

Lifestyle, Cardiometabolic and Inflammatory markers in Schoolchildren and their Associations with Body Mass Index

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Abstract. *Background:* Unhealthy lifestyle behaviors are key elements for weight gain, leading to several chronic diseases. The aim of this study was to evaluate lifestyle, cardiometabolic and inflammation markers and their associations with body mass index (BMI) in children. *Methods:* Schoolchildren (n = 225; G/B = 109/116); aged 7–10 years were recruited. Waist circumference (WC), and BMI were determined. Daily energy intake (DEI), total energy expenditure (TEE), energy balance (EB), physical activity level (PAL), and quality diet using KidMed index were evaluated. Cardiometabolic and inflammatory markers were estimated. *Results:* Anthropometric classification showed that 62% of children were normal weight (NW), 19% overweight (OW), 9% obese (O), and 10% thin (T). Compared to NW, OW and O presented respectively higher WC ($p < 0.05$; $p < 0.01$), weight, DEI and EB ($p < 0.01$; $p < 0.001$), and lower PAL ($p < 0.01$; $p < 0.001$), TEE and KidMed score ($p < 0.05$; $p < 0.01$), while T presented lower weight, DEI, EB and KidMed score ($p < 0.05$). Uric acid (UA) values were higher ($p < 0.05$) in O, leptin, interleukin-6 (IL-6), and tumor necrosis factor- α (TNF- α) concentrations were higher ($p < 0.001$), and adiponectin levels were lower ($p < 0.01$), in both OW and O, whereas, leptin and TNF- α values were lower, and IL-6 levels were higher ($p < 0.001$) in T. Significant associations between WC, DEI, KidMed, leptin, adiponectin, IL-6, TNF- α and BMI were observed. *Conclusion:* In response to unhealthy diet, excess energy intake, and sedentary; excessive fat mass is noted inducing inflammatory status in children. These findings highlight the necessity of oriented strategies to track obesity and related diseases.

Key words: schoolchildren, BMI, waist circumference, quality diet, sedentary, cardiometabolic risk, inflammation

Introduction

Metabolic health in childhood is influenced by several factors such as dietary and physical activity (PA) patterns (1). In fact, dietary practices in these critical periods affect physical and cognitive development, and have consequences later in life (2). Furthermore, children who had inadequate PA had higher

risk to be affected by overweight, obesity, and several chronic diseases (3,4). Unhealthy lifestyle behaviors are key elements for weight gain (5,6). Obesity is defined as abnormal and excessive fat mass, and may impair health (7,8). It has been associated with dyslipidaemia (elevated triglycerides (TG), total cholesterol (TC), low density lipoproteins-cholesterol (LDL-C), and reduced high density lipoproteins-cholesterol (HDL-C)

concentrations), hypertension, abnormal glucose metabolism, insulin resistance (IR), and endothelial dysfunction, representing the first step in atherosclerosis development (9–11). Moreover, fat distribution in abdominal compartments is also associated with coronary heart diseases (CHD) markers (12). Indeed, increased WC is linked to high TG, and low HDL-C levels, lipid abnormalities development, hypertension, and IR, which are important markers of atherosclerotic process progression in childhood (12–15). Otherwise, adipose tissue is a highly active endocrine and metabolic organ, sensing energy requirements, and secreting hormones (adipokines), and cytokines (anti-inflammatory and pro-inflammatory cytokines) (16,17). Leptin and adiponectin are two key adipocyte secreted hormones which change inversely in relation to body mass index (BMI) (18,19). Effectively, typical obesity in humans is commonly associated with elevated leptin, and decreased adiponectin levels (20,21). This profile is involved in obesity pathogenesis, and obesity-related diseases, such as early atherogenesis (22–24). Excess adipose tissue contributes then to increased secretion of pro-inflammatory cytokines, like IL-6, and TNF- α , suggesting chronic inflammation (9,12,24). Thus, inflammatory mechanisms leading to several metabolic disorders, related to obesity, and metabolic syndrome (MS), play a central role in atherosclerosis pathogenesis, and progression, representing CHD risk factors in children future life, and this in response to energy intake (EI) excess (1,23,25). Therefore, healthful lifestyle behaviors including high quality diet are associated with ~80% risk reduction of cardiovascular diseases (CVD), whereas poor diet quality alone accounts for ~45% of CVD deaths (26,27). Thus, a Mediterranean-like dietary pattern is strongly supported to have a dual effect on CVD prevention, by improving classical risk factors, and also, by having intense anti-inflammatory effect since childhood, through biological ways and significant effects on body weight, WC, reducing then the obesity risk (1,28–32).

To our knowledge, there are no data on cardiometabolic risk and inflammation in Algerian children. Besides, data related to their lifestyle behaviors are scarce, we do not even know if their diet is close to the Mediterranean model given the geographical location of Algeria. So, the current study contributed to explore

such components determining their health. Therefore, the aim of this study was to evaluate in schoolchildren from Oran, an Algerian city overlooking the Mediterranean Sea, the associations between BMI and lifestyle parameters (Energy Balance (EB), Physical Activity Level (PAL), and Mediterranean Diet (MD) adherence) as causal factors of weight gain on the one hand, and cardiometabolic risk and inflammatory markers as consequences of weight gain on the other hand.

