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Associação entre marcadores inflamatórios, composição corporal e consumo alimentar em crianças e adolescentes

Association between inflammatory markers, body composition and food consumption in children and adolescents

Abstract

Introduction: There is a relationship between inflammation and chronic non-communicable diseases, which generally manifest in adulthood. However, it is possible to detect inflammatory changes in children and young people. Thus, it is necessary to study the factors associated with inflammation in this life stage, so that adequate interventions can be made to stop such alterations from prolonging into adulthood. *Objective:* To assess the association between inflammatory markers, overweight indicators and food consumption markers in children and adolescents. *Methods:* Transversal study with 8- to 14-year-old individuals, from public schools in Vitória/ES. To assess inflammation, we used leukocytes, C-reactive protein, and uric acid. As overweight indicators, we used waist circumference, waist-to-height ratio, BMI-for-age, and body fat percentage. To estimate the likelihood of association, we calculated prevalence ratios and their respective 95% confidence intervalsusingPoisson regression models, modified for sociodemographic characteristics. *Results:* We evaluated 296 individuals, averaging 10.7 years of age, 54.4% female, and 53.7% adolescents. All variables at risk of overweight indicators were significant with the risk of high uric acid, in addition to the risk of increasing waist-to-height ratio (PR = 1.14), BMI-for-age (PR = 1.08), and body fat (PR = 1.10) being significant with the risk of high CRP. *Conclusion:* We conclude that the risk of alterations in overweight indicators was related with the risk of increased inflammatory markers in school-aged individuals.

Keywords: Adolescent. Child. Lifestyle. Inflammation.

Resumo

Introdução: Existe umarelação entre inflamação e doenças crônicas não transmissíveis, que geralmente se manifestam na fase adulta. Entretanto, já é possível perceber alterações inflamatórias no público infanto-juvenil.Sendo assim, torna-se necessário o estudo dos fatores associados à inflamação ainda nessa fase, a fim de que sejam feitas intervenções cabíveis para impedir que taisalterações se prologuem até a vida adulta. *Objetivo*: Avaliar a associação entre marcadores inflamatórios, indicadores de excesso de peso e marcadores de consumo alimentar em crianças e adolescentes. *Métodos*: Estudo transversal com indivíduos de 8 a 14 anos, de escolas públicas de Vitória/ES. Para avaliar inflamação, utilizaram-se leucócitos, proteína C reativa e ácido úrico. Os indicadores de excesso de peso utilizados foram perímetro da cintura, razão cintura/estatura, IMC-para-idade e percentual de gordura corporal. Para estimar as probabilidades de associação, calcularam-se razões de prevalência e seus respectivos intervalos de confiança de 95%, por meio de modelos de regressão de Poisson,

ajustados para características sociodemográficas. *Resultados*: Avaliaram-se 296 indivíduos, com média de 10,7 anos, sendo 54,4% do sexo feminino e 53,7% adolescentes.Todas as variáveis com risco dos indicadores de excesso de peso mostraram-se significativas com o risco de ácido úrico elevado, além do risco de elevação da razão cintura/estatura (RP = 1,14), do IMC-para-idade (RP = 1,08) e da gordura corporal (RP = 1,10) serem significativos com o risco de PCR elevado. *Conclusão*: Conclui-se que o risco de alterações nos indicadores de excesso de peso esteve relacionado com o risco de elevação dos marcadores inflamatóriosem escolares.

Palavras-chave: Adolescente. Criança. Estilo de vida. Inflamação.

