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Dietary inflammatory index scores are associated with atherogenic risk in Brazilian schoolchildren

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Abstract

Objective: To investigate the association between the Children's Dietary Inflammatory Index (C-DII™) scores and atherogenic risk in Brazilian schoolchildren.

Design: A cross-sectional representative study. Three 24-h dietary recalls were performed to evaluate food consumption and to calculate C-DII scores. Blood samples were collected for the lipid profile analysis (serum total cholesterol (TC), HDL-cholesterol, LDL-cholesterol, VLDL-cholesterol and triglycerides (TAG)) and to determine atherogenic indexes (Castelli risk indexes I and II, lipoprotein combined index (LCI), and atherogenic index of plasma and atherogenic coefficient (AC)). A semi-structured questionnaire was used to obtain sociodemographic characteristics and screen time. Body fat was assessed by dual-energy X-ray absorptiometry. We compared the distributions of outcomes by C-DII categories using multivariable linear regression.

Setting: Viçosa, Minas Gerais, Brazil.

Participants: Three hundred seventy-eight children between the ages of 8 and 9 years.

Results: The mean C-DII score was 0·60 ± 0·94, and the prevalence of dyslipidaemia was 70 %. Children with hypercholesterolaemia and hypertriglyceridaemia had higher C-DII scores. The C-DII was directly associated with atherogenic risk. Every 1 SD of C-DII was associated with a 0·07 (0·01, 0·13), 1·94 (0·20, 3·67), 0·06 (0·002, 0·12) and 0·12 (0·02, 0·22) units higher TC:HDL cholesterol ratio, LCI, AC and accumulation of altered dyslipidaemia markers (high TC + high LDL-cholesterol + high TAG + low HDL-cholesterol), respectively.

Conclusions: Dietary inflammatory potential, as estimated by the C-DII, is directly associated with atherogenic risk in Brazilian schoolchildren. This results reinforce the importance of effective nutritional policies to promote healthy eating habits and improve children's lipid profiles.

Keywords
Inflammation
Child
CVD
Atherosclerosis
Nutritional epidemiology

Dyslipidaemias are disorders characterised by the presence of high total cholesterol (TC), high LDL-cholesterol, low HDL-cholesterol and high triglycerides (TAG)[1]. The increasing prevalence of dyslipidaemia in childhood[2–4] is considered a major public health concern worldwide, especially due to its vital role in the pathogenesis of atherosclerosis and the development of CVD[1,5] through their effect on inflammatory process[5,6].

In this context, the diet is an important moderator of systemic inflammation[7] and has been identified as a modifiable risk factor for managing dyslipidaemia and preventing atherosclerotic disease[1,8,9]. Furthermore, studies in adults have shown the association of a pro-inflammatory diet with unfavourable lipoprotein profile[10,11] and subclinical atherosclerosis[12].

A validated tool for assessing the inflammatory potential of diet in paediatric populations[13], the Children's Dietary Inflammatory Index (C-DII™), has been directly associated with cardiometabolic risk and inflammation in children and adolescents[13–15]. Moreover, we recently demonstrated the

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association between C-DII with anti- and pro-inflammatory adipokines in our sample from the Schoolchildren Health Assessment Survey[15].

In a study with adolescents, it was identified a direct association between C-DII with dyslipidaemia in overweight individuals (12–18 years), but not with isolated markers of lipid profile, reinforcing the need for further studies[16]. The effects of diet-related inflammation on lipid profile and atherosclerosis risk remain poorly explored at young ages[16–18], and to date, no studies with children have evaluated these associations using the new C-DII. Therefore, we aimed to investigate the relationship of the C-DII with atherogenic risk in Brazilian schoolchildren. We hypothesise that the C-DII scores are directly associated with atherogenic risk.

Methods

Participants and study design

This cross-sectional representative study was carried out with participants from the Schoolchildren Health Assessment Survey (*Pesquisa de Avaliação da Saúde do Escolar,* in portuguese). Data collection was conducted in 2015 at the Universidade Federal de Viçosa by trained nutritionists.

The sample size calculation and the sampling process have been described previously[19,20]. In brief, we recruited randomly 378 schoolchildren between the ages of 8 and 9 years from a total 1464 children in the same age group enrolled in one of the urban primary schools of Viçosa, Minas Gerais, Brazil.

Children were not included in the study when they used medications regularly or had a clinically diagnosed health condition that could interfere with nutritional status, body composition, lipid profile, blood pressure and/or glucose metabolism; whose parents did not sign informed consent form; or parents and guardian that, after three attempts, could not be reached.

Food intake and children's dietary inflammatory index computation

To assess children's food intake, we performed 24-h dietary recalls, completed by both mother/guardian and the child, across three non-consecutive days, including one weekend day. To enhance data reliability, the interviewers were previously trained. Moreover, we also used household utensils and a photograph album with food and beverage serving sizes to help the participants estimate the sizes of portions consumed[21].

The common household units for each food consumed were converted into g, mg or ml to evaluate daily energy (kcal) and nutrients intake. The food composition analysis was conducted in the software Dietpro® 5i, version 5.8 using the Brazilian Food Composition Table[20] and the USDA Food Composition Database[22,23].

We calculated the C-DII scores to determine the inflammatory potential of diet according to the recent method proposed for paediatric populations[13]. This index characterises the child's diet on a continuum scale from maximally anti- to pro-inflammatory. Briefly, the Pesquisa de Avaliação da Saúde do Escolar dietary data were related to a representative world database that provides a global estimate mean along with the standard deviation for each nutrient considered in the C-DII definition[13]. First, we created a *Z*-score to express the individual exposure of the child relative to the 'standard global mean'. Second, these *Z*-scores were converted to a centred proportion to avoid the effect of 'right skewing' (i.e. with values from 0 to 1), multiplied by 2 and then subtracting 1. As a result, we achieved a symmetrical distribution ranging from −1 (anti-inflammatory) to +1 (pro-inflammatory) and centred on 0 (null). Next, the scores were multiplied by the 'overall food parameter-specific inflammatory effect score'. Finally, we summed each food parameter-specific C-DII scores to obtain the overall individual C-DII score[13]. To minimise the energy intake difference among people, the energy-adjusted C-DII was used by converting all food to per 1000 kcal consumption.

