Diet quality, asthma and airway inflammation in school-aged children

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Summary

Background: Asthma is a major public health problem, with increasing prevalence in most countries, particularly among children. Poor dietary quality is also increasing in children, and evidence of the overall quality of children's food patterns effects on asthma is scarce.

Methods: This cross-sectional analysis (660 children: 49,1%females, aged 7-12years) evaluated the association between diet quality and asthma (n=56) and airway inflammation among school-aged children according to body mass index (BMI). Diet quality was assessed through the Healthy Eating Index (HEI)-2015, and categorized by tertiles. Higher scores represent a healthier diet. A questionnaire was used to enquire about self-reported medical diagnosis of asthma and asthma under medication. Lung function and airway reversibility were measured, and airway inflammation assessed measuring exhaled fractional nitric oxide (eNO). Two categories of BMI were considered: non-overweight/obese (P<85th), (n=491), and overweight/obese (P≥85th), (n=169). The associations between diet quality and asthma and airway inflammation were estimated using logistic regression models.

Results: Non-overweight/obese children in 2^{nd}tertile of HEI-2015 score had decreased odds of having eNO≥35ppb (OR=0.43, 95%CI 0.19;0.98), medical diagnosis of asthma (OR=0.18; 95%CI 0.04;0.84), and asthma treatment (OR=0.12; 95%CI 0.01;0.95), compared to children in the 1^{st}tertile.

Conclusions: Our findings suggest that a higher diet quality associates with lower levels of airway inflammation and reduced prevalence of asthma among non-overweight/obese school-aged children.

Keywords: Diet quality; Asthma; Obesity; Healthy Eating Index; Airway Inflammation; Children

Impact Statement: Non-overweight/obese children with higher diet quality have lower levels of airway inflammation and reduced prevalence of asthma. Nonetheless, the same associations are not observed in overweight/obese children.

1. Introduction

Asthma is a major global health concern, and its prevalence and incidence are higher among children, especially in high-income countries (1). According to the International Study of Asthma and Allergies in Childhood (ISAAC), the prevalence of asthma in children has increased in many countries (2). Environmental factors, in conjunction with genetic susceptibility, can play a significant role in asthma pathophysiology (3) and it's possible that its prevalence has risen as a result of lifestyle and environmental changes (4). Dietary changes, such as increased consumption of highly processed and refined foods and decreased consumption of vegetables and fruits, may be an important contributor to this increase in asthma prevalence trend (Figure **1**) (4). Dietary patterns with the above-mentioned traits are likely to lead to obesity, which is a major public health concern, being simultaneously a disease modifier and a risk factor for asthma(4). Asthma has been increasingly associated with obesity (4, 5) and both the diseases appears to be driven by genetic and lifestyle factors (5, 6). Obese individuals have an increased risk of asthma, as well as more frequent and severe symptoms and exacerbations, a lower quality of life, and a reduced response to asthma medications (3, 7). In fact, children who were overweight had an increased adjusted risk for incident asthma (relative risk [RR]: 1.17; 95% confidence interval [CI]: 1.10–1.25) and for obese (RR: 1.26; 95% CI: 1.18–1.34 (8).

Although the role of diet has undoubtedly recognized mechanisms in some diseases (9), it has not been identified as a causal factor for asthma development (3). In this perspective, the majority of studies on diet and asthma association are performed upon specific foods or foods components (10). Nonetheless, foods are ingested as complex combinations, which include bioactive components, nutrients, and their specific effects in the food matrix, which interact with each other and leads to synergist effects modulating and influencing metabolic and health effects according to different dietary patterns (3, 4).

It has been demonstrated that higher dietary acid loads may modulate asthma-related miRNAs among school-aged children (11). Additionally, eating a higher dietary diversity of vegetables was linked to a lower risk of airway inflammation and to a lower prevalence of self-reported asthma (12). It has also been shown that diet's inflammatory characteristics may have a role in modulating the effects of indoor air pollution on asthma, indicating that the exposure effect to PM2.5 and PM10 on children with asthma was significantly higher among those who have a pro-inflammatory diet compared to a more anti-inflammatory diet (13).

The influence of food on asthma, asthma symptoms and lung function is of growing interest (3) and diet scores that evaluate diet quality, have been broadly used (4, 14). Dietary scores that can assess diet quality, based on established knowledge on the role of dietary intakes in prevention of major chronic diseases, may be of particular interest when investigating the role of diet in asthma (15).

In this context, the aim of this study was to investigate the effect of diet quality on asthma and airway inflammation in children. Additionally, we explored the association between diet quality, airway inflammation and three different definitions of asthma, considering a stratification according to children BMI.

2. Materials and Methods

2.1 Study design and participants

This is a secondary analysis of a cross-sectional study conducted between 2014 and March 2015. A total of 1602 children aged 7-12 years old in the 3rd and 4th grades, from 20 public school located in Porto, Portugal, were invited to participate (12). A total of 686 (42.8%) did not present the signed informed consent and 58 (3.8%) declined to perform clinical procedures. Among the remaining 858 children (53.6%), 660 (76.9%) had complete nutritional data (HEI-2015) and were considered for the analysis (Figure **2**). Written consent was obtained from every child's legal guardian. The study was done in accordance with Helsinki Declaration and The Ethics Committee of the University Hospital São João approved the study (ARIA 248-13).

