index, blood pressure, dyslipidemia, inflammation.

## Introduction

Obesity is widely considered to be the greatest public health challenge for the 21<sup>st</sup> century, because of its role in causing disability and

crippling healthcare costs [1]. Childhood obesity has more than quadrupled in adolescents aged 12–19, increasing from 5% in 1980 to nearly 21% in 2012 [2].

Hypertension and atherosclerosis may begin in childhood and adolescents [3–5], and can persist into adulthood [6–8]. This has been attributed to high obesity prevalence, especially when it is predominantly abdominal and associated with the other features of the metabolic syndrome (MS); this phenomenon is well characterized in adults [9, 10] and adolescents [11, 12].

Indeed, obesity is associated with increased occurrence of numerous diseases, including hypertension, dyslipidemia, insulin resistance (IR), diabetes, and atherosclerosis [13].

Moreover, adipose tissue is not simply a fat storage deposit, but has been recognized as an endocrine organ contributing to the inflammatory process in obese subjects, in both vascular and nonvascular tissues [12, 13], producing various adipocytokines, such as leptin, adiponectin, tumor necrosis factor (TNF)- $\alpha$ , interleukin (IL)-6, IL-1 $\beta$ , and resistin [14, 15].

The plasma adiponectin concentration was negatively correlated with the degree of body fat and IR [16], whereas leptin and C-reactive protein (CRP) plasma concentrations were directly related to obesity severity [17, 18], and were significantly correlated with the main variables of MS [18]. Moreover, TNF- $\alpha$  and IL-6, secreted by fat cells, induced hepatic synthesis of CRP, and both molecules were associated with obesity and cardiovascular diseases [19, 20].

A few studies relating obesity to cardiovascular risk factors have been conducted among adolescents in developing countries [12, 21–23], but there was no study in Algerian adolescents concerning metabolic risk factors, except hypertension [3].

Therefore, the aim of this study was to evaluate blood pressure (BP), dyslipidemia, inflammation markers and hormone profile and their relationships with body mass index (BMI), in scholar adolescents.

## Material and methods

The study was carried out from April 2010 to May 2012 in Oran (West Algeria). A total of 210 adolescents (sex ratio G/B = 106/104), aged 11–16 years were recruited from three colleges.

### Anthropometric and BP measurements

Anthropometric measurements were taken at schools by trained operators using standard equipment. Waist circumference (WC) was measured to the nearest 0.1 cm in a standing position

at the midpoint between the lowest rib and the iliac crest and at the end of a normal expiration, using a measuring tape. Body weight (BW) was measured to the nearest 0.1 kg using a portable scale (Seca, Germany) with minimal clothing and no shoes. Height was measured to the nearest 0.1 cm using a height bar (2 m, dismantling) without shoes. Body mass index was calculated as weight in kilograms divided by the square of height in meters (kg/m<sup>2</sup>).

The weight status of each subject was categorized as thin (T), normal weight (NW), overweight (OW), or obese (O), according to the cut-off points adopted by the International Obesity Task Force (IOTF) and international cut-off points for BMI for thinness [24].

Adolescents were defined as O when their BMI was greater than the 95<sup>th</sup> percentile, OW with a BMI between the 85<sup>th</sup> and 95<sup>th</sup> percentile, and NW with a BMI less than the 85<sup>th</sup> percentile of the reference values for age and sex.

Blood pressure was measured in a sitting position after a 10 min rest period. The averages of two systolic (SBP) and diastolic (DBP) BP measures were recorded at 5 min intervals.

### Blood sampling and analysis

Blood samples were collected after 12 h fasting from antecubital venipuncture. All collections were made between 8:00 and 9:00 am. Plasma and serum were collected by low speed centrifugation at 3000  $\times$  g at 4°C, for 15 min. The samples were separated in aliquots and frozen immediately at –75°C, until determination could be performed.

Glucose, uric acid, urea, total cholesterol (TC) and triacylglycerols (TG) were measured by enzymatic colorimetric methods (Spinreact kits, Spain).

High-density lipoprotein cholesterol (HDL-C) was determined after precipitation of chylomicrons, very low-density lipoproteins (VLDL) and low-density lipoproteins (LDL), with phosphotungstic acid and magnesium ions (Spinreact kit, Spain). Concentration of LDL-cholesterol (LDL-C) was calculated using the Friedewald formula [25].