For the C-DII calculation, we included sixteen of the twenty-five possible food parameters[13], as follows: carbohydrate, protein, total fat, SFA, MUFA, PUFA, fibre, Fe, Zn, Mg, vitamin C, vitamin B_1, vitamin B_2, vitamin B_3, vitamin B_6 and vitamin D. Higher C-DII scores represent a more pro-inflammatory diet.

Lipid profile and atherogenic risk

The children's blood samples were collected at the Laboratory of Clinical Analysis of the Health Division of the Universidade Federal de Viçosa by venepuncture in the antecubital vein after 12 h of fasting. Bloods were packed in 1·5 ml microtubes and stored at −80°C until the lipid profile analysis was completed.

We evaluated serum TC, LDL-cholesterol, HDL-cholesterol, VLDL-cholesterol and TAG using an automated equipment (BioSystems 200 Mindray® model), according to the manufacturer recommendations (Bioclin® kits). Children with at least one of the following altered lipids were classified with dyslipidaemia: TC ≥ 170 mmol/l, HDL-cholesterol < 45 mmol/l, LDL-cholesterol ≥ 110 mmol/l and TAG ≥ 75 mmol/l[1].

Moreover, we calculated atherogenic indexes[24] such as the Castelli risk index I (TC/HDL-cholesterol), Castelli index risk II (LDL-cholesterol/HDL-cholesterol), lipoprotein combine index (LCI), atherogenic index of plasma and atherogenic coefficient (AC). LCI was calculated using the formula: (TC × TAG × LDL-cholesterol)/HDL-cholesterol. Atherogenic index of plasma is the base 10 log of the TAG/HDL-cholesterol. AC is the ratio of (TC − HDL-cholesterol)/HDL-cholesterol[24–26]. Furthermore, we evaluated the accumulation of altered dyslipidaemia

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markers (high TC + high LDL-cholesterol + high TAG + low HDL-cholesterol), which contribute to the initiation and progression of endothelial dysfunction increasing the atherosclerosis risk[27,28].

Sociodemographic characteristics and screen time

A semi-structured questionnaire was administer to parents and guardians to obtain sociodemographic characteristics and data on screen time. The collected data included: sex, age (years) and race (White, Brown and Black), household's per capita income (US$) and screen time (h/d).

Anthropometry and body composition

The children's anthropometric measurements were performed by a trained member of the research group. The children wore light clothes and were barefoot. Weight was measured using a digital electronic scale with a capacity of 150 kg and a sensitivity of 100 g (Tanita® Ironman Model BC 553; Tanita Corporation of America Inc.). The height was evaluated using a vertical stadiometer divided in cm and subdivided in mm (Alturexata®). We obtained height-for-age and BMI-for-age *Z*-scores using the WHO Anthro Plus software[29].

We assessed the children's body fat by dual-energy X-ray absorptiometry (Lunar Prodigy Advance; GE Medical Systems Lunar). The child was fasted during the exam wearing only light clothing and remained in supine position on the scanning bed until the end of the equipment evaluation.

Data analyses

Exposure

Children's Dietary Inflammatory Index (C-DII) scores were expressed in quintiles.

Outcome

Lipid profile (TC, HDL-cholesterol, LDL-cholesterol, VLDL-cholesterol and TAG), atherogenic indexes (Castelli risk indexes I and II, LCI, atherogenic index of plasma and AC) and accumulation of altered dyslipidaemia markers (high TC + high LDL-cholesterol + high TAG + low HDL-cholesterol), were all fit as continuous variables.

Covariates

Child's age, sex, race, screen time, the household's per capita income and body fat (%).

Statistical analyses

The normality of the variables was assessed by the Kolmogorov–Smirnov test. Comparisons of mean and standard deviation between groups were verified by Student's *t* test, and Pearson's χ^2 test was used to evaluate the relationships between categorical variables. We evaluated the distribution of dietary intake using mean and standard deviation (SD) according to C-DII categories from multivariable linear regression. Then, we compared the distributions of outcomes (lipid profile, atherogenic indexes and accumulation of altered dyslipidaemia markers) by C-DII categories (exposure), using mean differences and 95 % CI from unadjusted and multivariable linear regression models adjusted by age, sex, race, screen time, per capita income and body fat (%). All the possible confounders included in the analysis were chosen after a literature review. The robust estimates of the variance were specified in all models, which are consistent with heteroscedasticity and non-normality[30].

Analyses were performed using the software Stata® version 14 (StataCorp LP) and Statistical Package for the Social Science® software version 21 (SPSS Inc.). The significance level was 0·05 for all hypothesis tests.

Results

In our sample, 52·12 % were girls and 68·52 % were Non-White children. The prevalence of dyslipidaemia was 70 %. The means ± SD of serum TC, HDL-cholesterol, LDL-cholesterol and TAG were 152·29 ± 26·40 mmol/l, 50·07 ± 9·99 mmol/l, 86·96 ± 23·38 mmol/l and 78·83 ± 35·41 mmol/l, respectively (data not shown). The children with dyslipidaemia had higher BMI-for-age (0·59 ± 1·45) and body fat (25·61 ± 10·44) compared with those with normal lipid profile (−0·01 ± 1·19 and 21·01 ± 8·40, respectively). The mean ± SD of C-DII score was 0·60 ± 0·94 and ranged from −2·16 (maximum anti-inflammatory diet) to 2·75 (maximum pro-inflammatory diet) (Table 1). Furthermore, children with hypercholesterolaemia and hypertriglyceridaemia reported consuming a more pro-inflammatory diet (Fig. 1).

Table 2 shows the association of food intake with C-DII after adjustment for potentially confounding factors. The C-DII was inversely associated with energy intake and the consumption of carbohydrate, protein, PUFA, fruits, vegetables, whole grains, rice and beans, and dairy products. Conversely, C-DII was directly associated with total fat, MUFA, saturated fat and unhealthy food groups intake as crackers and chips, processed meat, fast-food and fried snacks, industrial juices and soft drinks, and sugar.

