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REVIEW

Dietary inflammatory potential, cardiometabolic risk and inflammation in children and adolescents: a systematic review

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ABSTRACT

The Dietary Inflammatory Index (DII®) is a tool developed for quantifying the dietary inflammatory potential of individuals' diets, with the goal of assessing the effect of diet-associated inflammation on health outcomes. With most studies focusing on adults, little is known about the consequences for health of a more proinflammatory diet early in life. Hence, this study analyzed the available evidence on the association between the DII or the children's C-DII (C-DII™) and cardiometabolic risk and inflammatory biomarkers in children and adolescents. This systematic review was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The search was performed at the LILACS, ScienceDirect, Cochrane and PubMed databases, without any restriction regarding the dates of the publications. A total of six observational studies qualified; including three cross-sectional and three longitudinal studies focused on children and adolescents between 3 and 18 years of age representing both sexes. All papers found a positive association between the DII or C-DII with cardiometabolic markers. These included adiposity (i.e., BMI, waist and hip circumference, waist-to-height ratio and fat mass index), and/or to inflammatory biomarkers (interleukins 1, 2 and 6, tumor necrosis factor-alpha, interferon gamma, and soluble vascular cell adhesion molecule-1). In conclusion, findings currently available in the literature indicate that a proinflammatory diet is associated with a higher risk of early development of cardiometabolic and inflammatory changes during childhood. Also, the findings show the applicability of the DII and C-DII in epidemiological studies and underscore the need for strategies to encourage healthy, anti-inflammatory diets to prevent chronical illnesses. Systematic Review Registration Number (PROSPERO: CRD42019123939).

Introduction

Obesity in children and adolescents has become one of the major public health concerns throughout the world, largely because of its association with the early development of several metabolic (WHO 2018; WHO 2017) and inflammatory (Suhett et al. 2019) complications. Therefore, studies that identify the risk factors associated with excess weight in childhood can lead to strategies to prevent future associated illnesses.

An important modifiable risk factor in the etiology of obesity is food consumption (WHO 2003). A healthy and balanced diet during childhood; i.e., one rich in fruits and vegetables, is related to adequate growth appropriate development, and good quality of life (Mellendick et al. 2018; Funtikova et al. 2015). On the other hand, an unhealthy diet, embodied in what is known as the Western diet, may contribute to a pro-inflammatory state (Silveira et al. 2018)

and increased cardiometabolic risk beginning in childhood (Zhen et al. 2018; Rocha et al. 2017).

The Dietary Inflammatory Index (DII®) is a tool to assess the inflammatory potential of the diet, that was designed with the purpose of enabling a quantitative classification of food intake ranging from maximally anti-inflammatory to maximally pro-inflammatory (Cavicchia et al. 2009). A total of 45 food parameters, including some whole foods, macronutrients, and micronutrients such as vitamins and minerals and other constituents such as flavonoids were identified in a careful search of the literature that was conducted to create this index (Shivappa et al. 2014). Based on essentially the same schema, the Children's Dietary Inflammatory Index (C-DII™) was recently developed and validated to be used in pediatric populations (Khan et al. 2018). Both the DII and the C-DII have been associated with systemic inflammation in both children and adults (Phillips et al. 2018; Khan et al. 2018; Shivappa et al. 2014).

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The utilization of the DII in nutritional epidemiology research allows us to assess diet-associated inflammation in relation to the incidence of non-communicable chronic diseases (Garcia-Arellano et al. 2019). Studies conducted in adults have shown positive associations between DII scores and adiposity (Muhammad et al. 2019; Meneguelli et al. 2019), cardiovascular diseases (Muhammad et al. 2019; Phillips et al. 2018; Park et al. 2018), metabolic syndrome (Ruiz-Canela, Bes-Rastrollo, and Martínez-González 2016) and mortality (Park et al. 2018; Garcia-Arellano et al. 2019). However, research with children and adolescents is still scarce. This review aims to analyze the available evidence on the association between the DII or C-DII and cardiometabolic risk and inflammatory biomarkers in children and adolescents.

Materials and methods

Study identification and selection

This systematic review was designed to address the following research question: "What is the evidence available regarding the association between the Dietary Inflammatory Index and cardiometabolic risk and inflammation biomarkers in children and adolescents?". The present study was designed and implemented within the period from April to October 2019, based on the recommendations of Preferred Reporting Items for Systematic Reviews and Meta-Analyzes (PRISMA) guidelines and registered in PROSPERO (CRD42019123939).