2.2. Participants assessment

2.2.1. Dietary and Diet Quality Assessment

Dietary information was collected using a single interviewer-administered 24-hour food recall questionnaire answered by the children, following standard procedures, and using a photograph atlas to estimate portion sizes. Participants were asked in detail about their food and beverages intakes from the previous 24h, including brands and quantities (16). Nutritional data and total energy intake (kcal) were estimated through the software Food Processor® (ESHA Research, USA), that encompasses databases of Portuguese nutritional food composition.

Diet quality was evaluated by using the HEI-2015, which has 13 components that sum to a total maximum score of 100 points (17). This index has two sections: adequacy and moderation. Higher scores are provided on the nine adequacy components (total fruits, whole fruits, total vegetables, greens and beans, whole grains, dairy, total protein foods, seafood and plant proteins and fatty acid ratio) and reflect higher intakes. The other four components are moderation components, which are calculated so that higher scores indicate lower intakes (refined grains, sodium, added sugars, and saturated fats). For most of the components the ratio of the dietary constituents are to 1000 kcal of energy, except for fatty acids. Fatty acids use the ratio of the sum of monounsaturated and polyunsaturated fatty acids to saturated fatty acids. Also, two components, saturated fat and added sugars, are conveyed on a percent of energy basis (17, 18).

Since all components of the index are considered equally important, the HEI components are weighted equally. Some diet groups are represented by two components, each with a maximum of 5 points. All other components receive up to ten points. Total fruits, whole fruits, total vegetables, greens and beans, total protein foods, seafood and plant proteins are components that are scored to a maximum of 5 points when: total fruits ≥ 0.8 cup equivalent, whole fruits≥ 0.4 cup equivalent, total vegetables ≥ 1.1 cup equivalent, greens and beans ≥ 0.2 cup equivalent, total protein foods ≥ 2.5 ounces equivalent, seafood and plant proteins ≥ 0.8 ounces equivalent. These components have 0 points when no foods from the component's groups are consumed (17). Whole grains, dairy, fatty acid ratio, refined grains, sodium, added sugars, and saturated fats can have a maximum of 10 points, when: whole grains ≥ 1.5 ounces equivalent, dairy ≥ 1.3 cup equivalent, fatty acid ratio ≥ 2.5 cup, refined grains ≤ 1.8 ounces equivalent, sodium ≤ 1.1 grams, added sugars ≤ 6.5% of energy, and saturated fats ≤ 8% of energy. The standard for having a minimum score (zero) is as follows: on the whole grains and dairy components implies no consumption; for fatty acids having a ratio that is ≤ 1.2; for refined grains ≥ 4.3 ounces equivalent; for sodium ≥ 2.0 grams; for added sugars ≥ 26% of energy; and for saturated fats ≥ 16% of energy. Intakes between the minimum and maximum standards are scored proportionately (17). As for arranging the components of the HEI-2015 score: "Total Fruits" includes 100% fruit juice and whole fruits; "Total Protein Foods" includes meat, poultry, eggs, seafood, nuts, seeds, soy products, legumes (beans and peas); "Seafood and Plant Proteins" component comprises seafood, nuts, seeds, soy products, legumes (beans and peas); "Greens and Beans" consist of legumes (beans and peas) and dark-green vegetables; "Total Vegetables" enclose legumes (beans and peas), dark-green vegetables and all other vegetables. "Dairy" component contains all milk products, such as fluid milk, cheese, and yogurt, and fortified soy beverages (17). For dairy, meat, poultry and eggs, saturated fat is counted separately; when considering nuts, seeds and soy products it encloses nuts, seeds, and soy products (other than beverages) (17). As information was registered in grams, "Portions and Weights, 2017-2018 Food and Nutrient Database for Dietary Studies - At A Glance" was used to transform dietary components from grams to cups (19). The higher the overall HEI-2015 score, the better is the diet quality and adherence to a healthy eating pattern (17, 18). The HEI-2015 score was categorized into three groups according to the tertile score (1^{st}:≤54.53; 2^{nd}:>54.53 and ≤ 65.37; 3^{rd}:>65.37). The use of nutritional supplementation (vitamins/minerals) by the children in the past year was also considered.

2.2.2. Anthropometry

Weigh was measured by a digital scale (Tanita™ BC-418 Segmental Body Analyzer) and recorded in kilograms, and height was measured by a portable stadiometer and recorded in centimeters (cm). BMI was obtained by the calculation of weight/$height^2$ and displayed in kilograms per square meters (kg/m^2). Participants were then divided into two groups, non-overweight/obese (P<85th) and overweight/obese (P≥85th) (20), according to specific age and sex percentiles provided by the US Centers for Disease Control and Prevention (21). The US CDC definition was grounded on an evaluation of the degree of agreement among several BMI classifications (US CDC, International Obesity Task Force, World Health Organization, and Percentage of Body Fat), with the US CDC showing the highest level of agreement with all the other classifications (data not presented) (22).

2.2.3. Airway Inflammation

To quantify airway inflammation, FeNO was measured using a NObreath analyzer (Bedfont Scientific Ltd., Rochester, Kent, UK). The results were stratified in accordance with the official American Thoracic Society (ATS) criteria for children (23) and expressed as parts per billion (ppb). Exhaled NO was dichotomized using a cut-off point of equal or above 35 ppb representing increased levels of eNO.