The C-DII was directly associated with atherogenic indexes, regardless of child's age, sex, race, per capita income, screen time and body fat (%). Compared with first, the fifth quintiles of C-DII were related to 0·17 (95 % CI −0·01, 0·35), 5·34 (95 % CI 0·43, 10·25) and 0·16 (95 % CI −0·02, 0·34) units higher TC/HDL-cholesterol ratio, LCI and AC, respectively. Every 1 SD of C-DII was associated with a 0·07 (95 % CI 0·01, 0·13), 1·94 (95 % CI 0·20, 3·67) and 0·06 (95 % CI 0·002, 0·12) units higher TC/HDL-c ratio, LCI and

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Table 1 Characteristics of participants according to the presence or absence of dyslipidaemia, Viçosa, Minas Gerais, Brazil, 2015

	Dyslipidaemia						
	Total (*n* 378)		No (*n* 115)		Yes (*n* 263)		
Characteristics	Mean	SD	Mean	SD	Mean	SD	*P*
Age (years)	8·51	0·50	8·45	0.·50	8·54	0·50	0·10
Sex (girls)‡	52·12		27·40		72·60		0·18
Race (non-white)‡	68·52		30·10		69·90		0·84
Per capita income (US$)†	242·28	276·61	231·04	255·16	247·20	285·82	0·60
Screen time (h/d)	3·53	1·46	3·31	1·42	3·63	1·46	0·05
Height-for-age (*Z*-score)	0·54	1·03	0·48	0·91	0·57	1·08	0·50
BMI-for-age (*Z*-score)	0·40	1·40	−0·01	1·19	0·59	1·45	<0·001*
Body fat (%)	24·21	10·08	21·01	8·40	25·61	10·44	<0·001*
C-DII	0·60	0·94	0·47	1.01	0·65	0·90	0·10

C-DII, Children's Dietary Inflammatory Index; SD, standard deviation.
*$P < 0·05$.
†Approximate exchange rates of real (R$) to dollar (US$) at the time of this study (US$1·00 = R$ 3·22).
Student's *t* test for continuous variables and ‡Pearson's χ^2 test for categorical variables.

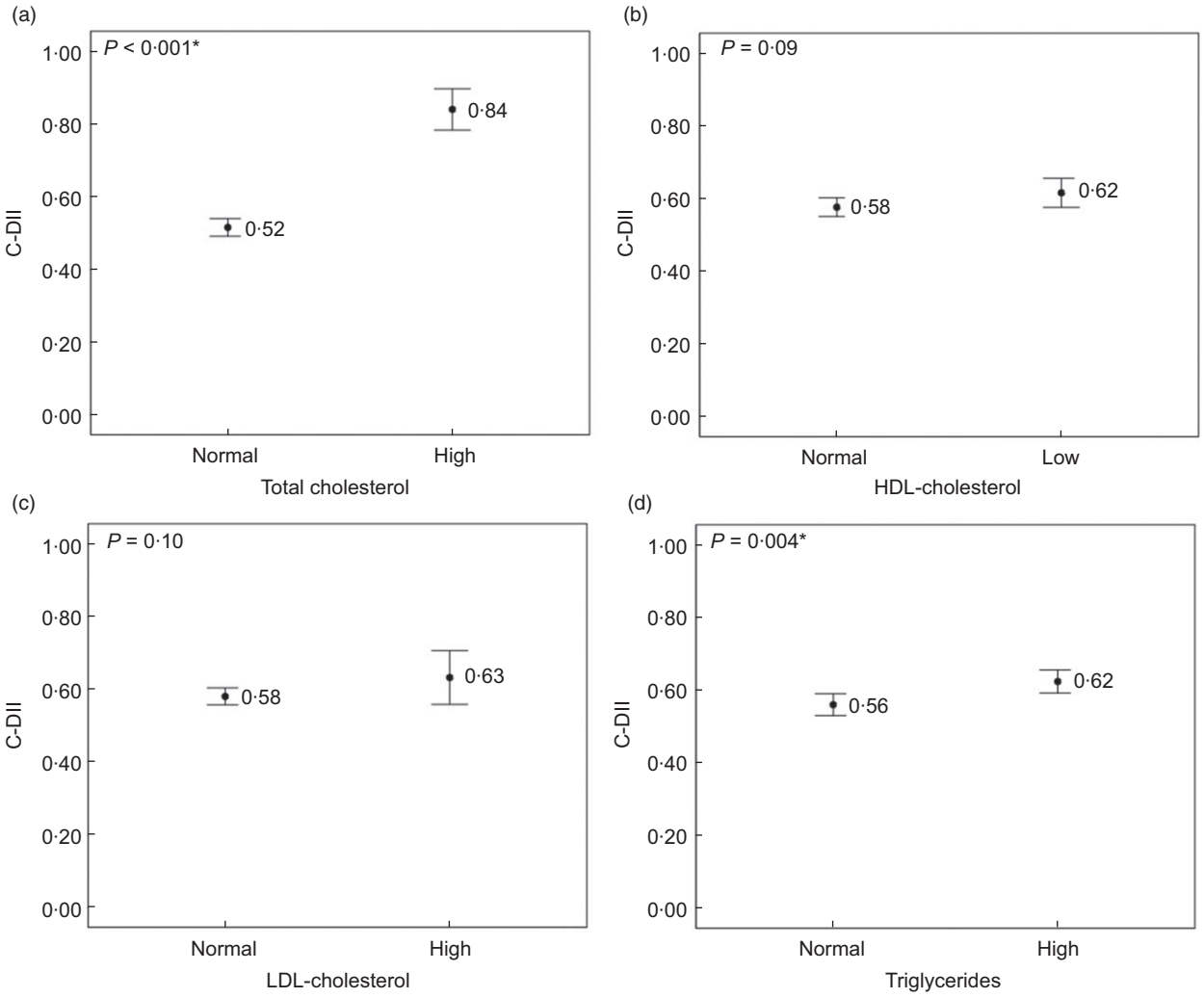

Fig. 1 Children's Dietary Inflammatory Index (C-DII) score according to the presence or absence of dyslipidaemia in schoolchildren from Viçosa, Minas Gerais, Brazil, 2015. Values are mean (95 % CI). Student's *t* test ($P < 0·05$*) adjusted for child's age, sex, race, per capita income, screen time and body fat

