

## Study on dietary constituents, hs-CRP serum levels and investigation of correlation between them in excess weight adolescents

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### Abstract

**Background:** The prevalence of childhood obesity has increased in Greece as well as worldwide. Mediterranean diet is considered the world's most popular healthy eating pattern. C-reactive protein (CRP) has been shown to play an important pathophysiological role between inflammation and cardiovascular diseases and has been linked to obesity. Our study aimed to investigate the adolescents' diet, their high-sensitivity CRP (hs-CRP) serum levels, and whether low-grade inflammation, present in obesity, is related to adolescents' diet.

**Methods:** The sample of the study consisted of 142 adolescents age- and gender- matched  $13.4 \pm 1.46$  years, divided into two groups: the study group and the controls. The study group of 71 excess body weight adolescents was further divided into two subgroups of 28 overweight and 43 obese respectively; 71 normal weight age- and gender-matched served as controls. Dietary constituents (food weight, energy intake, protein, carbohydrate and fat consumption, fiber, and sugars) were analyzed. Adherence to the Mediterranean diet was investigated, and hs-CRP serum levels were determined. The findings were compared between/among groups. Furthermore, the correlation of hs-CRP serum levels and food constituents between/among groups was investigated.

**Results:** We documented differences in several parameters among the groups: waist to hip ratio ( $p=0.001$ ), food weight ( $p=0.040$ ), energy intake ( $p=0.024$ ), protein intake ( $p=0.001$ ), total fibre ( $p=0.017$ ), sugars ( $p=0.001$ ), and the Mediterranean Diet Quality Index for children and adolescents (KIDMED;  $p=0.008$ ). No statistically significant difference was found for hs-CRP serum levels among the three groups. No correlation was found between hs-CRP serum levels and any of the dietary constituents.

**Conclusions:** Comparing the three groups (obese, overweight, and controls), we found statistically significant differences for food constituents but not for hs-CRP serum levels. In our study, inflammation was not found to be correlated with any of the dietary constituents. Further studies in a larger sample are required to consolidate these findings.

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**Keywords:** Childhood obesity, adolescents, inflammation, hs- CRP, Mediterranean diet, macronutrient intake

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### Introduction

The rate of overweight and obesity in adults and children has been increasing all around the world over the preceding decades. It has become a serious health issue due to its association with various chronic health disorders, such as cardiovascular diseases<sup>1</sup>. Chronic health issues that contribute to increased inflammation and elevation of inflammatory biomarkers seem to initiate in childhood, though their manifestations mainly occur in adulthood<sup>1,2</sup>. One of these chronic health issues is obesity.

There have been suggestions for healthy dietary patterns to avoid such manifestations<sup>3,4</sup>. Mediterranean diet is one of these dietary patterns characterized by low consumption of red meat, abundant consumption of fruit, vegetables, whole-grain cereal, and nuts, while olive oil

as one of the main nutrient characteristics, all known for anticoagulant and anti-inflammatory properties<sup>5,6</sup>.

Another factor related to obesity is C-reactive protein (CRP), an acute phase protein<sup>7</sup>, produced in the liver in response to increased cytokine levels, such as tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and interleukin-6 (IL-6)<sup>8</sup>. Adipose tissue, augmented in obesity, excretes these two cytokines, as well as other adipokines, promoting the production of CRP in low levels enhancing chronic low-grade inflammation. Many studies have shown a strong correlation between high-sensitivity CRP (hs-CRP) and cardiovascular diseases<sup>1,9</sup>. Thus, it can serve as a biomarker to identify people at risk<sup>2</sup>. The comparison of CRP serum levels between obese and normal-weight people has revealed higher levels of this protein in obesity in

the absence of any other obvious cause<sup>9</sup>.

The objectives of the present study were i) to compare waist-to-hip ratio, the consumed food (weight, total energy intake, macronutrient consumption, fiber, and total sugars), and the adherence to the Mediterranean diet between and among groups classified according to BMI, ii) to compare hs-CRP levels between and among groups classified according to BMI, and iii) to assess the possible correlation of hs-CRP serum levels with the consumed food (weight, total energy intake, macronutrient consumption, fiber, and total sugars), and the adherence to the Mediterranean diet.