2.2.4. Current asthma and respiratory symptoms assessment

The ISAAC in Childhood - based questionnaire was performed by the child's legal guardian. It enquired about social, demographic, and behavioural information and consisted of questions about the allergic/respiratory health and respiratory symptoms in the previous twelve months (24). Asthma symptoms (wheezing and cough symptoms) were defined by a positive answer to the question "Did your child has wheezing or whistling in the chest, in the past twelve months?"; and "Did your child suffer coughing at night in the last twelve months?" or "Did your child suffer coughing more than three months in the last year?". Self-report of asthma diagnosed by a physician was defined based on an affirmative answer to the question "Has your child ever been diagnosed with asthma by a physician?"

Airway reversibility and lung function, were recorded before and after 15 minutes of the inhalation of 400µg of salbutamol and evaluated through spirometry, following the official ATS/European Respiratory Society (ERS) guidelines (25).

Positive bronchodilation (+BD) was characterized by at least a 12% and over 200 mL increase in forced expiratory volume in one second (FEV1) as suggested by current GINA guidelines [include reference] and as a way to compare with the existing literature. Nevertheless, additionally, we also included in our analysis the new definition of +BD, suggested by the European Respiratory

Society: a change of >10% relative to the predicted value in forced expiratory volume in 1 second (FEV1). (26)

Three different definitions of asthma were considered as previously described (27): (i) ever asthma: self-reported medical diagnosis; (ii) +BD or medical diagnosis plus current asthma symptoms: self-reported medical diagnosis with reported symptoms (wheezing, dyspnoea, or dry cough) occurring in the past 12 months or positive BD (12% and over 200 mL increase in forced expiratory volume in one second); and (iii) medical diagnosis and under asthma treatment—self-reported medical diagnosis and currently under anti-asthma medication.

2.2.5. Atopy

Skin-prick tests (SPT) were performed on children's forearms using a QuickTest™ containing *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae* , a mix of weeds, a mix of grasses, *Alternaria alternata*, cat dander, and dog dander, a negative control, and a positive control containing histamine at 10mg/mL (Hall Allergy®, Netherlands), and the results read after 15 minutes.(28) According to standard procedures(28), atopy was defined by a positive SPT to at least one of the tested allergens (wheal ≥ 3 mm diameter) coupled to a positive histamine response (wheal ≥ 3 mm diameter) and no positivity in the negative control (wheal < 3 mm diameter).

2.2.6. Indoor Air quality

Air quality assessments were conducted by measuring concentrations of indoor pollutants, including PM2.5, PM10, ultrafine particles (UFP), carbon dioxide (CO2), ozone (O3), and nitrogen dioxide (NO2) at each school. These measurements took place over a 5-day period, specifically from Monday morning to Friday afternoon, during the winter season. To analyze PM2.5 and PM10, a portable TSI DustTrak DRX photometer (model 8533; TSI Inc) was utilized. This photometer employed laser technology and light scattering principles to measure particles. With an accuracy reading of ±0.1% at 1 µg/m3 and a measuring range of 1-150 × 103 µg/m3, the equipment provided reliable measurements. The photometer was equipped with an internal battery-powered diaphragm pump that allowed for a flow rate of 3.0 L/min. Continuous measurements were collected for a minimum of 8 hours (29, 30).

2.2.7. Socioeconomic Data

Parental education level was described as the number of completed school years. It was then divided into 3 categories established by the parent with the highest education level: ≤9 years, between ≥ 10 and ≤12 years, and >12 years, and was used to denote the socio-economic status(31, 32).

2.2.8. Statistical Analyses

All statistical analyses were performed using the SPSS ® statistical package software v27.0 and R studio software.

To check normality for continuous variables, skewness and kurtosis test was used. The characteristics of the participants are presented for the whole sample by sex as percentages for categorical variables, and as median (25^{th}–75^{th} percentile) for non-Gaussian distributed continuous variables, and as mean ± standard deviation (SD) for normal distributed continuous.

In order to determine differences between sexes, the independent-samples t-test for continuous variables and chi-squared test for categorical variables were used. The Mann-Whitney test was used for inferential analysis when non-Gaussian distributions were observed.

The associations between our independent variable, HEI-2015 score, (continuous and categorical) and airway inflammation and asthma, our dependent variables, were estimated using logistic regression models (OR, 95% CI).

When considering categories of the HEI-2015 score by tertiles: the reference and first tertile is ≤54.53, second tertile is >54.53 and ≤65.37, third tertile is >65.37.

The Hosmer-Lemeshow test was performed to assess the fit of the logistic regression model.
The selection of potential confounders was made through a combination of conceptual reasoning and empirical evidence(33). Factors such as age, sex, atopy, dietary factors, air quality, and parental education were chosen based on both our understanding of the subject matter and the evidence available in prior literature(34).

Confounders were considered such as age, sex(33), parental education(31-33, 35-38), atopy(33, 39) (40, 41), school(13, 30), total energy intake (TEI), and nutritional supplementation use (33). Significant differences were defined with an α-value of less than 5%, 95% confidence interval, ($p < 0.05$).

3. Results

The characteristics of participants included in the analyses are presented in table I. The mean (SD) age of children was 8.7 (0.8) years and 49.1% (n=324) were girls. A total of 6.8% (n=45) had a self-reported medical diagnosis of asthma; 8.5% (n=56) had a medical diagnosis with asthma symptoms or +BD; and 5.6% (n=37) had a medical diagnosis of asthma and were under asthma treatment. The prevalence of overweight/obese was 25.6% (n=169).