Subjects and Methods

Study design and ethical requirement

The present study derived from a school-based descriptive research, was conducted from January 2017 to May 2019, in Oran (West Algeria). It was approved by the Health and Population Directorate of the city, and commissioned by the Department of Educational Organization of the Education Directorate (Authorizations N°546/DE/DEO/2016, N°101/DE/DEO/2018). A total of 225 children (sex ratio G/B = 109/116), aged 7–10 years were consecutively recruited from two different schools. Parents or legal guardians, and their children were previously informed about study purpose and methodology, and written consent was obtained from parents, and verbal consent was provided by each child.

Anthropometric measurements

Anthropometric parameters of each participant were measured at schools, with standardized procedures, and equipments by a trained staff. Height and weight were performed using stadiometer and balance (Weighing Scale ZT 220, China), with minimal clothing and no shoes. BMI was computed as weight (kg)/height² (m) to define weight status, using IOTF (International Obesity Task Force) gender, and age related cut-offs for BMI (33,34). Children were classified into 4 groups: Normal-weight (NW), Overweight (OW), Obese (O) and Thin (T). WC was measured in a standing position to the nearest 0.1 cm at the level of the umbilicus, and at the end of a normal expiration, using a non-elastic tape.

Daily Energy Intake (DEI), Total Energy Expenditure (TEE), PAL and EB assessments

A dietary survey was carried out by 24 hours recall, followed by 3 days record. This method consisted on written or verbal report using an adapted questionnaire. Each child was asked to recall all food and beverages type and quantity consumed during the 4 days including one weekend day. Serving sizes were estimated by using a food portion model handbook. Dimensions of dishes, utensils, and consumed food portions were specified on photos (in three small, medium and large sizes). Day was organized chronologically in breakfast, morning snack, lunch, afternoon snack, and dinner. Meals were structured by entry, principal dish accompaniments, dessert, and drinks. Thus, increasing reliability of provided information. Quantitative DEI assessment was calculated, using the computerized nutritional survey management software GENI (35). Complete information on frequency, duration and intensity of physical activities during a typical week, including domains such as transport, household, fitness and sports activities were collected and treated by GENI (35). EB was calculated by subtraction (DEI-TEE).

Quality diet by adherence to MD

To assess adherence to MD, KidMed index was used (36). This index is based on 16-questions, which sustain the MD patterns principles, as well as, those that undermine it. Questions that present negative aspects in relation to MD are scored with a value of -1, and those with positive aspects with +1. The sum of all values from the administered test is categorized into three levels of MD adherence: high adherence (score ≥ 8 points); medium adherence (score 4–7 points), and low adherence (score ≤ 3 points).

Blood Pressure (BP) measurements and biochemical analysis

Systolic (SBP) and diastolic (DBP) BP were measured twice in the seated position with the left arm supported at the heart level after at least 10 minutes of rest. The mean value of 2 measurements was used for

analysis. If the two measurements differed by 2 mmHg or more, a third measure was taken.

Blood samples were obtained from each subject after a 12-h overnight fasting by antecubital venipuncture. Serum was collected by centrifugation at $3000 \times g$ at 4°C , for 15 min. Samples were separated in aliquots, and stored immediately at -80°C , until essays could be performed. Each parameter was measured in duplicate samples. Enzymatic colorimetric methods were used to measure serum levels of glucose, TC, TG, Urea (BioSystems kits, Spain), and UA (Biolabo kit, France). HDL-C was determined using precipitating reagent (BioSystems kit, Spain), and LDL-C was calculated using the Friedewald formula (37). Albumin was determined by colorimetric method (BioSystems kit, Spain), and creatinine with calorimetric-kinetic method (SpinReact kit, Spain). Leptin and adiponectin concentrations were determined using Enzyme Linked Immuno Sorbent Assay (ELISA) (SPI-Bio Bertin Pharma kits, France), permitting measurements within the range of 1–50 ng/mL for leptin, and 0.1–10 $\mu\text{g/mL}$ for adiponectin. All samples were above the limits of detection (leptin: 0.2 ng/mL, and adiponectin: 7 ng/mL). TNF- α and IL-6 were assayed by immunometric assay kits (ELISA) (Cayman Chemical Company, USA), permitting measurements within the range of 3.9–250 pg/mL for both cytokines. The lower limit of detection was 3.9 pg/mL for TNF- α , and 7.8 pg/mL for IL-6.