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INTRODUCTION

Following a global trend, the Brazilian population has undergone an important change in its anthropometric profile, which has resulted in the decrease of malnutrition indices and a fast and significant increase in overweight and obesity.[1,2] Characteristics of children and adolescents follow the national trend, since, according to the Family Budget Survey (POF; Portuguese acronym), the percentage of overweight 5- to 9-year-old boys has increased from 10.9% in 1974-1975 to 34.8% in 2008-2009. A similar outlook is seen for girls of the same age, as, overweight went from 8.6% to 32.0% in the same period. Among adolescents, its prevalence has gone from 3.7% to 21.7% for males and from 7.6% to 19.4% in females in the same period of time.[3]

Adopting inadequate eating habits, with diets that are hypercaloric, high in sugar, rich in fats, and that arelow in fruits, vegetables, and whole grains, is referred to as one of the main factors linked to changes in body composition and their respective metabolic alterations.[4,5] This lifestyle, when associated with the increase in adipose tissue, triggers uncontrolled inflammatory responses, leading to low-grade systemic inflammation and metabolic disorders, which are linked to the appearance of chronic non-communicable diseases (CNCD).[6]

Low-grade systemic inflammation is characterized by an increase in the concentration of circulating pro-inflammatory cytokines, and it isinvolved in the pathogenesis of obesity, diabetes *mellitus*, cardiovascular diseases, and metabolic syndrome.[7] We can consider as markers of the inflammatory process: leukocytes, uric acid, and C-reactive protein (CRP). Leukocytes and uric acid are associated with several components of metabolic syndrome, such as hyperglycemia, high Body Mass Index (BMI), dyslipidemia, and cardiovascular diseases.[8] Although the mechanism through which uric acid increases inflammation is not yet fully elucidated, Orlando et al.[9] have shown that hyper uricemia may contribute to the development of cardiovascular diseases due to inducing inflammation at the vascular level, and Kimura et al.[10] have found that the decrease in plasma uric acid levels suppressed inflammation in humans. CRP, an important marker for systemic inflammation, is linked to an increase in BMI and to vascular endothelial growth factor, being involved in the beginning and progression of atherosclerosis in children and adolescents.[11]

From that perspective, knowledge on food consumption and its association with inflammatory markers can provide greater understanding of the complex relationship between diet, excess weight, and CNCDs.[12] This investigation is even more relevant in the early stages of life, as that is the ideal time for establishing actions which aim to intervene and lead to healthy habits.[13] However, studies associating inflammatory markers with overweight indicators and food consumption markers in this age group are still scarce.[14] As such, the current study aims to assess the associations of inflammatory markers with overweight indicators and food consumption markers within a sample of Brazilian children and adolescents.

METHODS

Study Design, Participants, and Recruiting

This is a transversal study derived from a broader study,[15] with children and adolescents of 8 to 14 years of age, studying in public schools in the Maruípe region, in the city of Vitória (ES). The sample size was calculated (n=296) to detect a difference of 10mg/dL between the cholesterol sample means from the children and adolescents, with a safety level of 95%, study power of 90% and an estimated standard deviation of 25mg/dL for the chosen variable, "Total Cholesterol". To this, we added 10% to compensate for possible losses, reaching a total of 291 individuals. The sample was obtained according to the convenience of proximity to the data collection site, and nine schools were included in the research.

As exclusion criteria, we vetoed the participation of pregnant and/or lactating individuals; users of pacemaker and/or orthopedic protheses; disabled people; those who informed through the questionnaire that they had infections and/or inflammations that altered the inflammatory profile or presented them at the time of collection (such as allergies or autoimmune diseases), as well as those who said they were using medicines which could alter blood biochemical levels (corticosteroids, anticonvulsants and anti-inflammatory drugs).

Data collection occurred from July 2016 to February 2017, at Universidade Federal do Espírito Santo (Federal University of Espírito Santo – UFES; Portuguese acronym), in Maruípe-Vitória/ES. The anthropometric and body composition evaluations were carried out by a nutritionist, whereas the blood sample collection was performed on the same day by a nursing technician, all trained specifically for their tasks.

This study was conducted according to the guidelines set out in the Declaration of Helsinki, and all procedures involving the research participants were approved by the Ethics Committee (1.565.490/2016). Informed consent was obtained in writing from all participants.