No significant differences were found among boys and girls except for TEI, and dietary sodium obtained from the 24-hour recall questionnaire. Boys presented higher values for TEI [2228 kcal (1966; 2581) vs. 2065 kcal (1760; 2403)] and dietary sodium [2206mg (1689; 3030) vs. 1923mg (1441; 2591)] compared to girls.

Additionally, there were also significant differences between boys and girl for both definitions of positive bronchodilation: +BD (a change of >10% relative to the predicted value in FEV1)(26) and +BD (12% and over 200 mL increase in FEV1) (25).

The score of the HEI-2015 showed no differences between sexes, with a total score of 59.6 ± 11.7 for girls and 58.8 ± 11.1 for boys. Components of the HEI-2015 among boys and girls are presented in table II. No statistically significant differences were observed.

After adjustment for age, sex, atopy, supplementation used in previous 12 months, parental education level, school, and total energy intake, non-overweight/obese children in the 2nd tertile of HEI-2015 score had decreased odds of having eNO ≥ 35ppb (OR = 0.43; 95%CI 0.19;0.98), ever asthma (OR = 0.18; 95%CI 0.04;0.84) and asthma under treatment (O R= 0.12; 95%CI 0.01;0.95), as presented on Table III.

The Hosmer-Lemeshow test was performed to assess the fit of the logistic regression model and it indicated a calculated chi-square value of 5,279 with a p-value of 0.727. At a significance level of 5%, we cannot reject the null hypothesis. Therefore, we can conclude that the model was adequately adjusted.

4. Discussion

This study revealed that having a higher-quality diet appears to reduce the odds of having higher airway inflammation, asthma diagnosed by a physician, and asthma under medication treatment among school-aged children who are not overweight or obese.

Other studies have proposed a beneficial effect of a higher-quality diet on asthma and airway inflammation, which is consistent with our findings (42-46). In a longitudinal study, lower scores in the Revised Brazilian Healthy Eating Index score increased the odds of wheezing in the previous year among young adults (18 and 22 years old) (OR = 1.97, 95%CI 1.33; 2.91 and OR = 1.98, 95%CI 1.36; 2.87, respectively). Accordingly, remaining on a poor diet from age 18 to 22, raised by more than three-fold the odds of chest wheezing (OR = 3.28; 95%CI 1.84; 5.84) compared to continuing on a high quality diet (42). Findings from the PARIS birth cohort revealed that children in the higher tertile group of adherence to the Mediterranean diet, considered to have a higher diet quality, had a lower risk of having current asthma compared to children in the lowest tertile group (aOR = 0.28, 95%CI 0.12; 0.64) (44). Also, adults with high adherence to the traditional Mediterranean diet were more likely to have asthma under control as measured by lung function, symptoms, and exhaled NO (OR = 0.22; 95% CI = 0.05–0.85) (47). A recent systematic review revealed a protective role of the Mediterranean diet on childhood asthma (45). Moreover, the Mediterranean diet has been shown to modulate the production of some inflammatory mediators known to play a pathogenetic role in asthmatic airways as IL-4 and IL-17 (46) and eNO (48).

Cardinale et al. (40) sugested that high levels of pro-inflammatory cytokines could increase the activity of iNOS enzyme (40). Considering the previous hypothesis by Cardinale et al., a higher dietary quality present various dietary component with antioxidant and anti-inflammatory properties that may reduce the production of pro-inflammatory cytokines (3), and thus decreasing NO production and airway inflammation. A low antioxidant dietary intake, as usually reflected by a low consumption of fruits and vegetables, as well as an intake of foods or following dietary patterns associated with increased oxidative stress, such as saturated fat consumption and adhering to a typical western diet, can increase oxidative damage to the airways via the generation of ROS (49). Because nutrients are not consumed in isolation, the additional and synergistic effects of combining the overall nutrient and phytochemical content acquired from various food matrix and overall diet with higher quality may explain the current study's negative associations (50).

In our study, the protective effect of diet was only observed among children who were not overweight or obese. These results may be due to the low number of overweight/obese individuals. However, a previous study including French adults also found that higher dietary scores assessed by three different indexes were associated with a lower asthma symptom score (4). Nevertheless, in the referred study, when separating individuals based on their BMI and analyzing the association of a higher diet quality with asthma symptom score, some statistically significant associations were lost when BMI was ≥ 25 and <30 kg/m^2 and nearly all were lost when BMI was ≥ 30 kg/m^2 (4). Individuals with obesity can present higher circulating concentrations of many inflammatory markers (51) and the GINA guidelines have in its recommendations weight loss as a component of the strategy of asthma management in obese individuals (52). Also, according to a systematic review, for obese asthmatic adults, the more effective dietary intervention appears to be energy restriction, regardless of the specific dietary components or dietary pattern (53). Given that obesity is a strong risk factor for asthma, having a high dietary quality may not be enough to compensate the negative consequences of being overweight or obese. Furthermore, asthma and obesity have an intricate mechanistic interaction, and comorbidities caused by excess body weight may aggravate or even mimic asthma symptoms, leading to misdiagnosis (54). Moreover, obesity is known to stimulate inflammatory pathways, but most studies among obese children with asthma either observed no correlation or found a negative correlation between exhaled NO and obesity, and similar results were seen in adults (55, 56). There seems to exist a mechanical effect of weight at the thoracic level that inhibits the production and diffusion of nitric oxide (57) or an increase in oxidative stress might cause a higher production of reactive oxygen species with consequential conversion of airway nitric oxide into reactive nitrogen species (55).