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Table 2 Distribution of nutrients and food groups intake according to Children's Dietary Inflammatory Index (C-DII) in schoolchildren from Viçosa, Minas Gerais, Brazil, 2015

	C-DII (quintiles)										
	Q1 (–2·16 to –0·19) (*n* 75)		Q2 (–0·20 to 0·41) (*n* 76)		Q3 (0·42 to 0·86) (*n* 76)		Q4 (0·87 to 1·41) (*n* 76)		Q5 (1·42 to 2·75) (*n* 75)		
Dietary intake	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	P_{trend}†
Energy (kcal)	1500·48	356·74	1481·12	438·58	1424·70	519·99	1304·22	467·57	1275·28	398·42	<0·001*
Macronutrients (% EI)											
Carbohydrate	60·78	6·29	59·78	6·28	59·22	6·07	58·11	5·90	57·56	5·64	<0·001*
Protein	15·25	2·93	14·61	2·70	13·53	2·78	12·91	2·66	13·04	2·92	<0·001*
Total fat	26·70	5·52	26·49	4·92	27·80	4·79	29·34	4·78	29·49	4·94	<0·001*
MUFA	8·23	1·85	8·25	1·93	8·63	2·03	9·32	1·94	9·73	2·12	<0·001*
PUFA	6·04	1·90	5·50	1·74	5·87	2·07	5·53	1·97	4·70	1·78	<0·001*
Saturated fat	8·94	2·17	8·89	2·25	9·16	2·12	9·78	2·40	9·96	2·16	0·001*
Food groups (% EI)											
Fruits and vegetables	12·44	7·59	9·14	7·94	8·13	6·01	6·50	4·39	6·31	6·35	<0·001*
Fruits and natural juices	7·42	6·56	4·87	5·58	4·11	4·64	3·00	3·34	2·68	2·86	<0·001*
Red, yellow and green veggies	0·69	0·60	0·78	1·53	0·54	0·88	0·34	0·49	0·36	0·97	0·01*
Whole grains	0·93	3·13	0·44	1·44	0·32	1·08	0·16	0·63	0·32	1·00	0·004*
Dairy products	11·46	6·25	9·45	5·78	9·37	5·78	9·45	6·65	7·68	6·16	<0·001*
Meat, fish and eggs	12·78	5·90	12·16	6·55	11·61	5·93	12·36	6·38	10·89	6·37	0·29
Rice and beans	16·01	7·70	14·96	7·77	13·33	6·59	14·44	7·75	13·56	7·78	0·001*
Crackers and chips	6·61	6·55	8·90	9·51	8·00	8·16	9·82	8·37	11·18	9·60	0·003*
Processed meat	3·10	3·77	3·15	3·82	4·00	4·21	4·38	4·39	4·90	4·70	0·01*
Fast-food and fried snacks	3·82	4·90	5·91	6·61	6·27	7·90	6·88	8·85	8·12	10·11	<0·001*
Industrial juices and soft drinks	3·23	3·13	4·85	3·77	4·88	3·30	5·15	3·89	5·23	5·00	<0·001*
Added sugar	15·98	6·12	17·05	5·70	18·51	7·41	19·21	6·74	19·97	7·42	<0·001*

EI, energy intake; MUFA, monounsaturated fat; PUFA, polyunsaturated fat; SD, standard deviation.
*$P < 0·05$.
†From linear regression models with a variable representing ordinal C-DII categories introduced as continuous. Robust estimates of variance were specified in all models. Adjusted for child's age, sex, race, per capita income, screen time and body fat.

AC, respectively (Table 3). Additionally, a pro-inflammatory diet was associated with the accumulation of altered dyslipidaemia markers (high TC + high LDL-cholesterol + high TAG + low HDL-cholesterol). Children with the most pro-inflammatory diet (fifth quintile) had 0·32 (95 % CI 0·01, 0·63) unit higher accumulation of altered dyslipidaemia markers than children with the most anti-inflammatory diet (first quintile) (Fig. 2). Every 1 SD of C-DII was associated with a 0·12 (95 % CI 0·02, 0·22) unit higher accumulation of altered dyslipidaemia markers.

Discussion

Our cross-sectional study supports the hypothesis that a pro-inflammatory diet is associated with a higher atherogenic risk in schoolchildren.

The findings showed a direct association between C-DII and atherogenic indexes, but not individual parameters. Previous studies with paediatric population[16,18] also found no significant associations between the pro-inflammatory diet and isolated traditional markers of lipid profile, corroborating with our results. However, the atherogenic indexes are good indicators of CVD risk because these consider the balance between atherogenic and protective lipoproteins, thus, increasing their predictive capacity compared with isolated traditional markers[24,31]. In this context, the assessment of atherogenic indexes, also obtained at young ages, should be encouraged in paediatric clinical practice as interesting complementary methods of screening and monitoring cardiometabolic risk[32,33].

Current studies with adults have shown the association between a pro-inflammatory diet and an increased risk of dyslipidaemia[10], elevated TAG/HDL-cholesterol ratio and apoB[11], as well as the development of CVD and increased mortality[12,34–36]. Though results do exist in adults, the investigations regarding the impacts of dietary inflammatory potential on children's lipid profiles are limited[17,18]; to date, no studies have been found evaluating the relationship between C-DII and atherogenic indexes. Taken together, more research conducted in children is needed to clarify this issue.