Statistical Analysis

All analyses were performed using STATA: version 12 SE. Descriptive statistics with means \pm SD or percentages (numbers) were used for participants characteristics. The dependent variable was the BMI. The Shapiro-Wilk test was used to verify whether variable distribution was normal. The χ^2 test was used to rule out the influence of “sex” variable on BMI. Student *t*-test was used to compare different variables in T, OW, and O groups with those of NW. Differences according to BMI classification were determined by analysis of variance (ANOVA). A small number of missing outcome data were handled *via* multivariate imputation based on Markov chain Monte Carlo methods (38). Ordinal logistic regression was performed in two steps: univariate (20%), and multivariate (5%). The

dependent variable was encoded as an ordinal variable from 1 to 4 representing T, NW, OW, and O respectively. Odds ratio (OR) was estimated for each factor separately to evaluate its influence on BMI. A p -value of 0.05 was considered statistically significant with the confidence interval (CI) of 95%.

Results

Children descriptive characteristics are presented in Table 1. Anthropometric classification showed that 62% of children were NW, 19% OW, 9% O, and 10% T. There was no significant difference according to gender, age, and height between the different groups. However, body weight (BW) was 1.28- and 1.66-fold higher, in OW and O, respectively, and 1.1-fold lower in T, than in NW. Moreover, WC increased by 12% and 41% in OW ($p < 0.05$), and O ($p < 0.01$) respectively. Furthermore, DEI enhanced in OW ($p < 0.01$), and O ($p < 0.001$), and

lowered in T ($p < 0.05$), whereas, TEE decreased in OW ($p < 0.05$), and O ($p < 0.001$), compared to NW. Indeed, PAL was similarly decreased in the same groups, since all O had a low PAL, and only 5% of OW had a high PAL. As a result, OW and O children presented positive EB, while T group had a negative EB. Besides, KidMed was increased in OW, O, and T compared with NW, in fact, in the three groups, over 80% had a low score.

As shown in table 2, there was no significant difference in SBP, DBP, glucose, TC, HDL-C, LDL-C, TG, TG/HDL-C ratio, albumin, urea, and creatinine between the different groups, excepted for UA values which increased in O ($p < 0.05$), compared to NW.

Inflammatory biomarkers are presented in Table 3. Compared to NW, OW and O children presented high leptin, IL-6 and TNF- α levels ($p < 0.001$), whereas, T group had low leptin and TNF- α values, and elevated IL-6. In contrast, adiponectin concentrations were reduced in OW and O, and leptin to adiponectin ratio (L/A) was increased in both groups, compared to NW.

Table 1. Descriptive characteristics according to BMI

Characteristics	NW	OW	O	T	P-value
N(%)	140 (62)	43 (19)	20 (9)	22 (10)	
Sex ratio (Girls/Boys)	69/71	21/22	7/13	10/12	NS
Age (years)	8.7 \pm 1.1	8.6 \pm 1.1	8.8 \pm 1.1	8.9 \pm 1.2	NS
Weight (kg)	28.6 \pm 4.4	36.6 \pm 6.0**	49.7 \pm 9.0***	25.9 \pm 5.3*	< 0.001
Height (m)	1.3 \pm 0.1	1.3 \pm 0.1	1.4 \pm 0.1	1.3 \pm 0.1	NS
BMI (kg/m ²)	16.6 \pm 1.3	20.2 \pm 1.3**	26.2 \pm 2.7***	14.5 \pm 0.7**	< 0.001
WC (cm)	60.4 \pm 4.2	67.4 \pm 7.8*	85.0 \pm 4.2**	58.3 \pm 3.8	< 0.001
DEI (Mj/d)	7.7 \pm 0.6	8.5 \pm 0.5**	11.0 \pm 0.2***	6.6 \pm 0.4*	< 0.001
TEE (Mj/d)	7.6 \pm 1.3	6.8 \pm 1.0*	6.5 \pm 0.4**	8.0 \pm 0.7	0.05
EB= DEI-TEE (Mj/d)	0.2 \pm 0.1	1.7 \pm 0.4**	4.5 \pm 0.3***	-1.4 \pm 0.2*	< 0.001
PAL	1.74 \pm 0.2	1.5 \pm 0.1**	1.3 \pm 0.1***	1.73 \pm 0.1	< 0.001
Low (%)	0	28	100	0	
Medium (%)	51	67	0	50	
High (%)	49	5	0	50	
KidMed Score	5 \pm 2	3 \pm 1*	2 \pm 1**	3 \pm 1*	0.002
Low (%)	33	83	87	83	
Medium (%)	59	17	13	17	
High (%)	8	0	0	0	

BMI: Body Mass Index, WC: Waist Circumference, DEI: Daily Energy Intake, TEE: Total Energy Expenditure, EB: Energy Balance, PAL: Physical Activity Level, NS: Not Significant. Values are expressed as mean \pm standard deviation or percentage. Significance was calculated by ANOVA followed by Student t-test: Normal weight (NW) vs Overweight (OW), Obese (O), and Thin (T). * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Table 2. Cardiometabolic markers according to BMI