Besides, children who are overweight or obese may have a higher index quality score at the expense of elements and food groups that have not been found to be asthma protective such as fruit juice consumption which leads to a higher score in the "Total Fruits" category. In some studies, fruit juice consumption has been linked to an increased risk of asthma (58, 59). When analysing 100% fruit juice intake, the mean ± SD value in cups, is higher for the overweight/obese group when compared with the non-overweight/obese group (0.19 ± 0.52 cups vs. 0.13 ± 0.41 cups); although not statistically significant, it results in higher values in the component "Total Fruit" at the expense of fruit juice. Likewise, non-overweight/obese children, have overall higher final scores in components that have revealed positive impacts on asthma, namely Whole Fruits, Total Vegetables, Whole Grains, Greens and Beans, and Saturated Fats (data not shown), compared to overweight/obese children. This may also explain the no significant results observed among children in the highest tertile of the HEI-2015 score (Table 3).

In concordance, the U.S.-based Nurses' Health Study revealed that high AHEI-2010 scores were not associated with decreased risk of adult-onset asthma (60). A research with the aim of studying the association between a pro-inflammatory diet (as measured by the energy-adjusted Dietary Inflammatory Index [E-DII]) or a high dietary quality (as measured by the AHEI-2010) with current asthma, current asthma symptoms, and lung function in Hispanic adults, observed that a higher E-DII score (representing a more pro-inflammatory diet) was associated with current asthma (OR for quartile 4 vs. 1: 1.35, 95%CI 0.97;1.90) and asthma symptoms (OR for quartile 4 vs. 1: 1.42, 95%CI 1.12;1.81). However, the AHEI-2010 score was not significantly associated with any of the referred outcomes (61), and Han et al.(61) suggests that E-DII may be a better indicator of dietary patterns leading to airway inflammation than the AHEI-2010 (61).

In the same line, the index used in the present study (HEI-2015), assigns a positive score not only to the consumption of fruit juices, but also to dairy products, and both components exhibit no positive effects on asthma (58, 59, 62). Even though, not statistically significant, when analysing 100% fruit juice intake, the mean ± SD value in cups is higher for the third tertile (0.20 ± 0.53 cups) compared with the second (0.16 ± 0.42 cups) and first (0.08 ± 0.34 cups) tertiles, creating higher values in the component Total Fruit. As for dairy, we also observed the same pattern, the third tertile has higher dairy values mean ± SD in cups, than the second and first tertile (7.67 ± 2.58; 6.74 ± 2.85, and 6.19 ± 2.97 cups, respectively).

Furthermore, although HEI-2015 has vegetables intake into consideration, favouring the consumption of green vegetables, it does not have the whole diversity of eaten vegetables into consideration. Mendes et al. (12) showed that a higher diversity of vegetables, independently of the amount of the vegetables consumed, was associated with less self-reported asthma and airway inflammation (12). The HEI-2015, likewise, does not take into account the n-6:n-3 PUFA ratio that a number of studies have demonstrated to be relevant in asthma (63, 64), as well as trans saturated fats intake that has been associated with an increase in sputum % neutrophils in asthmatic patients (65). Moreover, this score does not take into consideration the protective influence of microbes and commensal organisms' exposure on the development of asthma and allergy (66). As food-borne microbes may hold a protective effect on asthma (67), cooked or raw vegetables and fruit consumption can impact outcomes (68, 69).

We acknowledge a various number of limitations in our research. Firstly, because this is a cross-sectional study, reverse causation may occur (70), and we can speculate that children who have previously been diagnosed with asthma may have already changed their consumption behaviour to a healthier diet, affecting the results. Also, the cross-sectional design precludes the establishment of causal relationships between diet quality with airway inflammation and asthma. Secondly, the HEI-2015 is not validated or adapted for Portugal nor Portuguese children and the recommendations present on this index may not fit this population. Nevertheless, epidemiologic studies are crucial for establishing potential causes of allergic diseases such as asthma, particularly when experimental study designs are challenging to do (71). The same research team gathered detailed health data, assuring a relative unbiased evaluation of outcome prevalence. Moreover, respiratory, allergic, and dietary outcomes were assessed at the same point in time, even so, symptoms were based on the prior twelve months, identifying individual that have long-term asthma (27). Other limitation is that we used a 24-hour recall questionnaire, a method primarily centered on short-term intake, and does not take seasonality into consideration. Nevertheless, detailed data about common size containers, ingredients used in mixed dishes, and commercial product brand names were gathered, permitting a good quality characterization of consumption and dietary intake. Moreover, because one single day does not represent usual intake, multiple recalls are preferred to report an individual's habitual intake (72). Nonetheless, a 24-hour recall questionnaire can estimate the current diet without inducing alterations in children's dietary behaviors as a result of the time-consuming task of recording or knowing that their diet is being assessed (73). Despite the fact that children were asked to recall all of the foods and beverages they had consumed the day before, a more difficult cognitive task, such as comparing their food intake in the last 24 hours to a typical day, was not considered. Dietary data collected may be influenced by recall bias and indirect reporting, particularly because, due to limited food knowledge and memory, children's self-reports of diet are more prone to have errors (74). However, knowing that portion size is hard to estimate correctly and to avoid misreporting in dietary consumption, nutritionists and specially trained interviewers obtained 24-hour food recall questionnaires from the children, using photographs and food models to quantify portion sizes, with the advantage that they have experience probing information from children without suggesting responses (75). The 24-hour dietary recall detailed good agreement and adequate reporting between energy intake and measured total energy expenditure at group level (16). It may be easier for children to remember the most recent foods consumed and the 24-hour recall may be preferable when determining the usual dietary intake of large groups of subjects (76). Other researches have also used 24h questionnaires-reports to assess dietary quality (77, 78), and Kirkpatrick et al. (78) found that HEI-2015 scores based on 24-hour dietary recall data are generally well estimated (78). Also, even though confounders were selected centered on preceding research and knowledge of their link with diet and the outcomes studied, residual confounding could still be present.