We also observed a positive association of the C-DII with the accumulation of lipid abnormalities characterising a dyslipidaemia pattern. This result suggests a potential role of diet in the early occurrence of CVD through inflammatory modulation mechanisms. The adherence to an anti-inflammatory diet with a higher intake of nutrients and antioxidant compounds sources as fruits and vegetables may improve lipid profile[37,38] and reduce inflammation[39,40] and atherosclerosis risk[36]. In contrast, a poor-quality diet that includes excessive intake of pro-inflammatory food

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Table 3 Crude and adjusted analyses of the association of the Children's Dietary Inflammatory Index (C-DII) with lipid profile and atherogenic indexes in schoolchildren from Viçosa, Minas Gerais, Brazil, 2015

	C-DII (quintiles)						
Markers	Q1 (−2·16 to −0·19) (*n* 75)	Q2 (−0·20 to 0·41) (*n* 76)	Q3 (0·42 to 0·86) (*n* 76)	Q4 (0·87 to 1·41) (*n* 76)	Q5 (1·42 to 2·75) (*n* 75)	Per 1 SD§	P_{trend}‖
TC (mmol/l)							
Mean	148·35	152·95	151·29	154·17	154·91		
SD	25·11	27·08	22·14	31·10	26.19		
Unadjusted difference (95 % CI)†	Reference	4·60 (−3·75, 12·95)	2·94 (−4·64, 10·52)	5·64 (−3·41, 14·69)	6·56 (−1·68, 14·80)	1·63 (−0·92, 4·19)	0·21
Adjusted difference (95 % CI)‡	Reference	4·86 (−3·17, 12·91)	3·98 (−3·57, 11·53)	6·37 (−2·69, 15·44)	8·09 (0·05, 16·13)	2·17 (−0·35, 4·68)	0·10
LDL-c (mmol/l)							
Mean	85·46	91·00	83·91	89·31	85·12		
SD	21·70	26·09	18·36	27·99	21·41		
Unadjusted difference (95 % CI)†	Reference	5·54 (−2·14, 13·21)	−1·55 (−7·98, 4·88)	3·85 (−4·22, 11·92)	−0·34 (−7·26, 6·58)	−0·36 (−2·58, 1·85)	0·75
Adjusted difference (95 % CI)‡	Reference	6·21 (−0·99, 13·42)	0·53 (−5·77, 6·85)	5·68 (−2·35, 13·72)	2·09 (−4·54, 8·73)	0·7 (−1·44, 2·85)	0·62
HDL-c (mmol/l)							
Mean	50·64	49·91	50·22	49·15	50·43		
SD	9·26	10·19	9·35	10·90	10·44		
Unadjusted difference (95 % CI)†	Reference	−0·73 (−3·85, 2·38)	−0·42 (3·39, 2·56)	−1·48 (−4·71, 1·75)	−0·21 (−3·38, 2·95)	−0·48 (−1·45, 0·49)	0·33
Adjusted difference (95 % CI)‡	Reference	−0·34 (−3·51, 2·81)	−0·11 (−3·19, 2·95)	−1·14 (−4·40, 2·12)	0·27 (−2·87, 3·40)	−0·38 (−1·37, 0·60)	0·49
VLDL-c (mmol/l)							
Mean	15·14	15·27	15·62	16·17	16·69		
SD	6·16	6·92	7·87	7·04	7·40		
Unadjusted difference (95 % CI)†	Reference	0·13 (−1·97, 2·22)	0·48 (−1·78, 2·74)	0·76 (−1·38, 2·90)	1·54 (−0·64, 3·73)	0·46 (−0·29, 1·21)	0·23
Adjusted difference (95 % CI)‡	Reference	−0·08 (−2·01, 1·85)	0·42 (−1·82, 2·66)	0·61 (−1·48, 2·71)	1·79 (−0·26, 3·84)	0·53 (−0·16, 1·22)	0·13
TAG (mmol/l)							
Mean	75·71	76·34	78·12	80·86	83·44		
SD	30·82	34·60	39·34	35·20	37·01		
Unadjusted difference (95 % CI)†	Reference	0·63 (−9·84, 11·21)	2·41 (−8·89, 13·71)	4·87 (−5·73, 15·46)	7·73 (−3·20, 18·67)	2·46 (−1·31, 6·24)	0·20
Adjusted difference (95 % CI)‡	Reference	−0·17 (−9·77, 9·42)	2·49 (−8·69, 13·68)	4·58 (−5·61, 14·77)	9·30 (−0·91, 19·51)	2·94 (−0·46, 6·34)	0·09
TC/HDL-c							
Mean	2·99	3·14	3·08	3·22	3·15		
SD	0·55	0·65	0·58	0·71	0·63		
Unadjusted difference (95 % CI)†	Reference	0·15 (−0·04, 0·34)	0·09 (−0·08, 0·27)	0·23 (0·02, 0·43)	0·16 (−0·03, 0·35)	0·07 (0·01, 0·13)	0·03*
Adjusted difference (95 % CI)‡	Reference	0·14 (−0·05, 0·32)	0·10 (−0·08, 0·28)	0·22 (0·02, 0·43)	0·17 (−0·01, 0·35)	0·07 (0·01, 0·13)	0·02*
LDL-c/HDL-c							
Mean	1·73	1·89	1·72	1·89	1·75		
SD	0·49	0·62	0·44	0·69	0·55		
Unadjusted difference (95 % CI)†	Reference	0·16 (−0·04, 0·34)	0·01 (−0·16, 0·13)	0·13 (−0·06, 0·33)	0·02 (−0·15, 0·18)	0·01 (−0·04, 0·06)	0·69
Adjusted difference (95 % CI)‡	Reference	0·16 (−0·01, 0·33)	0·02 (−0·13, 0·17)	0·16 (−0·05, 0·36)	0·05 (−0·11, 0·21)	0·03 (−0·03, 0·08)	0·38
AIP							
Mean	0·35	0·36	0·36	0·44	0·45		
SD	0·45	0·50	0·52	0·52	0·46		
Unadjusted difference (95 % CI)†	Reference	0·01 (−0·14, 0·17)	0·01 (−0·14, 0·17)	0·01 (−0·10, 0·24)	0·01 (−0·05, 0·24)	0·04 (−0·01, 0·08)	0·14
Adjusted difference (95 % CI)‡	Reference	0·00 (−0·15, 0·14)	0·00 (−0·15, 0·16)	0·01 (−0·10, 0·22)	0·10 (−0·04, 0·24)	0·04 (−0·01, 0·08)	0·09
LCI							
Mean	20·74	24·71	21·68	27·10	24·52		
SD	13·90	21·31	17·18	23·63	19·11		