Dependent variables

We chose the markers of inflammatory process (leukocytes, CRP, and uric acid) as dependent variables. For blood collection, the participants were instructed to fast for 12 hours, being careful not to go over the 14-hour limit, and then collection proceeded via venous puncture. We assessed total leukocytes based on the complete blood count, CRP with the turbidimetry method, and uric acid with the enzymatic method. We classified leukocytes as "no risk" (≤10,000/mm³) and "at risk" (>10,000/mm³).[16] CRP and uric acid, on the other hand, were evaluated according to sex and age group, being categorized as "no risk" (<90th percentile [p90] of the sample) and "at risk" (≥p90 of the sample).

Independent variables

As independent variables, we included the overweight indicators (waist circumference, waist-to-height ratio, BMI-for-age, and body fat percentage) and the

food consumption markers obtained through the Previous Day Food Questionnaire (PDFQ-3).

Overweight indicators were measured according to a standard protocol.[17] Weight was obtained through vertical electrical bioimpedance with eight tactile electrodes (Inbody230®), with a maximum capacity of 250 kg; and height was obtained with a wall-mounted stadiometer (Seca®), with 2.21 m in length. With these data, we calculated BMI and, using the BMI-for-age index, we classified the anthropometric state of the participants[18] as "no excess weight" (< +1 z-score) and "overweight" (≥ +1 z-score) according to sex and age.

Waist circumference was obtained with an inelastic and flexible measuring tape with 1.5 m of length, measuring the midpoint between the lower margin of the last rib and the iliac crest at the end of a normal exhalation, in the horizontal plane.[19] As there are no validated cutoff points for children and adolescents, we characterized waist circumference according to sex and age group, classifying individuals as "no risk" (<p90 of the sample) and "at risk" (p≥90 of the sample). Waist-to-height ratio was calculated by dividing the waist (cm) by the height (cm), and then classified as "no risk" (<0.5) and "at risk" (≥0.5).[20]

To estimate the body fat percentage of the participants, we used a vertical electrical bioimpedance device with eight tactile electrodes (Inbody230®), with a 250kg maximum capacity and 100g precision. The exam was carried out in the morning, after the participants had fasted for 12 hours, following an assessment protocol.[21] The classification of %BF was done following the proposition by Freedman et al.,[22] according to age groups and sex, and considering moderate and high values as inadequate. Therefore, we used the following criteria to classify excess body fat for male individuals: values over 22%, 24%, and 23% for boys under 9, from 9 to 11.9, and from 12 to 14.9 years of age, respectively. For the female individuals, we classified as having excess body fat the values of 27%, 30%, and 32% for girls under 9, from 9 to 11.9, and from 12 to 14.9 years of age, respectively.

To assess food consumption markers, we employed the Previous Day Food Questionnaire (PDFQ-3), in which the participant checks which food items they consumed on the day prior to the survey, validated in 2009 by Assis et al.[23] The questionnaire is illustrated, and shows the meals in chronological order (breakfast, morning snack, lunch, afternoon snack, dinner, and evening snack), each with 21 options of foods and/or food groups. Among these food items, we analyzed eight markers of food consumption, namely: i) beans; ii) leafy and/or leguminous vegetables; iii) fresh fruit; iv) beef; v) poultry, pork, and/or fish meat; vi) sugary drinks; vii) savory ultra-processed foods; and viii) stuffed cookies, sweets, and/or candy. "Sugary drinks" include soda, powdered drinks, artificial juice, and other industrialized drinks; "savory ultra-processed foods" include chips, pizzas, hamburgers, and hot-dogs; and "sweets and/or candy" correspond to ice creams, chocolate, chewing gum, hard candy, and lollipops

Covariables

To modify the analyses, we used sociodemographic characteristics, which comprised of sex, age group, race and ethnicity, mother's schooling level, and socioeconomic level. "Sex" was classified as "female" and "male". Age group was dichotomized into "childhood" (8-9 years of age)

and “adolescence” (10-14 years of age).[17] “Race and ethnicity” was self-declared, and classified as “white” or “nonwhite” (“black”, “brown”, “yellow”, or “indigenous”).[24] The schooling level of their mothers was categorized into “incomplete middle school”, “complete middle school or incomplete high school”, “complete high school or incomplete higher education”, and “complete higher education”. The socioeconomic aspect was assessed with the scale from Associação Brasileira de Empresas de Pesquisa (Brazilian Association of Research Companies),[25] in which the participants and their guardians provide data regarding aspects of the place where they reside and the educational level of the head of the family. The categorization was split into classes “A”, “B1”, “B2”, “C1”, “C2”,and “D-E”.