Tumor necrosis factor  $\alpha$ , IL-6, and IL-1 $\beta$  were determined in duplicate samples with commercial enzyme-linked immunosorbent assay kits (ELISA) (Cayman Chemical's ACE EIA kit) with a range of 0–250 pg/ml. The lower limit of detection was 3.9 pg/ml for TNF- $\alpha$  and IL-1 $\beta$ , and 7.8 pg/ml for IL-6. The CRP marker was measured in duplicate samples with an immunometric assay kit (ELISA) (Cayman Chemical's ACE EIA kit) with a range of 0–3000 pg/ml, and with a detection limit of approximately 50 pg/ml.

Adiponectin was measured in duplicate samples with an immunometric assay kit (ELISA) (SPI Bio Bertin Pharma), with a range of 0–10  $\mu$ g/ml

and with a limit detection of approximately 7 ng/ml. Similarly, leptin analysis was performed in duplicate samples with an immunometric assay kit (ELISA) (SPI Bio Bertin Pharma), with a range of 0–50 ng/ml, and with a limit of detection of 0.2 ng/ml. Insulin was assayed in duplicate samples for the quantitative measurement of human insulin concentrations in serum (ELISA) (abcam) with a range of 0–300  $\mu$ IU/ml and with a limit of detection of 4  $\mu$ IU/ml.

### Statement of ethics

Informed written consent was obtained from the parents or tutors, and verbal consent was provided by each adolescent. The study was approved by the Preventive Directory of the Ministry of Health.

### Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics version 20. All values were expressed as mean  $\pm$  SD. The Shapiro-Wilk test was used to verify whether variable distribution was

normal. Differences according to BMI classification were determined by analysis of variance (ANOVA). The Student *t*-test was used to compare different variables in T, OW and O groups with those of NW. The level of significance was set as  $p < 0.05$ . Correlations between variables were calculated using Pearson's coefficient. The odds ratio (OR) was estimated for each factor separately to evaluate its influence on BMI. A  $p$ -value = 0.05 was considered statistically significant with the confidence interval (CI) 95%. Odds ratio was estimated using logistic regression analysis.

### Results

The characteristics of adolescents according to BMI are presented in Table I. The adolescent classification showed that 15% were T, 63% had NW, 13% were OW and 9% were O (Table I). There was no significant difference according to age or gender between the different groups. However, BW (kg) was higher in OW ( $p < 0.05$ ) and O groups ( $p < 0.01$ ) than in NW, whereas no significant difference in height was noted between all the