Parameter	NW	OW	O	T	P-value
SBP (mmHg)	93.1 ± 11.1	96.5 ± 7.4	105 ± 7.1	93.3 ± 12.1	NS
DBP (mmHg)	58.1 ± 8.8	58.4 ± 5.6	65.0 ± 7.1	60.0 ± 10.9	NS
Glucose (mmol/L)	4.9 ± 0.4	5.1 ± 0.5	4.9 ± 0.3	4.5 ± 0.3	NS
TC (mmol/L)	4.0 ± 0.7	4.1 ± 0.5	4.2 ± 0.7	4.1 ± 0.7	NS
HDL-C (mmol/L)	1.2 ± 0.3	1.4 ± 0.4	1.2 ± 0.7	1.3 ± 0.3	NS
LDL-C (mmol/L)	2.7 ± 0.6	2.8 ± 0.4	2.9 ± 0.7	2.7 ± 0.6	NS
TG (mmol/L)	0.5 ± 0.3	0.6 ± 0.3	0.4 ± 0.1	0.4 ± 0.2	NS
TG/HDL-C	0.4 ± 0.2	0.4 ± 0.2	0.3 ± 0.1	0.3 ± 0.2	NS
Albumin (g/L)	34 ± 5	37 ± 6	31 ± 1	36 ± 6	NS
UA (μmol/L)	213 ± 36	223 ± 55	291 ± 30*	239 ± 32	0.05
Urea (mmol/L)	4.3 ± 1.0	3.6 ± 1.0	4.6 ± 1.0	3.7 ± 0.5	NS
Creatinine (μmol/L)	67 ± 20	67 ± 29	81 ± 49	78 ± 22	NS

SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, TC: Total Cholesterol; HDL-C: High-Density Lipoprotein-Cholesterol, LDL-C: Low-Density Lipoprotein-Cholesterol, TG: Triglycerides, UA: Uric Acid, NS: Not Significant. Values are expressed as mean ± standard deviation. Significance was calculated by ANOVA followed by Student t-test: Normal weight (NW) *vs* Overweight (OW), Obese (O), and Thin (T). * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Table 3. Inflammatory biomarkers according to BMI

Parameter	NW	OW	O	T	P-value
Leptin (ng/mL)	3.6 ± 1.1	13.0 ± 2.7***	18.0 ± 2.8***	2.5 ± 0.2***	< 0.001
Adiponectin (ng/mL)	11.7 ± 0.9	7.6 ± 1.3**	7.5 ± 0.7**	10.4 ± 1.3	< 0.001
Leptin/Adiponectin	0.3 ± 0.1	1.8 ± 0.5**	2.4 ± 0.6***	0.2 ± 0.0	< 0.001
IL-6 (pg/mL)	10.6 ± 3.1	24.0 ± 4.2***	30.0 ± 3.4***	20.0 ± 2.2***	< 0.001
TNF-α (pg/mL)	10.0 ± 1.1	13.0 ± 1.5***	16.0 ± 1.4***	9.3 ± 0.3***	< 0.001

IL-6: Interleukin-6, TNF-α: Tumor Necrosis Factor. Values are expressed as mean ± standard deviation. Significance was calculated by ANOVA followed by Student t-test: Normal weight (NW) *vs* Overweight (OW), Obese (O), and Thin (T). * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Ordinal logistic regression analysis of BMI *versus* all studied parameters was represented in Table 4.

Finally, after adjusting confounding variables, ordinal regression final model revealed significant positive associations of BMI with WC (OR: 1.18; IC 95%, $p = 0.01$), and leptin (OR: 1.92; IC 95%, $p < 0.001$) (Table 5).

Discussion

The aim of this study was to evaluate lifestyle, cardiometabolic risk, and inflammation markers and their

associations with BMI in scholar children. Our results demonstrated trends in the prevalence of overweight, obesity, and also thinness in this population, and explained the associations between overweight/obesity and unhealthy behaviors, like poor quality diets characterized by high energy intakes and low nutritional value, in combination with sedentary or light physical activity. Moreover, this study revealed the disturbed cardiometabolic and inflammatory status consequently to weight gain.

As reported by Li *et al* (39), easy anthropometric measurements, such as BMI and WC have been proposed in early stages to assess relationships

Table 4. Ordinal logistic regression: unadjusted association between variables and BMI

Variable	OR (Brut)	95% CI	P-value
Age	0.49	0.28 - 0.87	NS
Gender			
Girl	-	-	NS
Boy	1.36	0.51 - 3.67	
WC	1.27	1.14 - 1.42	< 0.001
DEI	16.63	5.58 - 49.59	< 0.001
KidMed	0.738	0.56 - 0.96	0.01
TEE	0.661	0.44 - 0.99	0.04
PAL	1.32	1.15 - 1.82	NS
SBP	1.03	0.98 - 1.09	NS
DBP	1.006	0.94 - 1.07	NS
Glucose	1.12	1.01 - 1.24	NS
TC	1.01	0.93 - 1.09	NS
HDL-C	1.12	0.96 - 1.29	NS
LDL-C	1.03	0.94 - 1.12	NS
TG	1.11	0.95 - 1.30	NS
Albumin	1.03	0.93 - 1.13	NS
UA	1.004	0.98 - 1.01	NS
Urea	0.95	0.51 - 1.75	NS
Creatinine	1.002	0.99 - 1.01	NS
Leptin	4.79	1.50 - 15.22	0.001
Adiponectin	0.47	0.30 - 0.73	0.001
IL-6	1.18	1.07 - 1.30	0.001
TNF- α	7.12	2.41 - 21.05	< 0.001

WC: Waist Circumference, DEI: Daily Energy Intake, TEE: Total Energy Expenditure, PAL: Physical Activity Level, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, TC: Total Cholesterol; HDL-C: High-Density Lipoprotein-Cholesterol, LDL-C: Low-Density Lipoprotein-Cholesterol, TG: Triglycerides, UA: Uric Acid, IL-6: Interleukin-6, TNF- α : Tumor Necrosis Factor, OR: Odds Ratio, CI: Confidence Interval, NS: Not Significant.