In terms of anthropometry, weight classifications were determined using BMI. BMI does not take into account body composition (79) and body adiposity appears to be more appropriate when studying asthma (80-82). BMI was calculated using measured height and weight, avoiding parental self-perceptions of weight categories, as most parents underestimated their children's overweight/obesity status (83).

Our study also has a variety of strengths. To the best of our knowledge, this study is the first one evaluating the association between diet quality with the Healthy Eating Index-2015 with asthma and airway inflammation in children. This research involved a large number of individuals and objectively measured spirometry with bronchodilation, combining it with ISAAC self-reported responses to characterize different asthma definitions, and three different definitions were used. (27). Although previous studies observed a good agreement in parental reporting of offspring asthma onset (84), according to Silva et al. (27), a standardized definition of asthma should comprise a questionnaire score as well as airway reversibility as these measures address different manifestations of asthma. Our research took into account important potential confounders such as atopy, parental education level, nutritional supplementation, total energy intake, surrounding environment, all of which have been considered relevant when addressing asthma-related outcomes in schoolchildren (33, 34).

The Healthy Eating Indexes have the benefit of being constantly revised and updated to agree with the latest guidelines for Americans (17). Even if the HEI-2015 is not adapted for Portugal nor Portuguese children, this index has the benefit of being scored on a density basis (17, 18), utilizing a less restrictive approach to defining standards for maximum scores, and enabling it to be employed to different groups, including children. The HEI-2015 evaluates quality over quantity (17). This index targets food subgroups that are most frequently low in diets and that have an exceptional nutrient profile, as legumes, dark green vegetables and seafood (17). Additionally, it has the benefit of not requiring any single food to have higher scores, having into regard food intake as a whole to characterize diet quality (17) carrying a more rounded approach to evaluate dietary intake that takes into consideration the potential interactions between the diverse components of the diet.

This study suggests that in non-overweight/obese school-aged children, a higher dietary quality is associated with a lower prevalence of self-reported medical diagnosis of asthma, self-reported medical diagnosis of asthma under asthma treatment, and lower levels of airway inflammation. This work underlines the significance of promoting a diet that is high quality as for example diets that are rich in vegetables, fruits, whole grains, greens and beans, healthy fats, high quality and diverse protein sources and that is low in saturated fats, added sugars, sodium, and refined grains. Understanding the potential effect of food consumption on asthma and airway inflammation might support the introduction of clinical guidelines and public health recommendations. Nevertheless, there are still significant gaps in the interpretation of the types of foods or diets that the population should incorporate in order to improve their respiratory health.

Funding: This research was funded *Fundação para a Ciência e Tecnologia* through the Project NORTE-01-0145-FEDER-000010 – Health, Comfort and Energy in the Built Environment (HEBE), cofinanced by *Programa Operacional Regional do Norte (NORTE2020)*, through *Fundo Europeu de Desenvolvimento Regional (FEDER)* and EXALAR 21 project financed by FEDER/FNR and by *Fundação para a Ciência e Tecnologia* (EXALAR 21 02/SAICT/2017 - Project nº 30193).

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by The Ethics Committee of the University Hospital São João.(ARIA 248-13, date of approval: 20 of September of 2013).

Author Contributions: Conceptualization, AM and PM; Data curation, IP, JCR and DS; Formal analysis, MCR, FCM, LD, AM and PM; Funding acquisition, AM; Investigation, MCR, FCM, PP, RB, IP, JCR and DS; Methodology, MCR, FCM, AM and PM; Project administration, AM; Writing – original draft, MCR, FCM and PM; Writing – review & editing, IP, PP, RB, JCR, DS, LD and AM.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Conflicts of Interest: The authors declare no conflict of interest.

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Table I. Summary of participants characteristics.