## Methods

The study commenced in May 2011, and the sample enrolment proceeded until May 2015. Participants (controls and increased weight) were children from families originating from different areas of Northern Greece, with a medical history of cardiovascular diseases that were examined in the Outpatient Clinic of Lipids and Cardiovascular Diseases Prevention from Childhood, of the 2<sup>nd</sup> Pediatric Department, in AHEPA University Hospital of the Aristotle University of Thessaloniki, Greece. To ensure eligibility of the study, children and their parents/guardians were fully informed regarding the procedure and the purpose of the study. Adolescents consented verbally and, afterward, parents/guardians signed an informed consent form. The study was approved by the Bioethics and Ethics Committee of the Medical Faculty of Aristotle University of Thessaloniki (decision No 2; 23/3/2016).

Exclusion criteria were set to eliminate potential bias. Therefore, blood was drawn, according to institutional protocols, from all adolescents for white blood cells count, investigation of serum hs-CRP levels, liver function enzymes [serum glutamic-pyruvic transaminase (SGPT), serum glutamic oxaloacetic transaminase (SGOT), and gamma-glutamyltransferase ( $\gamma$ -GT)], and thyroid function [thyroid-stimulating hormone (TSH)]. Adolescents with abnormal TSH and liver enzyme levels or with any other clinical condition were excluded from the study.

The final sample consisted of 142 adolescents (66 girls and 76 boys), aged  $13.4 \pm 1.46$  years. Participants were initially divided into two groups, the excess weight and the normal-weight adolescents (controls). We further divided the excess weight adolescents into obese and overweight groups. Comparisons were made between excess weight adolescents and controls followed by comparisons between obese and controls, overweight and controls, obese and overweight, and finally among all three groups for the anthropometry, the results of the 24hr recall dietary analysis, the Mediterranean Diet Quality Index for children and adolescents (KIDMED) score and the hs-CRP serum levels.

### *Anthropometric measurements*

Height was measured to the nearest 0.1 cm with a

Raven Minimater (Raven Equipment Limited, Essex, United Kingdom). Weight was measured to the nearest 100 grams with the Tanita HD351 model weighing scale. Body mass index (BMI) was calculated with the formula  $BMI = \text{weight}/\text{height}^2$ . Participants were then classified into overweight, obese, and normal-weight based on the age and sex cut-off points for BMI, according to the International Obesity Task Force recommendations<sup>10</sup>. Seventy-one adolescents of excess body weight (28 overweight and 43 obese) formed the study group. The normal-weight group (control group) consisted of 71 age- and gender-matched adolescents.

Waist circumference and hip circumference were measured to the nearest 0.1 cm by using a SECA measuring tape (SECA GmbH & Co., Hamburg, Germany). Waist-to-hip (W/H) ratio was then calculated.

### *Nutritional habits*

Two questionnaires for the assessment of the dietary habits of the adolescents were used and completed by the participating children and their parent/guardian. The first one was the 24-hour recall (completed for two days). It was used to calculate the total weight of food and its mean content in macronutrient consumption (total fat, protein, and carbohydrates), sugars, and fibers. Collected data was analyzed using the nutritional software Horizon 2010 (Ermis Informatics, Athens, Greece).

The second questionnaire completed, to assess adherence to the Mediterranean diet, was the KIDMED score. KIDMED score is an index assessing the quality of diet and the adherence to the Mediterranean dietary pattern in children and adolescents. It consists of 16 questions scored +1 or -1, and the maximum score of positive answers is 12. The total score is classified into three levels. The first level  $\leq 3$  indicates a diet pattern away from the Mediterranean type and of very low quality. The second level (score: 4-7), indicates that some aspects are followed in accordance with the Mediterranean diet, but improvements are needed in diet quality. The third level of this classification (score  $\geq 8$ ) indicates compliance of the diet with the Mediterranean dietary pattern and high-quality diet<sup>11</sup>.

### *hs-CRP measurement procedure*

In order to measure hs-CRP serum levels, a blood sample was analyzed with the Latex High Sensitivity method by Roche in the Cobas Integra 400, Roche analyzer.