Table 5. Ordinal logistic regression: adjusted association between variables and BMI

Variable	OR (Adjusted)	95% CI	P-value
WC	1.18	1.04 - 1.33	0.01
Leptin	1.92	1.37 - 2.69	< 0.001

WC: Waist Circumference, OR: Odds Ratio, CI: Confidence Interval

between childhood obesity and cardiometabolic risk. However, there are a few studies about thinness prevalence in early childhood, despite potential negative consequences for health and development (40).

In fact, anthropometric classification of our scholar children showed that more than half of them presented NW, and 19% OW, whereas both O and T groups percentages were approximately similar. Many observations indicate this double burden of malnutrition (41). Besides, our OW and O children exhibited significant high BW, and BMI, when the reverse profile was found in T, compared to NW children, as observed in Danish and Polish children (19,40). Furthermore, WC showed a similar association with cardiometabolic risk factors, especially for TG, insulin, and MS (42). Our results showed that WC increased significantly in OW and O, the same result was previously reported in United Arab Emirates children (43).

Gain and loss weight originate from an imbalance between EI and EE, quantified by the energy imbalance (44), which can be large or sustained over longer time resulting in detectable body composition changes (45). Indeed, in our population, EI and EB were higher, whereas EE was lower in both OW and O children than their peers. These results are according to other studies (43,46). Therefore, reduction of energy intake will be essential for preventing or reducing weight gain (47), but not only. Activity-induced energy expenditure, as determined by the activity pattern including exercise, is the most variable component of DEE (45). In our study, PAL score used as a healthy pattern index, showed that OW and O children were less active than NW and T. In the same way, Li *et al* (48) found a negative correlation between BMI and PAL in Chinese children. Increased PA alone is insufficient to address the energy imbalance, so, healthy eating measures are essential for weight management. In fact, body weight is sensitive to dietary EI excess, but quality diet contributes also to weight stability, managing cardiometabolic risk (47). The traditional MD has a positive impact on children lifestyle with beneficial effects on BW, WC, blood lipid levels, fasting blood glucose, BP, inflammation, oxidative stress, and endothelial function (1,31,32,49,50). In our population, a very low percentage of children with high MD adherence was observed, and NW children had a higher KidMed score than that of OW, O, and T. In contrast, recent studies indicated that there was no significant difference between weight status and MD adherence (51,52).

The existence of overweight/obesity led to consequences on the cardiometabolic and inflammatory level. In our population, there was no significant difference in SBP, DBP, glucose, TC, HDL-C, LDL-C, TG, and TG/HDL-C, between the different groups. A similar profile was found by Donma *et al* (23), in O children, excepted for DBP and TG values which were higher, whereas, hypertension, and dyslipidaemia were found in adolescents (53, 54).

UA level, considered as an indicator for metabolically unhealthy obesity, contributing to inflammatory reaction and endothelial dysfunction disease (55,56), was significantly higher in O children than that of NW, and this was in accordance with results of Rocha *et al* (57).

Moreover, as mentioned above, changes in body composition, especially in fat mass and its distribution, are associated with alterations in adipokines secretion by adipose tissue (40). Regarding inflammatory profile, our OW and O children exhibited higher leptin concentrations, and L/A ratios, as well as, lower adiponectin concentrations, compared to NW children. These results were similar to those reported by Frithioff-Bøjsøe *et al* (19). In addition, leptin values were lower in T, compared to NW, as reported by Ambroszkiewicz *et al* (40).

Obesity is currently conceptualized as a low grade, chronic inflammatory disease (58). Our results showed a significant increase in IL-6 and TNF- α in schoolchildren with excess fat, this result is in accordance to Aburawi *et al* study (41). High plasma TNF- α and IL-6 levels are known to affect endothelial function, and stimulating inflammation-oxidative stress pathways (59–61). This knowledge underlines the link between inflammation and vascular dysfunction and atherosclerosis hypothesis (62).

Finally, ordinal logistic regression showed that although significant associations with DEI, KidMed, adiponectin, IL-6, and TNF- α were observed in the unadjusted analysis, only WC, and leptin were significantly associated in the adjusted analysis. As a result, in our population, these parameters were strongly predictive of increased BMI. Consequently, both OW and O had a tendency to present MS risk factors, the same profile was observed in adolescents of the same city (53).