Table 3 *Continued*

Markers	C-DII (quintiles)					Per 1 SD§	P_{trend}‖
	Q1 (−2·16 to −0·19) (*n* 75)	Q2 (−0·20 to 0·41) (*n* 76)	Q3 (0·42 to 0·86) (*n* 76)	Q4 (0·87 to 1·41) (*n* 76)	Q5 (1·42 to 2·75) (*n* 75)		
Unadjusted difference (95 % CI)†	Reference	3·96 (−1·78, 9·72)	0·93 (−4·06, 5·93)	6·35 (0·10, 12·61)	3·77 (−1·59, 9·14)	1·37 (−0·58, 3·33)	0·17
Adjusted difference (95 % CI)‡	Reference	3·98 (−1·28, 9·25)	1·84 (−3·23, 6·91)	7·07 (0·74, 13·39)	5·34 (0·43, 10·25)	1·94 (0·20, 3·67)	0·03*
AC							
Mean	1·99	2·14	2·08	2·22	2·15		
SD	0·55	0·65	0·58	0·71	0·63		
Unadjusted difference (95 % CI)†	Reference	0·15 (0·04, 0·34)	0·10 (−0·08, 0·28)	0·20 (−0·01, 0·41)	0·16 (−0·03, 0·35)	0·06 (0·00, 0·12)	0·05
Adjusted difference (95 % CI)‡	Reference	0·13 (−0·06, 0·32)	0·09 (−0·09, 0·27)	0·18 (−0·03, 0·40)	0·16 (−0·02, 0·34)	0·06 (0·002, 0·12)	0·04*

95 % IC, 95 % confidence interval; SD, standard deviation; AC, atherogenic coefficient; AIP, atherogenic index of plasma; HDL-c, high-density lipoprotein cholesterol; LCI, lipoprotein combine index; LDL-c, low-density lipoprotein cholesterol; LDL-c/HDL-c, low-density lipoprotein cholesterol/high-density lipoprotein cholesterol ratio; TC, total cholesterol; TC/HDL-c, total cholesterol/high-density lipoprotein cholesterol ratio; TAG, triglycerides; VLDL-c, very-low-density lipoprotein cholesterol.
*$P < 0·05$.
†From linear regression models with each lipid marker as a continuous outcome and C-DII as predictor. Robust estimates of variance were specified in all models.
‡From linear regression adjusted for child's age, sex, race, per capita income, screen time and body fat.
§From linear regression model with each lipid marker as continuous outcome and C-DII per 1 SD (continuous) as predictor.
‖Test for linear trend when a variable representing ordinal C-DII categories were introduced as a continuous predictor in the linear regression.

parameters, such as sugar and dietary fats (e.g. ultraprocessed foods), increases lipogenesis[41,42], activates the NF-kB pathway[43,44] and may subsequently alter lipid profile in children[45,46]. Moreover, emerging evidence demonstrate that the pro-inflammatory diet is directly associated with the secretion of pro-inflammatory cytokines and expression of adhesion molecules[13,47,48] which contributes to vascular tissue inflammation, endothelial dysfunction[5,6] and carotid intima-media thickening[16]. Atherosclerosis is a chronic inflammatory disease[5,6] that often originates in childhood[49] and is related to future cardiovascular events[50]. Therefore, a diet rich in anti-inflammatory properties might benefit children's health and growth, preventing the early onset of the atherosclerotic process and subsequent heart diseases in adulthood.

Some strengths of this study should be pointed out. First, this is a representative study with the sample composed exclusively of children, an important group in which to investigate food consumption because eating habits are created in childhood. Second, we evaluated the association of C-DII and atherogenic risk using traditional lipoproteins as well as non-traditional atherogenic indexes. Furthermore, body composition was analysed with dual-energy X-ray absorptiometry, a gold-standard method for assessing body composition, and the models were adjusted by body fat (%). We highlight that, according to our knowledge, this is the first epidemiological study to evaluate the relationship of C-DII with atherogenic risk in children. Our study provides novel information to public health practice and a better understanding of the role of the inflammatory dietary factors in the early occurrence of dyslipidaemia and underlying atherosclerosis.

This study has some limitations. First, the application of 24-h dietary recalls may present memory bias; however, the interviewers were previously trained, and the 24-h dietary recalls were administered on three non-consecutive days, using food a photo album and standard measurement tools; and all are recognisably methodological strategies to guarantee better accuracy. Second, we calculated the C-DII score with sixteen of the total twenty-five food parameters included in the C-DII definition. Nevertheless, our C-DII scores were similar to previous paediatric studies[18,51]. Finally, the cross-sectional design makes it impossible to establish causal relationships. Thus, further longitudinal studies with paediatric population are required to confirm our findings and determine the long-term effects of dietary-related inflammation on lipid profile and cardiovascular risk.

We conclude that pro-inflammatory diet, as indicated by higher C-DII scores, is associated with higher atherogenic risk in Brazilian schoolchildren. These results reinforce the importance of effective nutritional policies to promote healthy eating habits, improve the children's lipid profile and prevent later CVD.