The search was performed at the Latin-American and Caribbean System on Health Sciences Information (LILACS), ScienceDirect, Cochrane and National Library of Medicine, Bethesda, MD (PubMed) databases, without any restriction regarding the dates of the publications. The following search terms were used with combinations of descriptors available at the Medical Subject Headings (MeSH) index and keywords related to the subject: ("dietary inflammatory index" OR "inflammatory diet" OR "anti-inflammatory diet" OR "dietary inflammatory score") AND ("cardiovascular diseases" OR "cardiometabolic risk" OR "obesity") AND ("child" OR "adolescent"); ("dietary inflammatory index" OR "inflammatory diet" OR "anti-inflammatory diet" OR "dietary inflammatory score") AND ("inflammation" OR "subclinical inflammation" OR "inflammatory biomarker") AND ("child" OR "adolescent"). The search was restricted to papers written in the English language.

The researchers defined a protocol for identification and selection of original articles (Figure 1). The papers were independently and simultaneously analyzed and selected by two researchers (L.G.S. and B.C.C.). All studies whose selection was not unanimous between the researchers were discussed by them, with the purpose of reaching a consensus or, if necessary, ask for the opinion of a third reviewer. Initially, 350 papers were identified, which were evaluated by their titles and abstracts. Following the assessment of eligibility criteria, six papers were included in the present review.

Eligibility criteria

1. Inclusion: Observational studies with children and adolescents (aged 2 to 19 years) that assessed the association of DII or C-DII with cardiometabolic risk and/or inflammatory biomarkers.
2. Exclusion: Studies with adults, pregnant women, animals or *in vitro* experiments; papers that did not meet the inclusion criteria (association between DII or C-DII and other factors; or those that did not assess DII or C-DII); review papers; book sections; conference proceedings; encyclopedias; editorials; gray literature; monographs, theses, dissertations; publications whose full texts were not available; duplicates.

Data extraction

The information gathered regarding the selected papers were: authorship; year of publication; country; title of the study; study design; sample; method for assessing food consumption; number of food items for DII calculation; DII interpretation; outcome variables; main statistical analyses; adjustment variables; main results; statistically significant result (yes/no).

Assessment of study quality

Study quality was assessed through the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist (von Elm et al. 2014). Each reviewer (L.G.S. and B.C.C.) independently scored the overall quality of the papers, by attributing a score for each item in the paper. Following this assessment, all studies received a score between 0 and 22 points from each reviewer. The scores were averaged in order to generate a final score. Also, following a criterion established by the authors, the scores given by the reviewers could not differ from one another by more than one point. The final score was displayed as a percentage for better visualization of study quality.

Results

Study selection and description of the included studies

In total, 350 references were identified through the combinations of the descriptors listed above. Of these, six original papers were selected and included in the present review (Figure 1). All of these were observational studies carried out in children and adolescents of both sexes; three were cross-sectional, and three were cohorts. Half of them (n = 3) recruited their participants from schools, and sample sizes varied from 329 to 5427 individuals, aged 3 to 18 years (Table 1). Linear multiple regression was the most common statistical test performed in the studies (n = 4).