### *Statistical analysis*

Data were analyzed with the use of IBM SPSS Statistics for Windows, Version 20 (IBM Corp., Armonk, NY). The Kolmogorov-Smirnov test was utilized to check the normality of the distribution of the variables, which expressed as medians (minimum-maximum in brackets). The Mann-Whitney U-test was used for all non-parametric comparisons between the two groups, while the Kruskal-Wallis test was used for comparisons among the

three groups. Spearman's correlation coefficient was calculated to investigate any possible correlation between independent parameters of hs-CRP serum levels, anthropometry measurements, and results of nutritional habits analysis. The level of statistical significance was set at  $p \leq 0.05$ .

## Results

Results of the anthropometry, the 24hr dietary recall (dietary constituents), and the KIDMED score are presented in Table 1, comparing the different groups as classified according to the BMI. A statistically significant difference is evident in the W/H ratio ( $p = 0.001$ ) between groups. The higher W/H ratio is found in the obese group (0.87), followed by the overweight (0.84), and sequentially the controls (0.77). Additionally, the three groups differ in food weight intake ( $p = 0.040$ ). Specifically, there is a statistically significant difference only when comparing overweight adolescents with controls and obese with overweight adolescents: controls consume more food in weight (1,235 g) than overweight (1,019 g;  $p = 0.047$ ), while obese consume more (1,314 g) compared to overweight (1,019 g;  $p = 0.012$ ). When calculating the total energy intake, obese adolescents seem to ingest numerically more food in terms of calories compared to controls and overweight, as shown in Table 1, reaching a significant difference ( $p = 0.024$ ) among all three groups. It is clear that obese outnumber in calorie consumption when compared to overweight adolescents ( $p = 0.019$ ) as well as with controls ( $p = 0.018$ ). When comparing the excess weight group to controls, there is a difference of 374 calories, not reaching significance.

The results of dietary constituents are presented in Table 1. The protein consumption in paired groups reveals that the excess weight group, the obese, and the overweight subgroups consume more protein than controls ( $p = 0.001$  for all three comparisons). In Table 1 is apparent that obese and overweight adolescents consume almost the same amount of protein (18 % and 17 %, respectively), differing significantly from controls ( $p = 0.001$ ). Regarding the carbohydrate consumption, it is higher in the control group (44.3 %), followed by the overweight group (43 %) and the obese group (42 %). The only statistical significance was between control and obese and that was just about significant. Fat consumption is similar in all paired groups, as well as among the three groups ranging around 40 %. Fiber consumption differs among groups ( $p = 0.017$ ): controls consume the highest amount of fibers (14.3 g), followed by obese (11 g) and, finally, the overweight adolescents (10.1 g). Although the two overweight groups did not differ statistically between them, comparisons of either group with the controls reached significance (Table 1). Controls consume more sugars (52.2 g) than any other group. It is worth mentioning that in all paired groups comparisons with controls, the normal-weight adolescents outperform in sugars consumption ( $p = 0.001$ ).

The KIDMED score among groups is presented in

Table 1, revealing that the overweight group scores seven, controls six, and finally, the obese five. Among them, the difference is statistically significant ( $p = 0.001$ ). Out of all paired comparisons, only the comparisons of all other groups with the obese group reveal significant differences ( $p = 0.036$  and  $p = 0.002$ ).

The hs-CRP serum levels are also presented in Table 1. As shown, the overweight group has the higher hs-CRP levels (0.46 mg/dl); slightly higher than in the obese but not statistically significant (0.46 vs 0.38 mg/dl;  $p = 0.368$ ), while hs-CRP serum levels of the controls are almost half compared to the other two groups and decisively different ( $p = 0.001$ ).

Finally, in Table 2, we present the assessment of any possible correlation between hs-CRP serum levels with W/H ratio, the results of 24hr recall, and KIDMED, separately for the obese, the overweight adolescents, and the controls. No correlation was apparent between hs-CRP serum levels and W/H ratio, any of the dietary constituents, and finally, the KIDMED score.

## Discussion

Current study helps to shed some light on the characteristics of childhood obesity regarding the consumed nutrients, adherence to the Mediterranean diet, inflammation, and any possible correlation between the above.