**Table I.** Characteristics of adolescents according to BMI

Parameter	Thin (T)	Normal weight (NW)	Overweight (OW)	Obese (O)	P-value
Adolescents, n (%)	31 (15)	133 (63)	27 (13)	19 (9)	
Boys/girls	16/15	67/66	13/14	10/9	
Age [years]	12 $\pm$ 1	12 $\pm$ 1	13 $\pm$ 1	13 $\pm$ 1	NS
Weight [kg]	32.1 $\pm$ 3.9	42.2 $\pm$ 8.2	58.7 $\pm$ 7.6*	74.5 $\pm$ 13.2**	0.01
Height [m]	1.5 $\pm$ 0.1	1.5 $\pm$ 0.1	1.5 $\pm$ 0.1	1.6 $\pm$ 0.1	NS
Pubertal status I/II/III/IV/V	1/3/8/11/8	13/17/33/39/1	1/4/8/10/4	1/3/6/4/5	NS
BMI [kg/m <sup>2</sup> ]	15.0 $\pm$ 0.5*	18.6 $\pm$ 1.8	24.2 $\pm$ 1.9***	30.4 $\pm$ 3.1***	< 0.001
Waist circumference [cm]	66.6 $\pm$ 4.3*	72.6 $\pm$ 8.9	89.2 $\pm$ 5.1***	99.2 $\pm$ 3.5***	< 0.001
Systolic BP [mm Hg]	104 $\pm$ 6*	114 $\pm$ 5	127 $\pm$ 4***	138 $\pm$ 5***	< 0.001
Diastolic BP [mm Hg]	58 $\pm$ 5*	63 $\pm$ 6	75 $\pm$ 6***	83 $\pm$ 4***	< 0.001
Glucose [mmol/l]	4.0 $\pm$ 0.7	4.0 $\pm$ 0.8	4.6 $\pm$ 0.7**	4.8 $\pm$ 0.7**	0.06
TC [mmol/l]	4.1 $\pm$ 0.9	4.3 $\pm$ 0.9	4.3 $\pm$ 0.6	5.0 $\pm$ 0.8**	0.04
HDL-C [mmol/l]	1.2 $\pm$ 0.3	1.2 $\pm$ 0.2	1.1 $\pm$ 0.3*	1.1 $\pm$ 0.2*	< 0.001
LDL-C [mmol/l]	2.4 $\pm$ 0.6	2.5 $\pm$ 0.8	2.9 $\pm$ 0.5*	3.3 $\pm$ 0.7**	< 0.001
TG [mmol/l]	0.8 $\pm$ 0.4	1.0 $\pm$ 0.4	1.5 $\pm$ 0.5*	1.7 $\pm$ 0.4**	< 0.001
Urea [mmol/l]	4.1 $\pm$ 1.2	3.8 $\pm$ 1.4	4.2 $\pm$ 1.0	2.8 $\pm$ 1.0	NS
Uric acid [ $\mu$ mol/l]	229.1 $\pm$ 82.9	236.1 $\pm$ 101.6	260.4 $\pm$ 80.7**	255.1 $\pm$ 87.2**	< 0.001
Insulin [ $\mu$ IU/ml]	6.2 $\pm$ 0.4	6.1 $\pm$ 0.2	6.1 $\pm$ 0.4	6.3 $\pm$ 0.5	NS
TG/HDL-C	0.6 $\pm$ 0.1	0.8 $\pm$ 0.1	1.3 $\pm$ 0.2*	1.6 $\pm$ 0.2**	< 0.001

BMI – weight (kg)/height (m<sup>2</sup>), BP – blood pressure, TC – total cholesterol, HDL-C – high-density lipoprotein-cholesterol, LDL-C – low-density lipoprotein-cholesterol, TG – triglycerides. Values are mean  $\pm$  SD of 210 adolescents. Differences according to BMI classification were determined by ANOVA. Student *t*-test: NW vs. T, OW, O. \* $p < 0.05$ ; \*\* $p < 0.01$ ; \*\*\* $p < 0.001$ .

**Table II.** Inflammatory biomarkers according to BMI

Parameter	Thin	Normal weight	Overweight	Obese	P-value
IL-1 $\beta$ [pg/ml]	15.3 $\pm$ 5.9	19.6 $\pm$ 11.9	12.9 $\pm$ 11.9	17.6 $\pm$ 11.3	NS
IL-6 [pg/ml]	38.7 $\pm$ 7.4*	35.9 $\pm$ 8.1	40.2 $\pm$ 7.5**	43.8 $\pm$ 19.2***	< 0.001
Leptin [ng/ml]	3.9 $\pm$ 0.9*	6.4 $\pm$ 1.7	24.3 $\pm$ 4.9***	40.9 $\pm$ 5.0***	0.001
Adiponectin [ng/ml]	2.5 $\pm$ 1.0*	2.3 $\pm$ 0.9	1.1 $\pm$ 0.5**	1.1 $\pm$ 0.5**	0.001
TNF- $\alpha$ [pg/ml]	4.9 $\pm$ 1.7*	7.5 $\pm$ 2.7	10.9 $\pm$ 2.6***	13.9 $\pm$ 1.3***	< 0.001
CRP [pg/ml]	0.4 $\pm$ 0.1	0.5 $\pm$ 0.1	1.1 $\pm$ 0.5***	1.1 $\pm$ 0.5***	0.001

IL-1 $\beta$  – interleukin-1 $\beta$ , IL-6 – interleukin-6, TNF- $\alpha$  – tumor necrosis factor, CRP – C-reactive protein. Values are mean  $\pm$  SD of 210 adolescents (sex ratio girls/boys, 106/104). Differences according to BMI classification were determined by ANOVA. NS – not statistically significant. Student t-test NW vs. T, OW, O. \* $p$  < 0.05; \*\* $p$  < 0.01; \*\*\* $p$  < 0.001.

groups. Nevertheless, WC increased in both OW and O ( $p$  < 0.001), and diminished in T ( $p$  < 0.05), compared to NW.