	Girls, n= 324 (49,1%)	Boys, n= 336 (50,9%)	Total, n= 660	*p*-value
Age (years), mean ± SD	8.68 ± 0.8	8.69 ± 0.8	8.68 ± 0.8	0.907
BMI category				0.864
Non-overweight/obese	242 (74.7%)	249 (74.1%)	491 (74.4%)	
Overweight/obese	82 (25.3%)	87 (25.9%)	169 (25.6%)	
HEI-2015 Score, mean ± SD	59.6 ± 11.7	58.8 ± 11.1	59.2 ± 11.4	0.387
Carbohydrates, %VET	50.1 ± 7.1	50.9 ± 7.4	50.6 ± 7.3	0.142
Protein, %VET	17.8 ± 4.2	17.3 ± 3.8	17.5 ± 4.0	0.095
Fat %VET	28.8 ± 6.2	28.6 ± 6.4	28.7 ± 6.3	0.679
MUFA %VET	10.2 ± 3.0	10.2 ± 3.3	10.2 ± 3.1	0.815
PUFA %VET	3.8 ± 1.8	3.7 ± 1.5	3.8 ± 1.7	0.500
SFA %VET	9.0 ± 3.4	8.9 ± 3.1	9.0 ± 3.2	0.597
Fiber (g), median (25th – 75th)	17.9 (13.3; 24.3)	18.8 (14.4; 24.3)	18.4 (13.8; 24.3)	0.345
Sodium (mg), median (25th – 75th)	1923 (1441; 2591)	2206 (1689; 3030)	2053 (1513; 2769)	**<0.001***
Total energy intake (kcal), median (25th – 75th)	2065 (1760; 2403)	2228 (1966; 2581)	2865 (1868; 2476)	**<0.001***
Nutritional Supplementation, n (%)	44 (15.4%)	43 (14.4%)	87 (14.9%)	0.496
+BD (>10%), n%	73 (22.5%)	91 (27.1%)	164 (24.8%)	**0.027***
+BD (>12% and >200ml), n (%)	21 (6.5%)	15 (4.5%)	36 (5.5%)	**0.041***
Asthma Symptoms, n (%)	45 (13.9%)	44 (13.1%)	89 (13.5%)	0.820
Asthma medication, n (%)	45 (13.9%)	44 (13.1%)	89 (13.5%)	0.820
Increased levels of FeNO (≥ 35ppb)**, n (%)**	36 (11.1%)	50 (14.9%)	86 (13.0%)	0.150
Asthma definitions, n (%)				
Ever	23 (7.1%)	22 (6.5%)	45 (6.8%)	0.759
Medical diagnosis with asthma symptoms or +BD	33 (10.2%)	23 (6.8%)	56 (8.5%)	0.124
Medical diagnosis and under asthma treatment	21(6.5%)	16 (4.8%)	37 (5.6%)	0.337

Atopy, n (%)	106 (33.3%)	121 (36.3%)	227 (34.9%)	0.422
Parental education, n (%)				0.236
<9 years	81 (32.3%)	107 (38.5%)	188 (35.5%)	
10-12 years	84 (33.5%)	77 (27.7%)	161 (30.4%)	
>12 years	86 (34.3%)	94 (33.8%)	180 (34.0%)	

Note: * statically significant differences. Abbreviations: HEI: Healthy Eating Index. FeNO: Fractional exhaled nitric oxide. MUFA: Monounsaturated fatty acids; PUFA: Polyunsaturated fatty acids; SFA: Saturated fatty acids. +BD: Positive Bronchodilation; %VET: Percent of Total energy value.

Table II. Scores of the HEI-2015 components by sex.

	Girls, n= 324 (49,1%)	**Boys, n=336 (50,9%)**	**Total, n= 660**	***p*-value**
HEI-2015 Groups, mean ± SD				
Total Fruits, mean ± SD	3.44±1.95	3.23±1.96	3.34 ±1.96	0.171
Whole Fruits, mean ± SD	3.86±1.99	3.71±2.03	3.79±2.01	0.350
Total Vegetables, mean ± SD	1.91±1.46	1.77±1.38	1.84±1.42	0.194
Whole Grains, median (25th – 75th)	0.00 (0.00; 2.43)	0.00 (0.00; 2.06)	0.00 (0.00; 2.21)	0.434
Dairy, mean ± SD	6.90±2.93	6.83±2.81	6.87±2.87	0.729
Total Protein Foods, median (25th – 75th)	5.00 (4.71;5.00)	5.00(4.90;5.00)	5.00 (4.86;5.00)	0.512
Seafood & Plant Proteins, mean ± SD	2.69±2.42	2.96±2.40	2.83±2.41	0.148
Greens & Beans, mean ± SD	3.27±2.02	3.24±2.05	3.26±2.04	0.841
Fatty Acids, mean ± SD	3.86±3.57	3.71±3.40	3.78±3.49	0.564
Refined Grains, mean ± SD	2.63±3.31	2.44±3.12	2.53±3.21	0.454
Sodium, median (25th – 75th)	10.00 (8.31;10.00)	10.00 (8.29;10.00)	10.00 (8.29;10.00)	0.870
Added Sugars, median (25th – 75th)	10.00 (7.99; 10.00)	9.37 (7.64; 10.00)	9.59 (7.86;10.00)	0.098
Saturated fats, mean ± SD	7.79±2.77	7.88±2.59	7.84±2.68	0.644

Note: Abbreviations: HEI: Healthy Eating Index.

Table III. Association between diet quality and airway inflammation and asthma.