Other characteristics, such as author and year of publication, title and location of the study and outcome variables (cardiometabolic risk and inflammatory biomarkers) are described in Table 1. Table 2 displays the main statistical
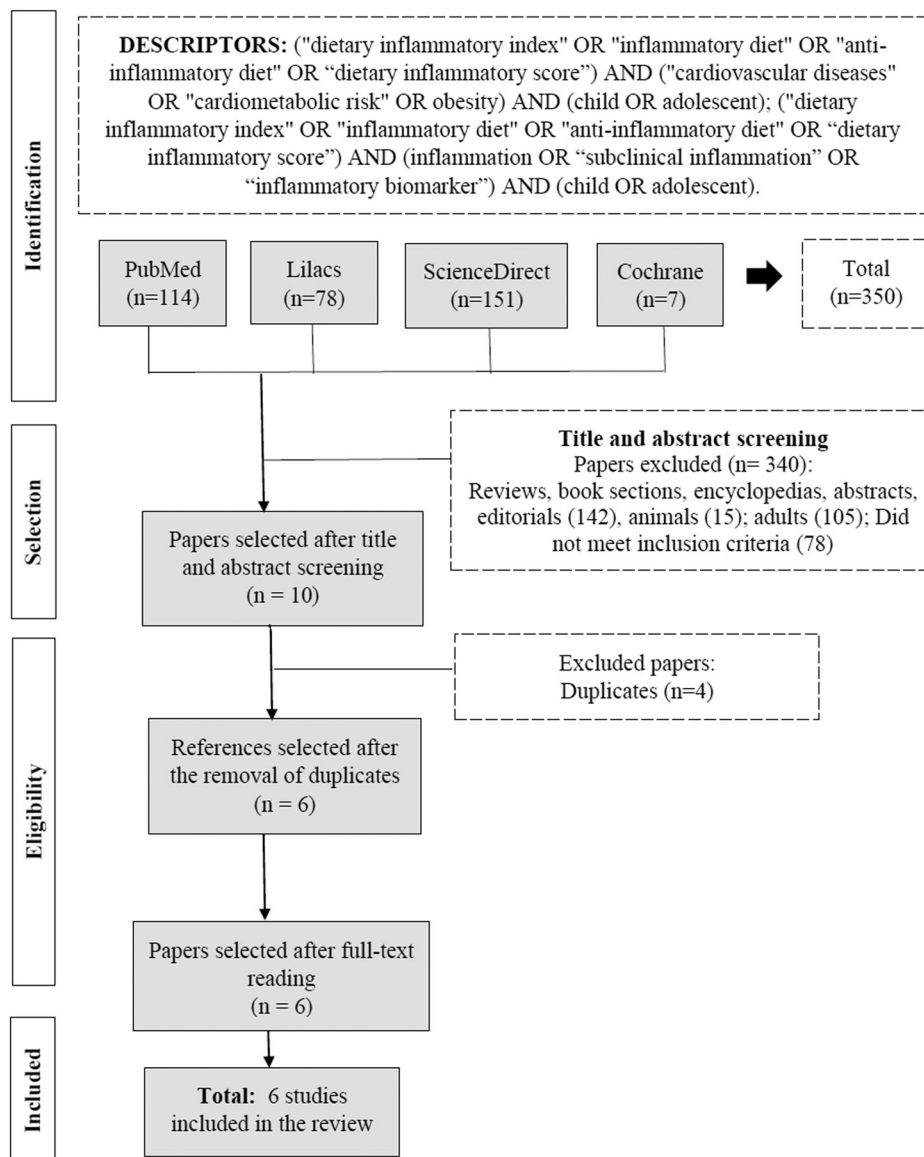
Figure 1. Protocol of identification and selection of studies eligible for the systematic review on the association between Dietary Inflammatory Index (DII® or C-DII™) and cardiometabolic risk and inflammatory biomarkers in children and adolescents.

analyses, adjustment variables, main results and study quality assessment.

Figure 2 displays the cardiometabolic risk markers and inflammatory biomarkers associated to DII and C-DII in children and adolescents, identified in the present study.

Dietary Inflammatory Index (DII) or Children's DII (C-DII)

In all of the studies food consumption was assessed using food frequency questionnaires (FFQ) (n = 4) or 24 h-dietary recalls (n = 2). Most of the studies (n = 5) performed the DII calculation by following the methodology developed by Shivappa et al. (2014); include 25 to 31 food items out of a total of 45 possible parameters. Only one of the studies used the new index proposed by Khan et al. (2018) to assess the quality of children's diets (C-DII) (Navarro et al. 2019). All of the studies used the DII as continuous as well as categorized into terciles (n = 3) or quartiles (n = 3) (Table 1). Three studies reported DII scores ranging between −5.36

and +4.26 (negative values indicate an anti-inflammatory diet, while positive values indicate a pro-inflammatory diet). Findings from three studies did not include the DII or C-DII ranges observed within the respective investigated populations (Navarro et al. 2019; Sen et al. 2018; Shivappa et al. 2017) (Table 2).

Statistical analysis and adjustment variables

In order to examine the association between the DII and cardiometabolic and inflammatory biomarkers, most of the studies employed the multiple linear (n = 4) or multiple logistic (n = 2) regression analysis, adjusted according to confusing factors such as: Gender, age, socioeconomic status, area of residence, city, puberty stage, body mass index (BMI), waist circumference (WC), caloric intake, screen time, playing outdoors, looking at books and traveling in a car/bus, physical activity, smoking habit from the child or

Table 1. Characteristics of the studies included in the systematic review.