The W/H ratio seems to correlate positively with increasing BMI, as expected. It should be noted that there are no cut-off points for children and adolescents regarding this ratio at present, according to World Health Organisation<sup>12</sup>. Still, the measurement of the ratio provides more information beyond BMI pertaining to the accumulation of fat in the abdomen and thighs<sup>13</sup>. Therefore, W/H ratio is considered a useful method for detecting adiposity distribution in children<sup>14</sup>, considering that central obesity (increased waist circumference) is a predisposing factor for the development of cardiometabolic diseases<sup>15</sup>. Such predisposition to future health risks cannot be anticipated solely based on the BMI, which demonstrates the volume of the body but not the fat content nor its distribution<sup>16</sup>.

Both the energy intake and the food weight intake are higher in the obese group, a somewhat expected finding as obese consume more than the needed calories, and thus, they gain weight. Apart from ingesting more calories, they usually consume more food in weight, in order to satisfy their satiety.

In reference to the comparison of nutrients consumption, protein consumption is increased both in the overweight and the obese group, revealing a deviation from the Mediterranean dietary pattern and an attachment to the western-type, characterized by increased meat consumption. Adequate protein consumption is required for optimal growth of children<sup>17</sup>; however, a consumption higher than required contributes to increased body weight<sup>18</sup>. It is attributed to the fact that in a western-type diet, protein-rich foods are high in fat content (processed meats, dairy products, etc.). Also, this kind of food, though rich in calories, does not promote satiety. In gen-

**Table 1:** Comparisons of waist-to-hip ratio, results of 24hr recall, KIDMED score, and hs-CRP serum levels i) between the adolescents of excess weight (including the overweight and the obese subgroups) and controls (Ex vs C), ii) between obese adolescents and controls (Ob vs C), iii) between overweight adolescents and controls (Ov vs C), iv) between obese and overweight adolescents (Ob vs Ov), and among all three groups, obese, overweight adolescents and controls (among Ob, Ov, C).

	Controls (n =71)	Excess weight (n =71)	P (Ex vs C)	Obese (n =43)	P (Ob vs C)	Overweight (n =28)	P (Ov vs C)	P (Ob vs Ov)	P (among Ob, Ov, C)
Waist-to-hip ratio (W/H)	0.77 (0.64-1.32)	0.85 (0.68-1.08)	<b>0.001*</b>	0.87 (0.68-1.71)	<b>0.001*</b>	0.84 (0.74-0.93)	<b>0.001*</b>	<b>0.007*</b>	<b>0.001*</b>
Food weight (g)	1235 (602-3040)	1220 (408-3196)	0.562	1314 (704-3196)	0.512	1019 (569-2818)	<b>0.047*</b>	<b>0.012*</b>	<b>0.040*</b>
Energy (calories)	1778 (603-5072)	2161 (788-5326)	0.154	2296 (1444-5326)	<b>0.018*</b>	1740 (788-4674)	0.692	<b>0.019*</b>	<b>0.024*</b>
Protein (%)	14.5 (6.7-22)	18 (11-31)	<b>0.001*</b>	18 (11-25)	<b>0.001*</b>	17 (14-31)	<b>0.001*</b>	0.682	<b>0.001*</b>
Carbohydrates (%)	44.3 (32-65)	42 (19-56)	<b>0.035*</b>	42 (30-55)	<b>0.05*</b>	43 (19-56)	0.138	0.792	0.105
Fat (%)	40.3 (27-58)	40 (17-59)	0.730	41 (24-52)	0.958	40 (17-59)	0.551	0.660	0.841
Fiber (g)	14.3 (3.1-69.4)	10 (2.4-36.7)	<b>0.006*</b>	11 (4-27)	<b>0.045*</b>	10.1 (2.4-23.4)	<b>0.009*</b>	0.462	<b>0.017*</b>
Total sugars (g)	52.2 (5.6-122)	29.5 (0-106)	<b>0.001*</b>	31 (2-106)	<b>0.001*</b>	22 (2-65)	<b>0.001*</b>	0.969	<b>0.001*</b>
KIDMED score	6 (1-11)	5 (0-11)	0.407	5 (0-9)	<b>0.036*</b>	7 (0-11)	0.221	<b>0.002*</b>	<b>0.008*</b>
hs-CRP serum levels (mg/dl)	0.2 (0.06-2.1)	0.43 (0.04-2.9)	<b>0.001*</b>	0.38 (0.02-2.51)	<b>0.001*</b>	0.46 (0.01-2.78)	0.227	0.563	0.368

Values are expressed as medians (minimum-maximum in brackets) while in bold are marked statistically significance differences; KIDMED: the Mediterranean Diet Quality Index for children and adolescents, hs-CRP: high sensitivity C-reactive protein, Ex: adolescents of excess weight, C: controls, Ob: obese adolescents, Ov: overweight adolescents.

eral, the westernized way of eating is considered a path for weight gain as it includes non-balanced diets, rich in fat and meat, but low in fruit, vegetables, and carbohydrates<sup>19</sup>.