The present study had a strength for being the first exploring cardiometabolic and inflammatory

profile in Algerian children. However; some limitations were reported including relatively small number of participants, and a lack of other possible confounders. Furthermore some results did not reach or were bordered on statistical significance. Moreover, the cross-sectional nature of this study does not allow us to confirm the causality between BMI and lifestyle parameters. Thus, longitudinal studies are needed for investigating lifestyle benefits on obesity-related disorders.

Conclusion

This study suggests obesity-related disorders in response to low MD adherence, excess EI, and sedentary. Our findings highlight the association between weight gain and serum levels of adipokines and cytokines as significant predictors of metabolically unhealthy status. Furthermore, subjects classified with a high WC, and leptin levels have the highest odds of expressing OW and O independently of others potential confounders. In regard to beneficial changes in BMI, and significant improvements in metabolic indicators, providing healthy pattern, like promoting well-tested traditional MD type, and PA, is required in young populations.

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References

1. Agostinis-Sobrinho C, Ramírez-Vélez R, García-Hermoso A, et al. The combined association of adherence to Mediterranean diet, muscular and cardiorespiratory fitness on low-grade inflammation in adolescents: a pooled analysis. *Eur J Nutr* 2019; 58(7): 2649–2656.
2. Kim J, Lim H. Nutritional Management in Childhood Obesity. *J Obes Metab Syndr* 2019; 28(4): 225–235.
3. Rosi A, Giopp F, Milioli G, et al. Weight Status, Adherence to the Mediterranean Diet, Physical Activity Level, and Sleep Behavior of Italian Junior High School Adolescents. *Nutrients* 2020; 12(2): 478–489.
4. González K, Fuentes J, Márquez J. Physical Inactivity, Sedentary Behavior and Chronic Diseases. *Korean J Fam Med* 2017; 38: 111–115.
5. Leech RM, McNaughton SA, Timperio A. The clustering of diet, physical activity and sedentary behavior in children and adolescents: a review. *Int J Behav Nutr Phys Act* 2014; 11(1): 4–12.
6. Bawaked RA, Fernández Barrés S, Navarrete Muñoz EM, et al. Impact of lifestyle behaviors in early childhood on obesity and cardiometabolic risk in children: Results from the Spanish INMA birth cohort study. *Pediatr Obes* 2019; 15(3). DOI:10.1111/ijpo.12590
7. Fujita Y, Kouda K, Ohara K, Nakamura H, Iki M. Leptin mediates the relationship between fat mass and blood pressure: The Hamamatsu School-based health study. *Medicine* 2019; 98(12). DOI:10.1097/MD.00000000000014934
8. WHO. World Health Organization: Obesity and overweight. 2018. Available at: <https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight>
9. Sulistyoningrum DC, Susilowati R, Huriyati E, Witari NPD, Luglio HF, Julia M. Tumour necrosis factor- α and risk of cardiovascular disease among overfat Indonesian adolescents. *Asia Pac J Clin Nutr* 2017; 26(S1): 50–56.
10. Al-Hamad D, Raman V. Metabolic syndrome in children and adolescents. *Transl Pediatr* 2017; 6(4): 397–407.
11. Bruyndonckx L, Hoymans VY, Lemmens K, Ramet J, Vrints CJ. Childhood obesity-related endothelial dysfunction: an update on pathophysiological mechanisms and diagnostic advancements. *Pediatr Res* 2016; 79(6): 831–837.
12. Dhawan D, Sharma S. Abdominal Obesity, Adipokines and Non-communicable Diseases. *J Steroid Biochem Mol Biol* 2020; 203. DOI:10.1016/j.jsbmb.2020.105737