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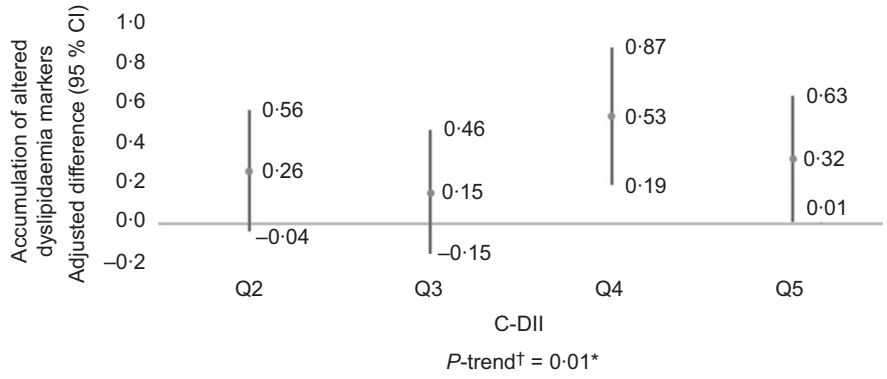

Fig. 2 Association between the Children's Dietary Inflammatory Index (C-DII) and the accumulation of altered dyslipidaemia markers (high TC + high TAG + high LDL-cholesterol + low HDL-cholesterol) in schoolchildren from Viçosa, Minas Gerais, Brazil, 2015. Q, quintiles; Q1: reference. †From linear regression models with the number of altered dyslipidaemia markers as continuous outcome and a variable representing ordinal C-DII categories introduced as continuous predictor. Robust estimates of variance were specified in all the models. Adjusted for child's age, sex, race, per capita income, screen time and body fat. ($P < 0{\cdot}05$*)

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References

1. Faludi AA, Izar MC, Saraiva JF *et al.* (2017) Atualização da diretriz brasileira de dislipidemias e prevenção da aterosclerose – 2017. *Arq Bras Cardiol* **109**, 1–76.
2. Furtado JM, Almeida SM, Mascarenhas P *et al.* (2018) Anthropometric features as predictors of atherogenic dyslipidemia and cardiovascular risk in a large population of school-aged children. *PLoS One* **13**, e0197922.
3. Ding W, Cheng H, Yan Y *et al.* (2016) 10-year trends in serum lipid levels and dyslipidemia among children and adolescents from several schools in Beijing, China. *J Epidemiol* **26**, 637–645.
4. Faria Neto JR, Bento VF, Baena CP *et al.* (2016) ERICA: prevalence of dyslipidemia in Brazilian adolescents. *Rev Saúde Pública* **50**, Suppl. 1, 10s. doi: 10.1590/S01518-8787.2016050006723.
5. Libby P, Ridker PM & Maseri A (2002) Inflammation and atherosclerosis. *Circulation* **105**, 1135–1143.
6. Ross R (1999) Atherosclerosis—an inflammatory disease. *N Eng J Med* **340**, 115–126.
7. Calder PC, Ahluwalia N, Brouns F *et al.* (2011) Dietary factors and low-grade inflammation in relation to overweight and obesity. *Br J Nutr* **106**, S1–S78.
8. Bamba V (2014) Update on screening, etiology, and treatment of dyslipidemia in children. *J Clin Endocrinol Metabol* **99**, 3093–3102.
9. Jellinger PS, Smith DA, Mehta AE *et al.* (2012) AACE task force for the management of dyslipidemia and prevention of atherosclerosis writing committee. *Endocr Pract* **18**, 270–293.
10. Khan I, Kwon M, Shivappa N *et al.* (2020) Proinflammatory dietary intake is associated with increased risk of metabolic syndrome and its components: results from the population-based prospective study. *Nutrients* **12**, 1196.
11. Mazidi M, Shivappa N, Wirth MD *et al.* (2018) Dietary inflammatory index and cardiometabolic risk in US adults. *Atherosclerosis* **276**, 23–27.
12. Bondonno NP, Lewis JR, Blekkenhorst LC *et al.* (2017) Dietary inflammatory index in relation to sub-clinical