The consumption of carbohydrates in the study was similar among all groups. This percentage was higher in the normal-weight group, which is expected as when following a diet rich in complex carbohydrates (up to 50 % of total energy intake), one can achieve satiety and weight control<sup>18</sup>.

Fat consumption was similar in all groups examined (around 40 %, Table 1). This finding could be attributed to the fact that in Greece, as in most Mediterranean regions, the main constituent of the diet is the olive oil, widely and abundantly used. The high-fat consumption is in accordance with our findings, indicating that there is some diet quality and adherence to the Mediterranean dietary pattern. In addition, high-protein consumption could also contribute to high-fat consumption, as meat is high in fat content. Furthermore, the way of cooking, especially fried food (meat or food accompaniments), might also be another factor contributing to high-fat consumption. Our investigation did not elaborate on the type of fats consumed. We can only hypothesize that controls ingested more vegetable oils and less animal fat.

Comparison among groups revealed that the control group consumed the highest quantities of fiber compared to both the excess weight groups (p =0.017). The fact that the controls also score six in KIDMED is an indication of partial adherence to the Mediterranean diet. It has been proven that fiber is abundant in the Mediterranean diet, and the co-existence of high fiber content and the Mediterranean dietary pattern contributes to weight control and satiety by decreasing the absorption and consumption of excess food<sup>20</sup>. This conclusion is also supported by our findings in Table 1, which indicates that the overweight group scores seven in KIDMED and has better weight control<sup>20</sup> than the obese who score five. To our knowledge, such a comparison is presented in the literature for the first time.

Regarding sugar consumption, our findings are in accordance with the increased consumption of sugars globally<sup>21</sup>. In general, adolescents with high sugar consumption may be affected by the advertisement on television<sup>22</sup>. Adolescence is also a period of starting the habit of going out with friends and consuming sweets or sweet beverages. In our study, the controls consumed the highest amount of sugars (52.2 g), followed by the obese (31 g), and the overweight (22 g) groups. The explanation of this fact may lie in different causes. First of all, all adolescents enrolled in our study come from an outpatient clinic for cardiovascular disease prevention from childhood; therefore, the controls may come from overweight and obese families and follow dietary patterns of their environment, possibly high in sugars. Furthermore, being aware of the fact of not having excess weight, controls could consume higher quantities of sugars without gaining weight<sup>23</sup>. Finally, they may do intense physical

**Table 2:** Correlation of hs-CRP serum levels with waist to hip ratio, food constituents and KIDMED score for all three groups (obese, overweight adolescents and controls).

	hs-CRP Rho (p)		
	Obese (n =43)	Overweight (n =28)	Controls (n =71)
Waist-to-hip ratio (W/H)	-0.059 (0.737)	-0.057 (0.828)	-0.003 (0.985)
Food weight (g)	0.048 (0.789)	0.011 (0.964)	-0.14 (0.331)
Energy (calories)	0.049 (0.781)	0.096 (0.704)	-0.058 (0.687)
Protein (%)	-0.014 (0.935)	-0.140 (0.580)	-0.041 (0.780)
Carbohydrates (%)	-0.089 (0.308)	0.227 (0.366)	-0.167 (0.247)
Fat (%)	-0.187 (0.291)	-0.183 (0.467)	0.174 (0.227)
Fiber (g)	-0.171 (0.334)	0.411 (0.101)	-0.267 (0.060)
Total sugars (g)	-0.098 (0.581)	-0.044 (0.866)	-0.121 (0.402)
KIDMED Score	-0.062 (0.725)	-0.140 (0.579)	-0.099 (0.503)