Statistical analysis

Sociodemographic characteristics, food consumption markers, overweight indicators, and inflammatory markers were described with absolute (n) and relative (%) frequencies, with 95% confidence intervals (CI 95%).

To estimate the likelihood of association between food consumption markers and overweight indicators (independent variables) with inflammatory markers (binary categorical dependent variables), we calculated prevalence ratios and their respective CI 95% using Poisson regression models, obtained with a robust covariance matrix, with and without modification for sociodemographic characteristics [sex (“female” or “male”), age (in years), race and ethnicity [“white” or “nonwhite” (“black”, “brown”, “yellow”, or “indigenous”)], mother’s schooling level (“incomplete middle school”, “complete middle school or incomplete high school”, “complete high school or incomplete higher education”, or “complete higher education”), and socioeconomic status (“A”, “B1”, “B2”, “C1”,“C2”,and “D-E”)].

These analyses were carried out with the IBM SPSS software (version: 20.0, © IBM Corp., EUA),with asignificance level of 5%.

RESULTS

We evaluated 296 children and adolescents, averaging 10.7 years of age (standard deviation = 1.98), 54.4% female and 53.7% adolescents. Regarding race and ethnicity, 15.5% were White and 84.5% were “nonwhite”, which comprised of 18.9% black, 56.4% brown, 2.7% yellow, and 6.4% indigenous. Regarding mother’s schooling level, 24.7% reported incomplete middle school education; 24.2% complete middle school or incomplete high school; 42.2% complete high school or incomplete higher education; and 9.0% complete higher education. When it comes to socioeconomic status, 1.8% was B1; 21.2% was B2; 27.0% was C1; 31.0% was C2; 19.0% was D-E; and no families belonged to class A. Regarding overweight indicators, we highlight that 40.2% were overweight according to BMI-for-age. For food consumption markers, 87.2% reported eating “beans” on the previous day, 22.3% consumed “fresh fruit”, and 24.7% consumed “stuffed cookies, sweets, and/or candy”. Regarding inflammatory markers, 5.7%, 9.1%, and 9.5% were at risk of elevated leukocytes, CRP, and uric acid, respectively. Further descriptive data are found in Tables 1 and 2.

Table 1. Food consumption markers and overweight indicators among children and adolescents (8-14 years old). Vitória, ES, Brazil, 2016-2017 (n = 296).

Overweight indicators		
Variables	n	% (CI 95%)†
Waist circumference††		
No risk	261	88.2 (84.2; 91.5)
At risk	35	11.8 (8.5; 15.8)
Waist-to-height ratio‡‡		
No risk	224	75.7 (70.6; 80.3)
At risk	72	24.3 (19.7; 29.4)
BMI-for-age§§		
No excess weight	177	59.8 (54.1; 65.3)
Overweight	119	40.2 (34.7; 45.9)
Body fat ||||		
No excess weight	179	60.5 (54.8; 65.9)
Overweight	117	39.5 (34.1; 45.2)
Food consumption markers		
Variables	n	% (CI 95%)†
Beans		
Yes	258	87.2 (83.0; 90.6)
No	38	12.8 (9.4; 17.0)
Leafy and/or leguminous vegetables		
Yes	135	45.6 (40.0; 51.3)
No	161	54.4 (48.7; 60.0)
Fresh fruit‡		
Yes	66	22.3 (17.8; 27.3)
No	230	77.7 (72.7; 82.2)
Beef		
Yes	197	66.6 (61.1; 71.8)
No	99	33.4 (28.2; 38.9)
Poultry, pork, and/or fish meat		
Yes	162	54.7 (49.0; 60.3)
No	134	45.3 (39.7; 51.0)
Sugary drinks§		
Yes	81	27.4 (22.5; 32.6)
No	215	72.6 (67.4; 77.5)
Savory ultra-processed foods||		
Yes	37	12.5 (9.1; 16.1)
No	259	87.5 (83.4; 90.9)
Stuffed cookies, sweets, and/or candy ¶		
Yes	73	24.7 (20.0; 29.8)
No	223	75.3 (70.2; 80.0)