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atherosclerosis and atherosclerotic vascular disease mortality in older women. *Br J Nutr* **117**, 1577–1586.
13. Khan S, Wirth MD, Ortaglia A *et al.* (2018) Design, development and construct validation of the children's dietary inflammatory index. *Nutrients* **10**, 993.
14. Suhett LG, Hermsdorff HHM, Cota BC *et al.* (2020) Dietary inflammatory potential, cardiometabolic risk and inflammation in children and adolescents: a systematic review. *Crit Rev Food Sci Nutr* **61**, 407–416.
15. Suhett LG, Hermsdorff HHM, Ribeiro SAV *et al.* (2021) The dietary inflammatory index is associated with anti- and pro-inflammatory adipokines in Brazilian schoolchildren. *Eur J Nutr*. Published online: 11 February 2021. doi: 10.1007/s00394021025008.
16. Sethna CB, Alanko D, Wirth MD *et al.* (2021) Dietary inflammation and cardiometabolic health in adolescents. *Pediatr Obes* **16**, e12706.
17. Rahbarinejad P, Asghari G, Yuzbashian E *et al.* (2019) Dietary inflammatory index in relation to carotid intima media thickness among overweight or obese children and adolescents. *Ann Nutr Metabol* **75**, 179–186.
18. Sen S, Rifas-Shiman SL, Shivappa N *et al.* (2018) Associations of prenatal and early life dietary inflammatory potential with childhood adiposity and cardiometabolic risk in Project Viva. *Pediatr Obes* **13**, 292–300.
19. Filgueiras MD, Suhett LG, Silva MA *et al.* (2018) Lower vitamin D intake is associated with low HDL cholesterol and vitamin D insufficiency/deficiency in Brazilian children. *Public Health Nutr* **21**, 2004–2012.
20. Milagres LC, Rocha NP, Filgueiras MS *et al.* (2017) Vitamin D insufficiency/deficiency is associated with insulin resistance in Brazilian children, regardless of body fat distribution. *Public Health Nutr* **20**, 2878–2886.
21. Zabotto CB, Vianna RPT & Gil MF (1996) Registro Fotográfico Para Inquéritos Dietéticos: utensílios e Porções. Goiânia: Nepa-Unicamp. https://www.fcm.unicamp.br/fcm/sites/default/files/2016/page/manual_fotografico.pdf (accessed November 2020).
22. Núcleo de Estudos e Pesquisas em Alimentação & Universidade Estadual de Campinas (2011) Tabela Brasileira de Composição de Alimentos – TACO, 4ª ed. rev. e ampl. Campinas: Nepa–Unicamp. http://www.nepa.unicamp.br/taco/contar/taco_4_edicao_ampliada_e_revisada.pdf?arquivo=taco_4_versao_ampliada_e_revisada.pdf (accessed November 2020).
23. US Department of Agriculture & Agricultural Research Service (2016) USDA National Nutrient Database for Standard Reference (Release 28). http://www.fnic.nal.usda.gov/food-composition/USDA-nutrient-data-laboratory (accessed July 2017).
24. Millán J, Pintó X, Muñoz A *et al.* (2009) Lipoprotein ratios: physiological significance and clinical usefulness in cardiovascular prevention. *Vasc Health Risk Manag* **5**, 757.
25. Wu TT, Gao Y, Zheng YY *et al.* (2018) Atherogenic index of plasma (AIP): a novel predictive indicator for the coronary artery disease in postmenopausal women. *Lipids Health Dis* **17**, 197.
26. Dobiášová M & Frohlich J (2001) The plasma parameter log (TG/HDL-C) as an atherogenic index: correlation with lipoprotein particle size and esterification rate in apob-lipoprotein-depleted plasma (FERHDL). *Clin Biochem* **34**, 583–588.
27. Pires A, Sena C & Seiça R (2016) Dyslipidemia and cardiovascular changes in children. *Curr Opin Cardiol* **31**, 95–100.
28. Kavey RE (2015) Combined dyslipidemia in childhood. *J Clin Lipidol* **9**, S41–S56.
29. de Onis M, Onyango AW, Borghi E *et al.* (2007) Development of a WHO growth reference for school-aged children and adolescents. *Bull World Health Organ* **85**, 660–667.
30. White H (1980) A heteroskedasticity-consistent covariance matrix estimator and a direct test for heteroskedasticity. *Econometrica* **48**, 817–838.
31. Criqui MH & Golomb BA (1998) Epidemiologic aspects of lipid abnormalities. *Am J Med* **105**, 48S–57S.
32. Castro AP, Hermsdorff HH, Milagres LC *et al.* (2019) Increased ApoB/ApoA1 ratio is associated with excess weight, body adiposity, and altered lipid profile in children. *J Pediatr* **95**, 238–246.
33. Sapunar J, Aguilar-Farías NI, Navarro J *et al.* (2018) Alta prevalencia de dislipidemias y riesgo aterogénico en una población infanto-juvenil. *Rev Méd Chile* **146**, 1112–1122.
34. Puddu PE, Shivappa N, Menotti A *et al.* (2020) Energy-adjusted dietary inflammatory index scores predict long-term cardiovascular disease mortality and other causes of death in an ecological analysis of the Seven Countries Study. *Eur J Prev Cardiol* **4**, 2047487320903866.
35. Garcia-Arellano A, Martínez-González MA, Ramallal R *et al.* (2019) Dietary inflammatory index and all-cause mortality in large cohorts: the SUN and PREDIMED studies. *Clin Nutr* **38**, 1221–1231.
36. Shivappa N, Steck SE, Hussey JR *et al.* (2017) Inflammatory potential of diet and all-cause, cardiovascular, and cancer mortality in National Health and Nutrition Examination Survey III Study. *Eur J Nutr* **56**, 683–692.
37. Giannini C, Diesse L, D'adamo E *et al.* (2014) Influence of the Mediterranean diet on carotid intima–media thickness in hypercholesterolaemic children: a 12-month intervention study. *Nutr Metabol Cardiovasc Dis* **24**, 75–82.
38. Cadario F, Prodam F, Pasqualicchio S *et al.* (2012) Lipid profile and nutritional intake in children and adolescents with type 1 diabetes improve after a structured dietician training to a Mediterranean-style diet. *J Endocrinol Invest* **35**, 160–168.
39. Sureda A, Bibiloni MD, Julibert A *et al.* (2018) Adherence to the Mediterranean diet and inflammatory markers. *Nutrients* **10**, 62.
40. Arouca A, Michels N, Moreno LA *et al.* (2018) Associations between a Mediterranean diet pattern and inflammatory biomarkers in European adolescents. *Eur J Nutr* **57**, 1747–1760.
41. Rupérez AI, Mesana MI & Moreno LA (2019) Dietary sugars, metabolic effects and child health. *Curr Opin Clin Nutr Metabol Care* **22**, 206–216.
42. Siri-Tarino PW & Krauss RM (2016) Diet, lipids, and cardiovascular disease. *Curr Opin Lipidol* **27**, 323–328.
43. Calder PC, Albers R, Antoine JM *et al.* (2009) Inflammatory disease processes and interactions with nutrition. *Br J Nutr* **101**, 1–45.
44. Galland L (2010) Diet and inflammation. *Nutr Clin Pract* **25**, 634–640.
45. Leffa PS, Hoffman DJ, Rauber F *et al.* (2020) Longitudinal associations between ultra-processed foods and blood lipids in childhood. *Br J Nutr* **6**, 1–8.
46. Rauber F, Campagnolo PD, Hoffman DJ *et al.* (2015) Consumption of ultra-processed food products and its effects on children's lipid profiles: a longitudinal study. *Nutr Metabol Cardiovasc Dis* **25**, 116–122.
47. Almeida-de-Souza J, Santos R, Barros R *et al.* (2018) Dietary inflammatory index and inflammatory biomarkers in adolescents from LabMed physical activity study. *Eur J Clin Nutr* **72**, 710–719.
48. Shivappa N, Hebert JR, Marcos A *et al.* (2017) Association between dietary inflammatory index and inflammatory markers in the HELENA study. *Mol Nutr Food Res* **61**, 1600707.
49. Holman RL, McGill HC Jr, Strong JP *et al.* (1958) The natural history of atherosclerosis: the early aortic lesions as seen in New Orleans in the middle of the 20th century. *Am J Pathol* **34**, 209.

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50. Willeit P, Tschiderer L, Allara E *et al.* (2020) Carotid intima-media thickness progression as surrogate marker for cardiovascular risk: meta-analysis of 119 clinical trials involving 100,667 patients. *Circulation* **142**, 621–642.

51. Navarro P, Shivappa N, Hébert JR *et al.* (2019) Predictors of the dietary inflammatory index in children and associations with childhood weight status: a longitudinal analysis in the lifeways cross-generation cohort study. *Clin Nutr* **39**, 2169–2179.

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