Author/ year	Study's country, name and design	Sample	Method of assessing the diet and number of food items used for DII® or C-DII™	Interpretation of DII® or C-DII™	Outcome variables
Navarro et al. (2019)	Ireland Lifeways Cross-Generation Cohort Study Prospective cohort Follow-up: 2001-2007	$n = 551$ 5 and 9 years NA	FFQ (149 items) 24 items	DII as continuous variable; Median C-DII $\leq$0.58 and >0.58; 1st Tertile (ref) vs. 3rd Tertile by considering the median C-DII score in each tertile.	Height, weight, BMI and WC.
Aslani et al. (2019)	Iran (Caspian)-IV Cross-sectional	$n = 5427$ 6-18 years Boys ($n = 2886$) Girls ($n = 2541$)	FFQ (168 items) 25 items	DII as continuous variable; 1st Quartile (ref:< −1.63) vs. 4th Quartile (>1.50).	Height, weight, WC, NC, wrist circumference, HC, BMI, WHtR, WHR.
Correa-Rodríguez et al. (2018)	Spain - Cross-sectional	$n = 428$ 9-17 years Boys ($n = 186$) Girls ($n = 242$)	24h Dietary recall (3 days) 28 items	DII as continuous variable; 1st Quartile (ref:$\leq$0.96) vs. 4th Quartile (>1.47).	Height, weight, BMI, WC, WHtR, WHR, body fat, BP, heart rate.
Almeida-de-Souza et al. (2018)	Portugal LabMed physical activity Study Cross-sectional	$n = 329$ 12-18 years Boys ($n = 145$) Girls ($n = 184$)	FFQ (91 items) 31 items	DII as continuous variable; 1st Tertile (ref:< −1.34) vs. 3rd Tertile (>1.41).	CRP, IL-6, C3, C4, Inflammatory Score.
Sen et al. (2018)	EUA Project Viva Pre-birth cohort Follow-up: on going	$n = 992$ pairs of mothers and children 3-5 years 6-10 years NA	FFQ (84 items) 28 items	DII as continuous variable; 1st Quartile (ref) vs. 4th Quartile.	Height, weight, BMI, WC, total body fat, truncal fat mass index, fat mass index, fat-free mass index, subscapular and triceps skinfolds, BP, fasting glucose, insulin, HOMA, TG, TC and fractions, LEP, CRP, cardiometabolic risk score.
Shivappa et al. (2017)	10 European cities Helena Cross-sectional	$n = 532$ 12-17,5 years NA	24h Dietary recall (2 days) 25 items	DII as continuous variable; 1st Tertile (ref) vs. 3rd Tertile.	CRP, TNF-α, IL-6, IL-1, IL-2, IL-4, IL-10, IFN-γ, sICAM, sVCAM.

BMI, body mass index; BP, blood pressure; C-DII, children's Dietary Inflammatory Index; C3, C3 component; C4, C4 component; CRP, C-reactive protein; DII, Dietary Inflammatory Index; HC, hip circumference; HOMA, homeostatic model assessment of insulin resistance; IL-1, interleukin-1; IL-2, interleukin-2; IL-4, interleukin-4; IL-6, interleukin-6; IL-10, interleukin-10; IFN-γ, interferon gamma; LEP, serum leptin; NC, neck circumference; sICAM, soluble intracellular adhesion molecule-1; sVCAM, soluble vascular cell adhesion molecule-1; TC, total serum cholesterol; TG, serum triglyceride; TNF-α, tumor necrosis factor alpha; WC, waist circumference; WHtR, waist-to-height ratio; WHR, waist/hip ratio.
NA: Distribution of the sample according to gender were not available in the article.

adolescent, and maternal characteristics (age, BMI, level of education, parity, smoking habit and ethnicity) (Table 2).

DII or C-DII and cardiometabolic risk markers

Four studies that assessed the association between DII and cardiometabolic risk in children and adolescents were included (Aslani et al. 2019; Correa-Rodríguez et al. 2018; Sen et al. 2018). It is noteworthy that from all cardiometabolic risk markers examined by the studies, only the adiposity markers were associated with DII scores. A recently published cohort study conducted in Ireland with 551 children aged 5 and 9 years showed that higher C-DII scores were associated with greater risk of childhood obesity at age 5 (OR = 1.09; 95% CI = 1.00-1.37) and overweight/obese status at 5 and 9 years (OR = 1.06; 95% CI = 1.01-1.09 and OR = 1.12; 95% CI = 1.07-1.18, respectively) (Navarro et al. 2019). Aslani et al. (2019), in their cross-sectional study with 5.427 Iranian children and adolescents,