Systolic and diastolic BP were significantly increased in OW and O groups ( $p$  < 0.001), and were reduced in T adolescents ( $p$  < 0.05).

Glucose concentrations were higher in OW and O than in NW ( $p$  < 0.01). Total cholesterol values increased in O adolescents ( $p$  < 0.01). Moreover, high LDL-C in OW ( $p$  < 0.05) and O ( $p$  < 0.01), and low HDL-C levels in both OW and O groups ( $p$  < 0.05) were observed, compared to NW (Table I). Triacylglycerols values were higher in OW ( $p$  < 0.05) and O ( $p$  < 0.01) than in NW. Indeed, TG/HDL-C represented 1.3  $\pm$  0.2 and 1.6  $\pm$  0.2 in OW and O versus 0.6  $\pm$  0.1 in T, compared to 0.8  $\pm$  0.1 in NW.

There was no significant difference in urea and insulin concentrations, whereas uric acid values were elevated in OW and O adolescents ( $p$  < 0.01).

Inflammatory biomarkers are presented in Table II. While IL-1 $\beta$  was not significantly different, IL-6, leptin, TNF- $\alpha$ , and CRP concentrations were increased ( $p$  < 0.001), whereas adiponectin values were reduced ( $p$  < 0.01), in both OW and O groups, compared to NW.

Strong relationships were found between WC, SBP, DBP, LDL-C, TC, TG, leptin and BMI. Inversely, negative correlations were noted between HDL-C, adiponectin and BMI (Table III).

Multiple regression analysis of BMI versus metabolic risk markers (WC, TC, LDL-C, HDL-C, TG, leptin, adiponectin, TNF- $\alpha$  and CRP) is shown in Table IV.

## Discussion

The aim of this study was to evaluate BP, dyslipidemia, inflammation markers and hormone profile and their relationships with BMI, in scholar adolescents.

Anthropometric classification showed that more than half of adolescents presented normal weight, whereas both T and OW groups were approximately similar, and O represented 9%. Significant relationships were found between BW, WC,

and BMI, as noted in several studies in adolescents [25–27].

Overweight is an important cardiovascular risk factor. Although the clinical manifestations of cardiovascular diseases occur in adulthood, studies have demonstrated that comorbidities, such as dyslipidemia, hypertension, and IR, may be present in childhood and adolescence [28, 29]. Indeed, our study showed that high SBP and DBP values were noted in 72% of OW and O, compared to

**Table III.** Pearson correlation between BMI and studied parameters

Parameter	r	P-value
Waist circumference	0.71	< 0.001
Systolic BP	0.50	< 0.001
Diastolic BP	0.75	< 0.001
Glucose	0.06	0.064
TC	0.179	0.009
HDL-C	-0.193	0.005
LDL-C	0.24	< 0.001
TG	0.65	< 0.001
TG/HDL-C	0.71	< 0.001
Urea	-0.13	NS
Uric acid	-0.008	NS
Insulin	0.116	NS
IL-1 $\beta$	-0.070	NS
IL-6	-0.075	NS
Leptin	0.74	< 0.001
Adiponectin	-0.267	0.001
TNF- $\alpha$	0.136	NS
CRP	-0.064	NS

NS – not statistically significant.

**Table IV.** Multiple regression analysis: association between BMI and metabolic risk markers

Parameter	OR	95% CI	P-value
Age	1.07	0.79–1.45	NS
Sex	0.98	0.44–2.12	NS
Waist circumference	1.33	1.22–1.46	< 0.001
DBP	3.23	3.80–10.2	< 0.001
SBP	2.95	2.41–11.2	< 0.001
Glucose	1.45	0.86–2.42	NS
TC	2.23	1.36–3.65	0.001
HDL-C	1.22	0.69–0.94	0.009
LDL-C	1.12	1.05–1.19	< 0.001
TG	1.34	1.19–1.50	< 0.001
Uric acid	1.001	0.99–1.00	NS
Insulin	1.01	0.95–1.28	NS
IL-1 $\beta$	1.011	1.01–1.03	NS
IL-6	1.006	0.86–1.02	0.621
Leptin	3.78	1.61–8.92	0.002
Adiponectin	0.98	0.96–1	0.04
TNF- $\alpha$	2.11	1.69–2.62	< 0.001
CRP	1.22	1.14–1.30	< 0.001

OR – odds ratio, CI – confidence interval, NS – not statistically significant.