Abbreviations: CI 95%, 95% confidence interval; BMI-for-age, body mass index for age.
† Refers to consumption on the day before the survey.
†† No risk: < 90th percentile of the sample, according to sex and age group. At risk: ≥ 90th percentile of the sample, according to sex and age group.
‡‡No risk: < 0.5. At risk: ≥ 0.5.
§§No excess weight: < +1 z-score.Overweight: ≥ +1 z-score.
||||Classification according to Freedman et al.[19], according to sex and age group.
‡ Excluding fruit juice.
§ Soda, powdered drinks, artificial juice, and other industrialized drinks.
|| Chips, pizzas, hamburgers, hot-dogs, etc.
¶ Sweets and/or candy: ice cream, chocolate, chewing gum, hard candy, lollipops, etc.

Table 2. Inflammatory markers among children and adolescents (8-14 years old). Vitória, ES, Brazil, 2016-2017 (n = 296).

Variables		n	% (CI 95%)
Leukocytes †			
	No risk	279	94.3 (91.2; 96.5)
	At risk	17	5.7 (3.5; 8.8)
CRP ‡			
	No risk	269	90.9 (87.2; 93.8)
	At risk	27	9.1 (6.2; 12.8)
Uric acid‡			
	No risk	268	90.5 (86.9; 93.5)
	At risk	28	9.5 (6.5; 13.1)

Abbreviations: CI 95%, 95% confidence interval; CRP, C-reactive protein.
† No risk: ≤ 10,000/mm³. At risk: > 10,000/mm³.
‡ No risk: < 90th percentile of the sample, according to sex and age group. At risk: ≥ 90th percentile of the sample,according to sex and age group.

All variables at risk of overweight indicators were significant with high uric acid risk (Table 3). Additionally, the risks of increasing waist-to-height ratio (PR = 1.14), BMI-for-age (PR = 1.08), and body fat (PR = 1.10) were significant with high CRP risk.

Table 3. Poisson regression models, obtained through a covariance matrix with a robust estimator, for the associations between inflammatory markers (binary categorical dependent variables) andoverweight indicators (independent variables) among children and adolescents (8-14 years old). Vitória, ES, Brazil, 2016-2017 (n = 296).

Variables	Inflammatory markers (binary categorical dependent variables)					
	Leukocytes †		CRP‡		Uric acid‡	
	Raw model	Modified model§	Raw model	Modified model§	Raw model	Modified model§
	PR (CI 95%)	PR (CI 95%)	PR (CI 95%)	PR (CI 95%)	PR (CI 95%)	PR (CI 95%)
Waist circumference‡						
No risk	Reference	Reference	Reference	Reference	Reference	Reference
At risk	1.03 (0.94; 1.13)	0.99 (0.89; 1.11)	1.08 (0.97; 1.21) *	1.10 (0.97; 1.24)	1.23 (1.09; 1.39) **	1.28 (1.11; 1.47) ***
Waist-to-height ratio||						
No risk	Reference	Reference	Reference	Reference	Reference	Reference
At risk	1.01 (0.95; 1.08)	1.02 (0.95; 1.09)	1.11 (1.03; 1.21) **	1.14 (1.04; 1.25) **	1.20 (1.10; 1.30) ***	1.23 (1.13; 1.35) ***
BMI-for-age ¶						
No excess weight	Reference	Reference	Reference	Reference	Reference	Reference
Overweight	0.99 (0.94; 1.04)	0.99 (0.93; 1.04)	1.06 (0.99; 1.12) *	1.08 (1.01; 1.16) **	1.16 (1.09; 1.24) ***	1.18 (1.10; 1.27) ***
Body fat††						
No excess weight	Reference	Reference	Reference	Reference	Reference	Reference
Overweight	1.01 (0.95; 1.06)	0.99 (0.94; 1.05)	1.09 (1.02; 1.16) **	1.10 (1.02; 1.19) **	1.16 (1.09; 1.24) ***	1.19 (1.11; 1.28) ***