aged 6 to 18 years, observed that participants with a more proinflammatory diet (fourth quartile group: DII > 1.50) displayed higher values of BMI, waist (WC) and hip (HC) circumferences, when compared to those from the first DII quartile group. Another cross-sectional study carried out in Spain with 428 schoolchildren aged 9-17, showed positive association between DII and waist-to-height ratio (WHtR) ($\beta = 0.128$; 95% CI =0.001-0.16) (Correa-Rodríguez et al. 2018). In a cohort conducted in the USA with 992 pairs of mothers and children aged 3 to 5 and 6 to 10, the children exposed to a more proinflammatory diet in the uterus and in the first childhood (3-5 y/o) displayed higher cardiometabolic risk at 6-10 years of age (Sen et al. 2018) (Table 2).

DII or C-DII and inflammatory biomarkers

As for the inflammatory biomarkers, a prospective cohort study in Portugal, with 329 adolescents, from 12 to 18 years

Table 2. Main statistical analyses, adjustment variables, findings and quality assessment of the studies that examined the association between DII® or C-DII™ with metabolic risk and inflammatory biomarkers in children and adolescents.

Author/year	Statistical analyses	Adjustment variables	Main findings	Statistically significant result (Yes/No)?	Score and % STROBE
Navarro et al. (2019)	Multiple logistic regression	Child gender, BMI, WC, time spent TV watching, playing outdoors, looking at books and traveling in a car/bus.	The C-DII average score was 0.56 ± 1.12. Higher C-DII scores indicating a more pro-inflammatory diet among children, were associated with greater risk of childhood obesity at age 5 (OR = 1.09; 95% CI = 1.00-1.37) and overweight/obese status at 5 and 9 years (OR = 1.06; 95% CI = 1.01-1.09 and OR = 1.12; 95% CI = 1.07-1.18, respectively).	Yes	18.8 81.8%
Aslani et al. (2019)	Multiple linear regression	Age, gender, area of residence, screen time, physical activity, socioeconomic status.	DII = $-4.42 - +4.26$. Individuals with the most pro-inflammatory diet (4th quartile) had a positive association with BMI ($\beta = 0.07$; 95% CI = 0.01-0.14), WC ($\beta = 0.89$; 95% CI= 0.07-1.70) and HC ($\beta = 1.13$; 95% CI =0.29-1.96) compared to those in the lowest quartile of DII (1st quartile). Considering the DII as continuous variable, a positive association was observed with the children WC ($\beta = 0.27$; 95% CI = 0.01-0.53) and HC ($\beta = 0.39$; 95% CI = 0.13-0.65). The pro-inflammatory diet is associated with higher rates of obesity.	Yes	19.8 90.0%
Correa-Rodríguez et al. (2018)	Multiple linear regression	Age, gender, caloric intake, pubertal stage.	DII= $-4.35 - +3.53$. DII average: 0.24 ± 1.67. The DII was associated to WHtR ($\beta = 0.128$; 95% CI = 0.001-0.16).	Yes	19.8 90.0%
Almeida-de-Souza et al. (2018)	Multiple logistic regression	Gender, age, puberty stage, BMI, caloric intake, socioeconomic status, time of sedentarism, physical activity, smoking habit.	DII = $-5.36 - +4.24$. Adolescents in the 3rd tercile of DII were more likely to have alterations in IL-6 (OR = 3.38; 95% CI = 1.24-9.20), C3 (OR = 1.71; 95% CI = 0.63-4.66), C4 (OR = 3.12; 95% CI = 1.21-8.10) and higher inflammatory score (OR = 5.61; 95% CI = 2.00-15.78) compared to those in the lowest tercile.	Yes	19.3 87.7%
Sen et al. (2018)	Multiple linear regression	Age and gender, family income and maternal characteristics (age, BMI, level of education, parity, smoking, ethnicity).	DII average (3-5 years): 0.3 ± 0.7. In girls, there were no significant differences between the DII of children aged 3-5 years with the anthropometric measures and cardiometabolic risk of children aged 6-10 years. In boys, the DII in early childhood (3-5 years) was associated with higher BMI values ($\beta = 0.16$; 95% CI = 0.02-0.29), and skinfolds ($\beta = 1.12$; 95% CI = 0.01-2.23) later in life (6-10 years). Boys exposed to a more pro-inflammatory diet	Yes	17.3 78.6%

Table 2. Continued.