6.5% of NW and T. These results are in accordance with those of Mexican [4], and East Algerian adolescents [3].

Furthermore, our results showed that TC and TG levels were more elevated in O. Indeed, increased LDL-C but lowered HDL-C were observed with BMI ( $p < 0.001$ ). These results are similar to those of Brazilian [11] and Japanese studies [30], which have shown that more overweight children presented significant high TG and low HDL-C values, but no relationship was noted between TC, LDL-C and BMI.

Lipid metabolism disorders, such as high LDL-C and low HDL-C, in children were reported as predictors of future atherosclerosis [31]. A report on increased HDL-C suggests the possibility of an association with a lower rate of mortality from ischemic cardiac disease, in Spanish children, compared with other developed countries [32].

In the pediatric population, TG : HDL-C ratio is related to IR and chronic inflammation [33, 34], suggesting that this marker was able to reflect cardiometabolic status, or the risk of developing cardiometabolic disease, later in life [35]. In our study, this ratio was increased with BMI

( $p < 0.001$ ). Uric acid, which is considered as a cardiometabolic risk factor [36], was increased in our OW and O adolescents, compared to NW.

Our results showed that OW and O adolescents presented a number of metabolic risk factors, such as high values of WC, BP, TG, LDL-C, TG : HDL-C, uric acid, and low HDL-C.

Moreover, inflammation markers, such as IL-6 and CRP levels, were elevated in OW and O adolescents. The high CRP concentrations in obese subjects might be explained by the expression of the cytokine IL-6 in adipose tissue [37] and its release into the circulation [38]. Indeed, IL-6 is a proinflammatory cytokine that stimulates the production of CRP in the liver.

On the other hand, increased TNF- $\alpha$  and lowered adiponectin values were observed relating to BMI. Tumor necrosis factor  $\alpha$  produced by white adipose tissue is markedly up-regulated in obesity and contributes to IR [39], possibly through down-regulation of GLUT-4, and inhibition of insulin receptor function and signaling [19]. Rubin *et al.* [40] suggested that high TNF- $\alpha$  concentrations inhibited adiponectin production, inducing overweight with IR during adolescence. Indeed, adiponectin is an anti-inflammatory and antiatherogenic hormone, exclusively synthesized in adipose tissue [41], with decreased levels in obese subjects [42, 43]. In our study, adiponectin values were significantly lower in OW and O adolescents, and inversely correlated with BMI ( $r = -0.2$ ,  $p < 0.001$ ).

Obesity was frequently associated with high plasma leptin concentration, which was correlated with IR and MS [44]. Leptin has been shown to be an independent risk factor for coronary heart diseases [45]. In our study, both OW and O groups had increased leptin levels, which was significantly associated with BMI ( $r = 0.74$ ,  $p < 0.001$ ).

The multivariate analysis revealed no significant association between age, gender, glucose, insulin, IL-1 $\beta$ , IL-6, uric acid, and BMI. However, relationships were observed with WC, SBP, DBP, TC, LDL-C, TG, TNF- $\alpha$ , CRP, leptin ( $p < 0.001$ ), HDL-C ( $p = 0.009$ ), adiponectin ( $p = 0.04$ ), and BMI.

This study has some limitations. Initially, the recruited obese group represented 50 adolescents, but only 38% of them agreed to participate in this study, resulting in a small sample size. Some results did not reach or were bordering on statistical significance. Therefore, further detailed studies, based on a larger population, are needed, for more comprehensive investigation.

In conclusion, this study shows a significant association between WC, BP, dyslipidemia, TNF- $\alpha$ , CRP, leptin, and BMI, indicating that both OW and O adolescents had a tendency to present MS risk factors.

Future studies are needed to better understand relationships in adolescents with and without



risk factor clustering to gain insight into prevention and/or treatment of high risk progression to chronic diseases over time.

The findings also highlight the need for longitudinal surveys to track the obesity development related to cardiometabolic diseases.

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### Conflict of interest

The authors declare no conflict of interest.

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