Abbreviations: CI 95%, 95% confidence interval; BMI-for-age, body mass index for age; CRP, C-reactive protein; PR, prevalence ratio.
†At risk: > 10,000/mm³.
‡ At risk: ≥ 90th percentile of the sample,according to sex and age group.
§Modified by sex ("female" or "male"), age (in years), race and ethnicity ["white" or "nonwhite" ("black", "brown", "yellow", or "indigenous")], mother's schooling level ("incomplete middle school", "complete middle school or incomplete high school", "complete high school or incomplete higher education", or "complete higher education"), and socioeconomic status ("A + B1", "B2 + C1", or "C2 + D-E").
|| At risk: ≥ 0.5.
¶ Overweight: ≥ +1 z-score.
†† Overweight: ≥ 25% (female); ≥ 20% (male).
* $p < 0.20$.
** $p < 0.05$.
*** $p < 0.001$.

For the associations between food consumption markers and inflammatory markers (Table 4), we found that not consuming "savory ultra-processed foods" on the previous day increased the likelihood of elevated leukocytes risk (PR = 1.05). And not consuming "stuffed cookies, sweets, and/or candy" on the previous day was linked to an elevated CRP risk (PR = 1.08).

Table 4. Poisson regression models, obtained through a covariance matrix with a robust estimator, for the associations between inflammatory markers (binary categorical dependent variables) and food consumption markers (independent variables) among children and adolescents (8-14 years old). Vitória, ES, Brazil, 2016-2017 (n = 296).

Variáveis ||	Inflammatory markers (binary categorical dependent variables)					
	Leukocytes †		CRP‡		Uric acid‡	
	Raw model	Modified model§	Raw model	Modified model§	Raw model	Modified model§
	PR (CI 95%)	PR (CI 95%)	PR (CI 95%)	PR (CI 95%)	PR (CI 95%)	PR (CI 95%)
Beans						
Yes	Reference	Reference	Reference	Reference	Reference	Reference
No	0.99 (0.93; 1.07)	0.98 (0.92; 1.05)	1.02 (0.92; 1.12)	1.01 (0.91; 1.12)	1.04 (0.94; 1.15)	1.02 (0.91; 1.14)
Leafy and/or leguminous vegetables						
Yes	Reference	Reference	Reference	Reference	Reference	Reference
No	0.98 (0.94; 1.04)	1.03 (0.98; 1.08)	1.00 (0.95; 1.07)	1.01 (0.94; 1.08)	1.00 (0.94; 1.06)	0.99 (0.93; 1.07)
Fresh fruit						
Yes	Reference	Reference	Reference	Reference	Reference	Reference
No	0.98 (0.92; 1.04)	0.98 (0.91; 1.05)	1.00 (0.93; 1.08)	0.97 (0.89; 1.06)	0.99 (0.92; 1.06)	0.96 (0.88; 1.04)
Beef						
Yes	Reference	Reference	Reference	Reference	Reference	Reference
No	1.01 (0.95; 1.06)	0.99 (0.94; 1.04)	1.00 (0.94; 1.07)	0.98 (0.91; 1.06)	1.01 (0.95; 1.08)	0.96 (0.89; 1.03)
Poultry, pork, and/or fish meat						
Yes	Reference	Reference	Reference	Reference	Reference	Reference
No	0.99 (0.94; 1.04)	1.03 (0.99; 1.09)	1.01 (0.95; 1.07)	1.00 (0.94; 1.08)	0.99 (0.93; 1.05)	1.02 (0.95; 1.09)
Sugary drinks††						
Yes	Reference	Reference	Reference	Reference	Reference	Reference
No	1.04 (0.99; 1.09) *	1.01 (0.96; 1.07)	0.96 (0.89; 1.03)	0.94 (0.86; 1.02)	1.01 (0.95; 1.08)	1.02 (0.94; 1.10)
Savory ultra-processed foods‡‡						
Yes	Reference	Reference	Reference	Reference	Reference	Reference
No	1.03 (0.98; 1.10)	1.05 (1.02; 1.08) **	0.98 (0.89; 1.08)	0.97 (0.87; 1.08)	1.04 (097; 1.13)	1.02 (0.96; 1.11)
Stuffed cookies, sweets, and/or candy§§						
Yes	Reference	Reference	Reference	Reference	Reference	Reference
No	1.02 (0.97; 1.08)	1.01 (0.95; 1.08)	1.05 (0.98; 1.11) *	1.08 (1.01; 1.15) **	1.00 (0.93; 1.07)	0.94 (0.86; 1.03)