Author/year	Statistical analyses	Adjustment variables	Main findings	Statistically significant result (Yes/No)?	Score and % STROBE
			(4th quartile) in the uterus and early childhood (3-5 years) presented a positive association with BMI ($\beta = 0.78$; 95% CI = 0.34-1.22) in the middle childhood (6-10 years), compared to children (3-5 years) in the lowest quartile of the DII (1st quartile). Boys and girls in the largest quartile of the DII (4th quartile) in the uterus and early childhood (3-5 years) were associated with higher values of fat mass index ($\beta = 0.67$; 95% CI = 0.06-1.27) and WC ($\beta = 2.36$; 95% CI = 0.14-4.59) when older (6-10 years).		
Shivappa et al. (2017)	Multiple linear regression	Age, gender, city, BMI, smoking habit of adolescents, physical activity.	Positive association between DII and TNF-α (β IIDt3vs1 = 0.13; 95% CI = 0.007-0.26), IL-1 (β IIDt3vs1 = 0.30; 95% CI = 0.02-0.58), IL-2 (β IIDt3vs1 = 0.42; 95% CI = 0.04-0.79), IFN-γ (β IIDt3vs1 = 0.58; 95% CI = 0.09-1.06), sVCAM (β IIDt3vs1 = 0.07; 95% CI = 0.01- 0.13). Positive association between continuous DII and TNF-α (β = 0.004; 95% CI = 0.002-0.07) and sVCAM (β = 0.03; 95% CI = 0.01-0.04).	Yes	17.3 78.6%

BMI, body mass index; BP, blood pressure; C-DII, children's Dietary Inflammatory Index; C3, C3 component; C4, C4 component; CI 95%, 95% confidence interval; CRP, C-reactive protein; DII, dietary inflammatory index; HC, hip circumference; HOMA, homeostatic model assessment of insulin resistance; IL-1, interleukin-1; IL-2, interleukin-2; IL-4, interleukin-4; IL-6, interleukin-6; IL-10, interleukin-10; IFN-γ, interferon gamma; LEP, serum leptin; NC, neck circumference; OR, odds ratio; sICAM, soluble intracellular adhesion molecule-1; sVCAM, soluble vascular cell adhesion molecule-1; TC, total serum cholesterol; TG, serum triglyceride; TNF-α, tumor necrosis factor alpha; WC, waist circumference; WHtR, waist-to-height ratio.

of age, showed that those individuals consuming a more inflammatory diet (third DII tercile group: DII > 1.41) had greater odds of having changes in interleukin-6 (IL-6) (OR = 3.38; 95% CI = 1.24-9.20), C3 complement (C3) (OR = 1.71; 95% CI = 0.63-4.66), C4 complement (C4) (OR = 3.12; 95% CI = 1.21-8.10) and higher inflammatory score (OR = 5.61; 95% CI = 2.00-15.78), when compared to the adolescents in the first DII tercile group (Almeida-de-Souza et al. 2018). Another cross-sectional study carried out with adolescents (12 to 17 y/o) from different European cities reported positive associations between the DII and tumor necrosis factor α (TNF-α), interleukin-1 (IL-1), interleukin-2 (IL-2), interferon gamma (IFN-γ), and soluble vascular cell adhesion molecule-1 (sVCAM) (Shivappa et al. 2017) (Table 2).

All of the included studies in this review that examined the relation between DII and C-reactive protein (CRP) serum concentration did not identify significant associations (Almeida-de-Souza et al. 2018; Sen et al. 2018; Shivappa et al. 2017). Besides, none of the studies evaluated the relationship between C-DII and inflammatory biomarkers.

Study quality

Considering a total of 22 points, the score of the studies varied from 17.3 to 19.8 points (78.6% to 90.0%) (Table 2). The criteria on which the studies were scored the least points were related to their not completely addressing the following items: reporting the study design within the title or abstract; presenting eligibility criteria, sources and methods of selection of participants; clearly defining all outcomes, exposures, predictors, potential confounders and effect modifiers; specifying all measures employed to avoid potential sources of bias; explaining how missing data were handled; describing the number of participants and reasons for loss of sample in each stage of the study; describing the non-adjusted estimations, as well as their accuracy (e.g., confidence intervals); discussing generalization of findings (i.e., external validity).