Rho: stands for correlation; KIDMED: the Mediterranean Diet Quality Index for children and adolescents, hs-CRP: high sensitivity C-reactive protein.

activity or be in sprout period, factors not examined in this study. Our results are in accordance with the study of Gasser et al, concluding that there was no correlation between sweets consumption and obesity<sup>24</sup>. Nonetheless, we need to mention that high sugar consumption is a dietary habit possibly linked to inflammation<sup>25</sup>.

hs-CRP serum levels of increased weight adolescents (0.43 mg/dl) are twice as much as those of controls (0.2 mg/dl). The study of Blake and Ridker revealed in 2002 that there was a correlation between high hs-CRP serum levels and BMI values<sup>9</sup>. It is noteworthy that the results in Table 1 show that the overweight group has the highest hs-CRP serum levels, even higher than the obese adolescents. There is no explanation for this finding; however, one could hypothesize that the excess weight of individuals in the pre-obese state is associated with relatively acute inflammation. In the case of obese individuals, the inflammation is assumed to be a chronic and exhausted state and therefore indicated by a reduction of CRP levels, possibly suggesting some adaptation to the established obesity. Obese participants, on the other hand, have been exposed to inflammation of adipose tissue excretion for longer, and therefore, hs-CRP levels may have been adapted and possibly reduced.

No correlation was found between the hs-CRP serum levels, indicating inflammation, and any of the dietary constituents. However, Gupta et al supported that inflammation indicated by increased hs-CRP serum levels was related to high sugar consumption<sup>26</sup>. Thus, we need a larger sample for safer results confirmation and consolidation. Similarly, we did not find any correlation between hs-CRP serum levels with KIDMED score (Table 2).

The present study has certain limitations: physical activity and socioeconomic conditions were not taken into consideration, and the number of adolescents ultimately recruited was small mainly due to practical difficulties (expenses for transportation and medical care could not be covered by additional funding). Nevertheless, presented data are indicative regarding the dietary intake and eating habits of adolescents of Northern Greece, as well as differences between overweight and obese adolescents, investigated for the first time, to our knowledge.

Further research with a greater number of participants is needed to provide more robust data.

In conclusion, inflammation seems to depend on the increase of BMI but does not correlate with any of the dietary constituents assessed in this study. Therefore, dietary education and intervention is necessary and seems obligatory in order to reduce childhood obesity rates and to eliminate low-grade inflammation and long-term health consequences, such as cardiovascular diseases. For this reason, there is a need for continuous effort in nutritional education from parents and relatives, healthcare professionals, school teachers, mass media, and governmental authorities. The role of Nutritionists/Dietitians, in cooperation with other healthcare professionals, is also very important as they can contribute to public education and entire family intervention programs to eliminate obesity prevalence.

#### Conflict of interest

Authors declare no conflict of interest.

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#### References

- Ha EE, Bauer RC. Emerging Roles for Adipose Tissue in Cardiovascular Disease. *Arterioscler Thromb Vasc Biol.* 2018; 38: e137-e144.
- Pires A, Martins P, Pereira AM, Marinho J, Vaz Silva P, Marques M, et al. Pro-inflammatory triggers in childhood obesity: correlation between leptin, adiponectin and high-sensitivity C-reactive protein in a group of obese Portuguese children. *Rev Port Cardiol.* 2014; 33: 691-697.
- Sears B. Anti-inflammatory Diets. *J Am Coll Nutr.* 2015; 34 Suppl 1: 14-21.
- Lewis JD, Abreu MT. Diet as a Trigger or Therapy for Inflammatory Bowel Diseases. *Gastroenterology.* 2017; 152: 398-414.e6.
- Bendall CL, Mayr HL, Opie RS, Bes-Rastrollo M, Itsiopoulos C, Thomas CJ. Central obesity and the Mediterranean diet: A systematic review of intervention trials. *Crit Rev Food Sci Nutr.* 2018; 58: 3070-3084.