13. D'Adamo E, Guardamagna O, Chiarelli F, et al. Atherogenic Dyslipidemia and Cardiovascular Risk Factors in Obese Children. *Int J Endocrinol* 2015. DOI:10.1155/2015/912047
14. Jena SK. Correlation of abdominal obesity indices with blood pressure in young adults: A cross-sectional study. *Adv Hum Biol* 2018; 8(1): 46–48.
15. Scheuer SH, Furch K, Philipsen A, et al. Abdominal Fat Distribution and Cardiovascular Risk in Men and Women With Different Levels of Glucose Tolerance. *J Clin Endocrinol Metab* 2015; 100(9): 3340–3347.
16. Reilly SM, Saltiel AR. Adapting to obesity with adipose tissue inflammation. *Nat Rev Endocrinol* 2017; 13(11): 633–643.
17. Vukovic R, Dos Santos TJ, Ybarra M, Atar M. Children With Metabolically Healthy Obesity: A Review. *Front. Endocrinol* 2019; 10:865.
18. Lausten-Thomsen U, Lund MAV, Frithioff-Bøjsøe C, et al. Reference values for leptin/adiponectin ratio in healthy children and adolescents. *Clin Chim Acta* 2019; 493: 123–128.
19. Frithioff Bøjsøe C, Lund MAV, Lausten Thomsen U, et al. Leptin, adiponectin, and their ratio as markers of insulin resistance and cardiometabolic risk in childhood obesity. *Pediatr Diabetes* 2020; 21(2): 194–202.
20. Li G, Xu L, Zhao Y, et al. Leptin-adiponectin imbalance as a marker of metabolic syndrome among Chinese children and adolescents: The BCAMS study. *PLOS ONE* 2017; 12(10). DOI:10.1371/journal.pone.0186222
21. Fasshauer M, Blüher M. Adipokines in health and disease. *Trends Pharmacol Sci* 2015; 36(7): 461–470.
22. Breitfeld J, Sabdvoss R, Schleinitz D, et al. Serum adiponectin and progranulin levels are associated with gallstone disease. *Exp Clin Endocrinol Diabetes* 2014; 122(10): 559–563.
23. Donma MM, Demirkol M, Ekmekci H, Ekmekci OB, Donma O. Pentraxin-3, Angiopoietin-Like Protein-3, Angiopoietin-Like Protein-4 and Angiopoietin-Like Protein-8 Levels in Morbid Obese Children. *Med One* 2017; 2(6). DOI:10.20900/mo.20170029
24. Donma MM, Ekmekci OB, Ekmekci H, Donma O. Evaluation of the Markers Affecting Obesity in Children. *Med One* 2018; 3. DOI:10.20900/mo.20180004
25. Dali-Youcef N. Inflammation métabolique et insulino-résistance : Les connaissances actuelles. *Médecine Mal Métaboliques* 2015; 9(3):279–291.
26. Whatnall M, Collins C, Callister R, Hutchesson M. Associations between Unhealthy Diet and Lifestyle Behaviours and Increased Cardiovascular Disease Risk in Young Overweight and Obese Women. *Healthcare* 2016; 4(3):57.
27. Willett WC, Koplan JP, Nugent R, Dusenbury C, Puska P, Gaziano TA. Prevention of Chronic Disease by Means of Diet and Lifestyle Changes. In: Jamison DT, Breman JG, Measham AR, et al., editors. *Disease Control Priorities in Developing Countries*. 2nd edition. Washington (DC) 2006; Chapter 44.
28. Castiglione D, Platania A, Conti A, Falla M, D'Urso M, Marranzano M. Dietary Micronutrient and Mineral Intake in the Mediterranean Healthy Eating, Ageing, and Lifestyle (MEAL) Study. *Antioxidants* 2018; 7(7):79.
29. Grosso G, Marventano S, Yang J, et al. A comprehensive meta-analysis on evidence of Mediterranean diet and cardiovascular disease: Are individual components equal? *Crit Rev Food Sci Nutr* 2017; 57(15):3218–3232.
30. Shah R, Makarem N, Emin M, Liao M, Jelic S, Aggarwal B. Mediterranean diet components are linked to greater endothelial function and lower inflammation in a pilot study of ethnically diverse women. *Nutr Res* 2020; 75:77–84.