Abbreviations: CI 95%, 95% confidence interval;CRP, C-reactive protein; PR, prevalence ratio.

† At risk: > 10,000/mm³.
‡At risk: ≥ 90th percentileof the sample,according to sex and age group.
§Modified by sex (“female” or “male”), age (in years), race and ethnicity [“white” or “nonwhite” (“black”, “brown”, “yellow”, or “indigenous”)], mother’s schooling level (“incomplete middle school”, “complete middle school or incomplete high school”, “complete high school or incomplete higher education”, or “complete higher education”), and socioeconomic status (“A + B1”, “B2 + C1”, or “C2 + D-E”).
|| Refers to consumption on the day before the survey.
¶ Excluding fruit juice.
†† Soda, powdered drinks, artificial juice, and other industrialized drinks.
‡‡ Chips, pizzas, hamburgers, hot-dogs, etc.
§§ Sweets and/or candy: ice cream, chocolate, chewing gum, hard candy, lollipops, etc.
* $p < 0.20$.
** $p < 0.05$.

DISCUSSION

The findings of the present study show that children and adolescents with alterations on their overweight indicators are at a higher risk of alterations on their inflammatory profile. However, for the food consumption markers, we unexpectedly found that not consuming of "savory ultra-processed foods" and "stuffed cookies, sweets, and/or candy" on the previous day increased the chances of an increase in leukocytes and CRP, respectively. This result may have occurred due to the representativity of the sample and the single-day food record, as some studies in the literature have revealed a link between a pro-inflammatory diet and inflammatory markers.[26-28]

Regarding overweight indicators, we found that the risk of increasing the waist-to-height ratio, BMI-for-age, and body fat percentage increased the risk of inadequate CRP and uric acid values, the latter also being associated with a risk of increase in waist circumference. Obesity has also shown to be linked to elevated CRP levels in a meta-analysis which included 51 studies with North American, European, and Asian children and adults. The pathophysiological mechanisms which link obesity to high CRP levels are well-known. The adipose tissue is an active endocrine organ which releases a variety of hormones and cytokines that contribute to increasing CRP.In obesity, the accumulation of free fatty acids activates pro-inflammatory enzyme cascades which then promote cytokine secretion, such as interleukin-6, which in turn triggers hepatic CRP synthesis. The liver is known for playing a central role in the expression and release of CRP, as it drains visceral adipose tissue, circulating triacylglycerol, and free fatty acids, to produce cytokines and promote an inflammatory milieu.[29]

Regarding uric acid, a study with 5.1-19.0-year-old Canadians has also shown that an increase in BMI was connected to an increase in the average uric acid concentration.[30] Other studies corroborate this result, endorsing the inflammatory role of uric acid. Cardoso et al.[31] found that elevated uric acid levels were associated with metabolic syndrome in children and adolescents, and Luciano et al.[32] found that hyperuricemia is associated with metabolic anomalies and, particularly, with waist circumference in childhood, highlighting the role of uric acid levels in the formation of cardiometabolic risk in childhood and adolescence.