6. Hennein R, Liu C, McKeown NM, Hoffmann U, Long MT, Levy D, et al. Increased Diet Quality is Associated with Long-Term Reduction of Abdominal and Pericardial Fat. *Obesity* (Silver Spring). 2019; 27: 670-677.
7. Sun J, Hartvigsen K, Chou MY, Zhang Y, Sukhova GK, Zhang J, et al. Deficiency of antigen-presenting cell invariant chain reduces atherosclerosis in mice. *Circulation*. 2010; 122: 808-820.
8. Torzewski J, Torzewski M, Bowyer DE, Fröhlich M, Koenig W, Waltenberger J, et al. C-reactive protein frequently colocalizes with the terminal complement complex in the intima of early atherosclerotic lesions of human coronary arteries. *Arterioscler Thromb Vasc Biol*. 1998; 18: 1386-1392.
9. Blake GJ, Ridker PM. Inflammatory bio-markers and cardiovascular risk prediction. *J Intern Med*. 2002; 252: 283-294.
10. Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. *BMJ*. 2000; 320: 1240-1243.
11. Serra-Majem L, Ribas L, Ngo J, Ortega RM, Garcia A, Perez-Rodrigo C, 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: 931-935.
12. World Health Organization. Waist Circumference and Waist-Hip Ratio: Report of a WHO Expert Consultation, 8-11 December 2008. Published: 2011, WHO. Available at: [https://apps.who.int/iris/bitstream/handle/10665/44583/9789241501491\\_eng.pdf?ua=1](https://apps.who.int/iris/bitstream/handle/10665/44583/9789241501491_eng.pdf?ua=1), date accessed: 20/12/2018.
13. Misra A, Vikram NK. Clinical and pathophysiological consequences of abdominal adiposity and abdominal adipose tissue depots. *Nutrition*. 2003; 19: 457-466.
14. Rolland-Cachera MF. Body composition during adolescence: methods, limitations and determinants. *Horm Res*. 1993; 39 Suppl 3: 25-40.
15. Liu X, Chen Y, Boucher NL, Rothberg AE. Prevalence and change of central obesity among US Asian adults: NHANES 2011-2014. *BMC Public Health*. 2017; 17: 678.
16. Himes JH, Roche AF. Subcutaneous fatness and stature: relationship from infancy to adulthood. *Hum Biol*. 1986; 58: 737-750.
17. Velázquez-López L, Santiago-Díaz G, Nava-Hernández J, Muñoz-Torres AV, Medina-Bravo P, Torres-Tamayo M. Mediterranean-style diet reduces metabolic syndrome components in obese children and adolescents with obesity. *BMC Pediatr*. 2014; 14: 175.
18. Introduction to Nutrition and Metabolism. Overweight and obesity. Taylor and Francis Group, London, New York, Canada, 2002.
19. Bartsch H, Nair J, Owen RW. Dietary polyunsaturated fatty acids and cancers of the breast and colorectum: emerging evidence for their role as risk modifiers. *Carcinogenesis*. 1999; 20: 2209-2218.
20. Slavin JL. Dietary fiber and body weight. *Nutrition*. 2005; 21: 411-418.
21. Siervo M, Montagnese C, Mathers JC, Soroka KR, Stephan BC, Wells JC. Sugar consumption and global prevalence of obesity and hypertension: an ecological analysis. *Public Health Nutr*. 2014; 17: 587-596.
22. Zhang G, Wu L, Zhou L, Lu W, Mao C. Television watching and risk of childhood obesity: a meta-analysis. *Eur J Public Health*. 2016; 26: 13-18.
23. Trier C, Fonvig CE, Bøjsøe C, Møllerup PM, Gamborg M, Pedersen O, et al. No influence of sugar, snacks and fast food intake on the degree of obesity or treatment effect in childhood obesity. *Pediatr Obes*. 2016; 11: 506-512.
24. Gaesser GA. Carbohydrate quantity and quality in relation to body mass index. *J Am Diet Assoc*. 2007; 107: 1768-1780.
25. Aeberli I, Gerber PA, Hochuli M, Kohler S, Haile SR, Gouni-Berthold I, et al. Low to moderate sugar-sweetened beverage consumption impairs glucose and lipid metabolism and promotes inflammation in healthy young men: a randomized controlled trial. *Am J Clin Nutr*. 2011; 94: 479-485.
26. Gupta L, Khandelwal D, Dutta D, Kalra S, Lal PR, Gupta Y. The Twin White Herrings: Salt and Sugar. *Indian J Endocrinol Metab*. 2018; 22: 542-551.