31. Godos J, Zappalà G, Bernardini S, Giambini I, Bes-Rastrollo M, Martinez-Gonzalez M. Adherence to the Mediterranean diet is inversely associated with metabolic syndrome occurrence: a meta-analysis of observational studies. *Int J Food Sci Nutr* 2017; 68(2): 138–148.
32. Garcia M, Bihuniak J, Shook J, Kenny A, Kerstetter J, Huedo-Medina TB. The Effect of the Traditional Mediterranean-Style Diet on Metabolic Risk Factors: A Meta-Analysis. *Nutrients* 2016; 8(3): 168–185.
33. Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. *BMJ* 2000; 320(7244): 1240–1245.
34. Cole TJ, Flegal KM, Nicholls D, Jackson AA. Body mass index cut offs to define thinness in children and adolescents: international survey. *BMJ* 2007; 335(7612): 194–201.
35. Musse JP, Musse. GENI (Gestion d'Enquêtes Nutritionnelles Informatisées). *Micro 6 (France)* 2000; Version 6.
36. Serra-Majem L, Ribas L, Ngo J, et al. Food, youth and the Mediterranean diet in Spain. Development of KIDMED, Mediterranean Diet Quality Index in children and adolescents. *Public Health Nutr* 2004; 7(7): 931–935.
37. Friedewald W, Levy R, Fredrickson S. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chemistry* 1972; 18: 499–502.
38. Royston P. Multiple imputation of missing values. *Stata J* 2004; 4(3): 227–241.
39. Li Y, Zou Z, Luo J, et al. The predictive value of anthropometric indices for cardiometabolic risk factors in Chinese children and adolescents: A national multicenter school-based study. *PLOS ONE* 2020; 15(1). DOI:10.1371/journal.pone.0227954
40. Ambroszkiewicz J, Gajewska J, Szamotulska K, Rowicka G, Klemarczyk W, Chełchowska M. Comparison of body composition and adipokine levels between thin and normal-weight prepubertal children. *J Pediatr (Rio J)* 2017; 93(4): 428–435.
41. Nugent R, Levin C, Hale J, Hutchinson B. Economic effects of the double burden of malnutrition. *The Lancet* 2020; 395(10218): 156–164.
42. Arellano-Ruiz P, García-Hermoso A, García-Prieto JC, Sánchez-López M, Vizcaíno VM, Solera-Martínez M. Predictive Ability of Waist Circumference and Waist-to-Height Ratio for Cardiometabolic Risk Screening among Spanish Children. *Nutrients* 2020; 12(2): 415–426.
43. Aburawi EH, Al Hamad S, Yasin J, Almekhaini LA, Souid AK. Dyslipidemia, subclinical inflammation, hepatic cholestasis and endothelial dysfunction in schoolchildren with excess fat: A study from the United Arab Emirates. *PLOS ONE* 2019; 14(1). DOI:10.1371/journal.pone.0210316
44. Fallah-Fini S, Ikeda N, Nishi N. Trends in Energy Imbalance Gap and Body Weight Status in the Japanese Adult Population: A System Dynamics Approach. *J Epidemiol* 2021; 31(5): 335–342.
45. Westerterp KR. Exercise, energy balance and body composition. *Eur J Clin Nutr* 2018; 72(9):1246–1250.
46. Azizi-Soleiman F, Motlagh ME, Qorbani M, et al. Dietary Habits and Health Related Behaviors in Iranian Children and Adolescents: The CASPIAN- IV Study. *Int J Pediatr* 2016; 4(7)31: 2087–2097.
47. Teasdale SB, Ward PB, Jarman R, et al. Is Obesity in Young People With Psychosis a Foregone Conclusion? Markedly Excessive Energy Intake Is Evident Soon After Antipsychotic Initiation. *Front Psychiatry* 2018; 9:725.
48. Li LB, Wang N, Wu XL, et al. Energy Balance-related Behaviors Are Related to Cardiometabolic Parameters and Predict Adiposity in 8–14-year-old Overweight Chinese Children One Year Later. *Biomed Env Sci* 2016; 29(10): 754–757.
49. Idelson PI, Scalfi L, Valerio G. Adherence to the Mediterranean Diet in children and adolescents: A systematic review. *Nutr Metab Cardiovasc Dis* 2017; 27(4): 283–299.
50. Castiglione D, Platania A, Conti A, Falla M, D'Urso M, Marranzano M. Dietary Micronutrient and Mineral Intake in the Mediterranean Healthy Eating, Ageing, and Lifestyle (MEAL) Study. *Antioxidants* 2018; 7(7): 79–95.
51. López-Gil JF, Brazo-Sayavera J, García-Hermoso A, Yuste Lucas JL. Adherence to Mediterranean Diet Related with Physical Fitness and Physical Activity in Schoolchildren Aged 6–13. *Nutrients* 2020; 12(2): 567–579.
52. Grassi T, Bagordo F, Panico A, et al. Adherence to Mediterranean diet of children living in small Southern Italian villages. *Int J Food Sci Nutr* 2020; 71(4): 490–499.
53. Ghomari-Boukhatem H, Bouchouicha A, Mekki K, Chenni K, Belhadj M, Bouchenak M. Blood pressure, dyslipidemia and inflammatory factors are related to body mass index in scholar adolescents. *Arch Med Sci* 2017; 13(1): 46–52.
54. Klisic A, Kavacic N, Ninic A. Serum cystatin C levels are associated with triglycerides/high-density lipoprotein cholesterol ratio in adolescent girls ages between 16–19 years old. *Eur Rev Med Pharmacol Sci* 2020; 24(20):10680–10686.
55. Özalp Kızılay D, en S, Ersoy B. Associations Between Serum Uric Acid Concentrations and Cardiometabolic Risk and Renal Injury in Obese and Overweight Children. *J Clin Res Pediatr Endocrinol* 2019; 11(3): 262–269.
56. Valle M, Martos R, Cañete MD, et al. Association of serum uric acid levels to inflammation biomarkers and endothelial dysfunction in obese prepubertal children. *Pediatr Diabetes* 2015; 16(6): 441–447.
57. Rocha EPAA, Vogel M, Stanik J, et al. Serum Uric Acid Levels as an Indicator for Metabolically Unhealthy Obesity in Children and Adolescents. *Horm Res Paediatr* 2018; 90(1): 19–27.
58. Stolarczyk E. Adipose tissue inflammation in obesity: a metabolic or immune response? *Curr Opin Pharmacol* 2017; 37: 35–40.
59. Popescu LA, Virgolici B, Stefan DCA, et al. Vascular Reactivity and Proinflammatory Cytokines in the Obese Children. *Rev Chim* 2017; 68(4): 758–762.

60. Gimbrone MA, García-Cardena G. Endothelial Cell Dysfunction and the Pathobiology of Atherosclerosis. *Circ Res* 2016; 118(4): 620–636.
61. 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): 441–455.
62. Marti A, Morell-Azanza L, Rendo-Urteaga T, et al. Serum and gene expression levels of CT-1, IL-6, and TNF- α after a lifestyle intervention in obese children. *Pediatr Diabetes* 2018; 19(2): 217–222.

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