	HEI Score: CrudeModel OR (95% CI)	HEIScore: aOR (95% CI)	HEI Score Tertiles: Crude Model OR (95% CI)		HEI Score Tertiles: aOR (95% CI)		
	Continuous (n=660)	Continuous (n=660)	>54.53 and ≤ 65.37 (n=220)	>65.37 (n=220)	Reference ≤54.53 (n=220)	>54.53 and ≤65.37 (n=220)	>65.37 (n=220)
Increased levels of eNO (≥ 35ppb)							
All participants	**0.98 (0.96;0.99)***	0.98 (0.96;0.99)	0.63 (0.36;1.09)	0.68 (0.4;1.18)	1.0	0.58 (0.29;1.17)	0.74 (0.38;1.45)
Non-overweight/obese	**0.97 (0.96;0.99)***	0.97 (0.94; 0.99)	**0.52(0.28;0.96)***	0.62 (0.34;1.13)	1.0	**0.39 (0.17;0.91)***	0.65 (0.30; 1.40)
Overweight/obese	0.99 (0.948;1.04)	0.999 (0.95; 1.05)	1.23 (0.34;4.52)	0.93 (0.24;3.65)	1.0	1.48 (0.32;6.91)	0.86 (0.17;4.36)
+ BD (>10%)							
All participants	1.00 (0.99;1.02)	1.00 (0.98;1.02)	1.3 (0.78,2.17)	1.3 (0.78,2.17)	1.0	1.37 (0.81,2.32)	1.36 (0.79,2.33)
Non-overweight/obese	0.99 (0.98;1.02)	0.99 (0.97;1.02)	1.85 (0.66,5.14)	1.62 (0.6,4.33)	1.0	1.93 (0.68,5.48)	2.05 (0.7,5.95)
Overweight/obese	1.02 (0.99;1.06)	1.04 (0.99;1.08)	1.2 (0.66,2.17)	1.22 (0.67,2.22)	1.0	1.24 (0.67,2.32)	1.27 (0.67,2.43)
Asthma							
Ever							
All participants	**0.97 (0.95;0.99)***	0.98 (0.95; 1.01)	0.61 (0.29;1.28)	0.63 (0.31;1.31)	1.0	0.45 (0.18;1.15)	0.71 (0.31;1.62)
Non-overweight/obese	0.96 (0.94;0.99)	0.96 (0.93;0.999)	0.43 (0.17;1.08)	0.55 (0.23;1.29)	1.0	**0.14 (0.03;0.69)***	0.53 (0.19;1.49)
Overweight/obese	0.99 (0.95;1.04)	0.999 (0.95;1.05)	1.38 (0.38,5.08)	0.93 (0.24;3.65)	1.0	1.62 (0.41;6.44)	1.19 (0.27;5.23)
Medical diagnosis w/asthma symptoms or +BD							
All participants	0.99 (0.97;1.02)	0.99 (0.97;1.02)	0.74 (0.38;1.47)	0.9 (0.47;1.72)	1.0	0.61 (0.27;1.41)	0.94 (0.44;2.01)
Non-overweight/obese	0.99 (0.96;1.02)	0.99 (0.96;1.02)	0.56 (0.25;1.27)	0.81 (0.38;1.72)	1.0	0.41 (0.14;1.24)	0.94 (0.38;2.32)

Overweight/obese	1.01 (0.96;1.06)	1.01 (0.96; 1.07)	1.51 (0.43;5.27)	1.18 (0.32;4.33)	1.0	2.09 (0.47;9.24)	1.6 (0.35;7.25)
Medical diagnosis and under asthma treatments							
All participants	0.98 (0.95;1.00)	0.98 (0.95;1.01)	0.45 (0.19,1.07)	0.69 (0.32;1.48)	1.0	**0.30 (0.09;0.94)***	0.76 (0.32;1.84)
Non-overweight/obese	0.97 (0.94;1.00)	0.97 (0.93;1.01)	0.37 (0.13,1.08)	0.61 (0.24;1.54)	1.0	**0.09 (0.01;0.78)***	0.62 (0.2;1.87)
Overweight/obese	0.99 (0.94;1.05)	0.92 (0.83;1.02)	0.71 (0.16,3.12)	0.93 (0.24;3.65)	1.0	0.82 (0.17;3.95)	1.08 (0.24;4.78)

Note: * statically significant differences. Abbreviations: aOR: Adjusted odds ratio; HEI: Healthy Eating Index; FeNO: Fractional exhaled nitric oxide. +BD: Positive Bronchodilation. Logistic regression was adjusted to age, sex, parental education, atopy, school, total energy intake, and nutritional supplementation use. Significant differences were defined with an α-value of less than 5%, 95% confidence interval, ($p < 0.05$)

Figure 1. Representation of the interaction between potential risk factors (as enviromental polution, education and socioeconomic status, weight and genetics) for asthma and airway inflammationand diet quality as a potential protector.

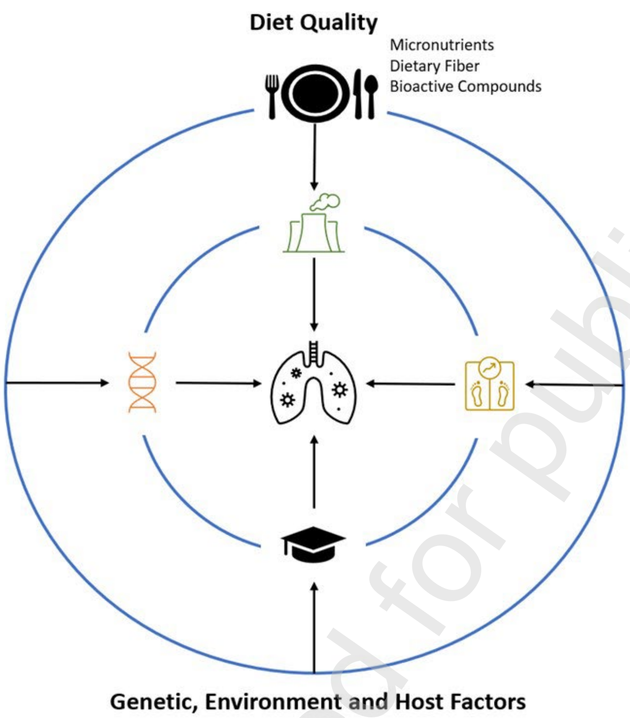

Figure 2: Flow chart of the included participants.