Discussion

The present systematic review is, to the best of our knowledge, the first to gather the available evidence on the association of the DII and C-DII with cardiometabolic risk and
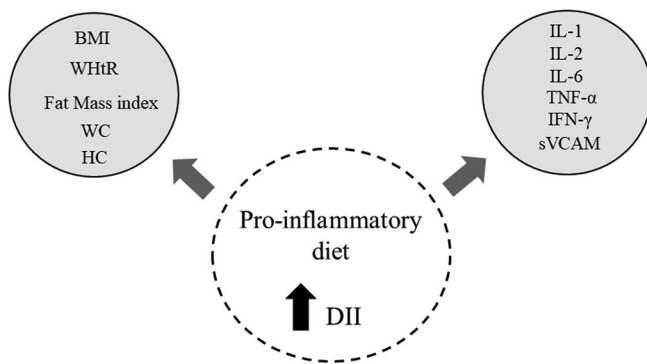
Figure 2. Cardiometabolic risk markers and inflammatory biomarkers associated to a pro-inflammatory diet evaluated by the DII® or C-DII™ in children and adolescents. DII, dietary inflammatory index; BMI, body mass index; IL-1, interleukin-1; IL-2, interleukin-2; IL-6, interleukin-6; IFN-γ, interferon gamma; WC, waist circumference; HC, hip circumference; sVCAM, soluble vascular cell adhesion molecule-1; TNF-α, tumor necrosis factor alfa.

inflammatory biomarkers in children and adolescents. Taking into account that nutrition is an important determinant of chronic diseases, and that childhood is a key stage for the development of healthy eating habits (Funtikova et al. 2015), it is relevant to understand the consequences of inappropriate food consumption early in life.

Unhealthy dietary patterns are associated to cardiometabolic changes in children and adolescents (Vieira-Ribeiro et al. 2019; Zhen et al. 2018; Rocha et al. 2017). Studies have shown that the low intake of whole fresh foods, such as fruits and vegetables (Mellendick et al. 2018; Navarro et al. 2017), as well as the high consumption of ultraprocessed foods (UPF) and excess sugar in the diet are associated with increased risk of developing obesity and other complications already in childhood (Vieira-Ribeiro et al. 2019; Sparrenberger et al. 2015). In a study with a representative sample of Brazilian children between 8 and 9 years of age (n = 378) from the *Pesquisa de Avaliação da Saúde do Escolar* (PASE – Schoolchildren Health Assessment Survey) it was found that those children with excess weight and body adiposity displayed higher adhesion to industrialized DP (mainly composed by UPF) and lower adherence to traditional DP (rice and beans) (Rocha et al. 2019). It is suggested that the excessive intake of proinflammatory foods may predispose the child to accumulation of body fat, leading to increased central and total adiposity and, consequently, higher levels of chronic systemic inflammation that is frequently observed in obesity (Mtintsilana et al. 2019).

Excessive intake of UPF, sugary drinks, sweets and candies was associated with several inflammatory biomarkers, favoring the occurrence of subclinical inflammation (González-Gil et al. 2018; Kosova, Auinger, and Bremer 2013), whilst antioxidant vitamins, polyunsaturated fatty acids (del Mar Bibiloni et al. 2013) and minerals (Suhett et al. 2018) seem to have anti-inflammatory properties. In addition, there is evidence that higher consumption of vegetables (González-Gil et al. 2016) and greater diversity of fruits and vegetables in the diet may have a protective effect against inflammation (Almeida-de-Souza et al. 2018).

In study with 464 European adolescents (13 to 17 y/o), individuals familiarized with the Mediterranean diet, mainly consisting of fruits, vegetables, olive oil, chestnuts, fish and whole grains (Grosso et al. 2014), displayed lower cardiovascular and inflammatory risk (Arouca et al. 2018). The Mediterranean diet is considered a healthy and anti-inflammatory DP (Grosso et al. 2014; Galland 2010), as the low adhesion to this pattern is directly associated to the worse plasmatic inflammatory biomarkers profile (Sureda et al. 2018). These results indicate that the diet has a key role for the onset of chronic diseases through the modulation of the inflammation (Hébert et al. 2019; Calder et al. 2011; Shivappa 2019).