The mechanism which leads to an increase in uric acid due to excess body fat is not yet clear; however, this substance has been identified to be produced and secreted by adipose tissue in mice. Uric acid secretion from adipose tissue was heightened in obese mice, and hyperuricemia was shown to be associated with the accumulation of visceral fat in humans.[30,33]

We highlight the use of waist-to-height ratio as an additional anthropometric measurement to assess obesity and central adiposity, and as a possible predictor of inflammatory alterations, as it was shown to have a strong link to CRP and uric acid. Due to its ease of measurement, waist-to-height ratio is a useful tool in the routine assessment of the nutritional status of children and adolescents, being practically equivalent, or even easier to use, than determining the BMI z-score. The waist-to-height ratio also provides an estimate of central adiposity, which is not true for the isolated use of BMI.[34] A study with 280 overweight or obese patients between 6 and 19 years of age and a control group of 112 children and adolescents with normal nutritional status by the Departamento de Nutrição Clínica (Clinical Nutrition Department) of JP Garrahan Hospital, in Argentina, has also found a link between waist-to-height ratio and CRP, indicating a connection between this anthropometric marker and subclinical inflammation, which endorses its use in clinical practice.[35]

Regarding food consumption markers, we found that not consuming "savory ultra-processed foods" on the day prior to the survey was linked to an increased leukocyte elevation risk. This finding is unexpected and controversial when compared to what is found in the literature, since despite a low number of studies

associating leukocyte count with food consumption markers, natural foods are described as having a protective effect against the increase in inflammatory markers. Menni et al.[36] found that high vegetable consumption is linked to a lower leukocyte profile, and this effect is mediated by the gut microbiome; Badimon et al.[37] reinforce that adhering to a mediterranean diet has been associated with a decrease in leukocyte count; and the relationship between this inflammatory marker and metabolic syndrome components (fasting blood glucose, waist circumference, triacylglycerol, HDL-cholesterol, and systolic blood pressure) is already known.[8] Therefore, its association with food must be better investigated.

Not consuming "stuffed cookies, sweets, and/or candy" on the day before the survey was linked to the increased risk of PCR inadequacy. This finding was also controversial in regard to the literature, as these food items are rich in sugar and fat. These compounds are reported to stimulate an inflammatory response in many ways, one of them being through the activation of the innate immune system for hours after each meal, potentializing the translocation of liposaccharides that directly activate the inflammatory system.[27] A study carried out based on data from the Food Frequency Questionnaire from Nurses' Health Study (n=1,350) showed that individuals within the greatest quintile of a dietary pattern rich in the consumption of regular and diet sodas, refined grains, and processed meat had higher CRP levels.[28] When evaluating an antioxidant and anti-inflammatory dietary pattern, rich in fruits and vegetables and low in chips, sugar, and white bread, which was developed by 1,531 English individuals, it was inversely associated to CRP.[38]

In this study, we failed to find a protective effect of natural foods, such as beans, vegetables, fresh fruit, and meat. However, healthy life habits, such as a balanced diet with low fat consumption and high fruit, vegetable, and whole grain consumption, have been well reported in the literature as a very effective way of preventing CNCDs, being associated with an improvement in the inflammatory state.[4,5,38]

These unexpected results regarding food consumption may have occurred due to some study limitations, such as sample representativity, as this is a study of secondary data analysis, in which the sample calculation was not carried out with this goal in mind; and using single-day food consumption markers, as a single day may not have been capable of faithfully reflecting their habitually eaten diet. Regardless, the association of food items with inflammatory markers needs to be more thoroughly investigated.

We highlight the analysis of factors associated with inflammatory markers in childhood and adolescence as a strength of this study, since it is little explored in the literature. We also highlight that rigorous methods of data collection and analysis were applied, following well-established protocols in the literature, which ensures high accuracy of the results, such as the identification of acute and/or light infection or subclinical inflammation episodes – for instance, allergic processes –, as they could interfere with the inflammatory profile of the participants.

CONCLUSION

Finally, we highlight that an association was found between inflammatory markers and overweight indicators already in childhood and adolescence, and we emphasize the importance of adopting a healthy lifestyle to prevent the appearance of CNCDs. We also highlight the importance of an early diagnosis of inflammatory alterations, so that the adequate interventions may be carried out and such alterations do not prolong into adulthood.

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