A diet of poor nutritional quality, mainly consisting of refined flours, sugar, saturated and trans fats may unleash an innate immune response, associated with the production and release of proinflammatory cytokines and a reduction of anti-inflammatory cytokines (Galland 2010; Giugliano, Ceriello, and Esposito 2006). This imbalance can favor the production of pro-inflammatory mediators, which, in turn, enable the occurrence of endothelial disfunction at the vascular level, thus fostering the low-grade chronic inflammatory state and increasing the risk of metabolic disorders (Muhammad et al. 2019; Phillips et al. 2018; Giugliano, Ceriello, and Esposito 2006). Another likely explanation involves the generation of oxidant compounds such as hydrogen peroxide and superoxide radicals during food metabolism, which, in turn, activate the NF-kB pathway, promoting inflammation (Kiecolt-Glaser 2010). Therefore, the consumption of foods rich in antioxidant compounds and vitamins may reduce the oxidative stress, as well as decrease the production of inflammatory mediators and serum concentration of adhesion molecules (sVCAM-1 and sICAM-1) (Calder et al. 2009; Giugliano, Ceriello, and Esposito 2006). It is important to disclose that none of the studies with children as sample assessed the relation between DII and inflammatory biomarkers, as the results were based exclusively on adolescent subjects.

Although the results with children and adolescents in this review did not reveal associations between DII and CRP serum concentration, the DII was associated with other inflammatory biomarkers, such as IL-6, which is considered a more sensible biomarker to cardiovascular diseases than CRP (Held et al. 2017). However, the inflammatory diet was associated to CRP in other populations (Phillips et al. 2018; Shivappa et al. 2014). Some of the differences in the results between the studies may be explained by factors such as sample size, utilization of different kinds of methods for assessing food consumption (FFQ vs. 24 h-dietary recalls), variation in the number of food items used to calculate DII. In addition, even though the C-DII has been validated with serum CRP in children and adolescents aged 6 to 14 years participants from NHANES (2005-2010) (Khan et al. 2018), none of the included studies evaluated the relationship of C-DII and inflammatory biomarkers yet. Therefore, further studies addressing this topic are necessary to elucidate potential associations with other mechanisms.

With respect to the quality of the papers included, only few of them described in the title or abstract the kind of experimental design applied. Nevertheless, all studies

included this information within the start of the Methods section. Still, the actions aiming to avoid potential sources of methodological bias were not entirely clear, since only a few limitations were discussed by most of the studies. The absence of descriptions regarding missing data and sample losses in the cohort studies could also be noted. Although some topics are not clearly described by the authors of the selected studies, they allow us to observe important associations that are poorly investigated, especially in young people.

Some of the strengths of the present review regards its systematic approach based on the PRISMA guidelines, peer-review and study quality assessment through the STROBE method (von Elm et al. 2014). However, a meta-analysis of data was not feasible due to the heterogeneity of the studies. The reduced number of studies included might be a limitation to assure the association between DII or C-DII and cardiometabolic and inflammatory risk. Although the search for the articles was made in 4 of the most important databases, other databases may include more articles that were not selected. Nevertheless, this paper provides new insights and highlights the necessity of more epidemiological studies, particularly longitudinal ones, with the utilization of the new children-specific DII calculation (C-DII) proposed by Khan et al. (2018).

In conclusion, the evidence presented in this review indicates that the DII and C-DII are useful tools for quantifying the inflammatory potential of the diet. We observed that a more pro-inflammatory diet was generally associated with cardiometabolic risk markers related to body adiposity (BMI, waist and hip circumference, waist-to-height ratio and fat mass index), and to inflammatory biomarkers (interleukins 1, 2 and 6, tumor necrosis factor alpha, interferon gamma, soluble vascular cell adhesion molecule-1) in children and adolescents. These findings reinforce the necessity of public health policies to implement effective actions of eating and nutritional education with children, families and schools, with the purpose of developing healthy eating habits that prevent current and future chronic and inflammatory diseases. The paucity of studies in this arena, underlined by our inability to conduct a meta-analysis, reinforces the need for more studies on the C-DII and health outcomes in children.

Disclosure statement

The authors declare no conflicts of interest. Dr. James R. Hébert owns controlling interest in Connecting Health Innovations LLC (CHI), a company that has licensed the right to his invention of the dietary inflammatory index (DII®) from the University of South Carolina in order to develop computer and smartphone applications for patient counseling and dietary intervention in clinical settings. Dr. Nitin Shivappa is an employee of CHI. The subject matter of this paper will not have any direct bearing on that work, nor has that activity exerted any influence on this project. The authors have no other potential competing interest to disclose.

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