Review

Diet and Allergic Diseases among Population Aged 0 to 18 Years: Myth or Reality?

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Abstract: Allergic diseases are an important health problem. However, epidemiological studies concerning childhood diet-related allergic diseases are scarce. This review examines published articles dealing with diet, dietary patterns and nutrition in relation with allergic diseases among population aged 0 to 18 years. Studies and trials were identified using MEDLINE/PubMed and Cochrane Database of Systematic Reviews and were limited to those published in English or French from 1992 until 2012. This manuscript also reviews the evidence for maternal diet during pregnancy and diet during early childhood and their association with childhood atopic diseases, taking into account the methodology used to evaluate dietary patterns. The evidence reviewed is derived from large epidemiological studies exploring the effects of different food categories on asthma, atopic dermatitis, and allergic rhinitis in children. Overall, maternal diet during pregnancy and a childhood diet rich in antioxidants and omega-3 fatty acids are considered as healthy diets that could be protective for allergic diseases in childhood.

Keywords: diet; dietary patterns; asthma; allergic rhinitis; atopic dermatitis; atopic diseases; children
1. Introduction

The prevalence of allergic diseases has risen in recent decades, especially among children and in the Western world [1]. This increase in prevalence has become a serious public health issue [2]. Although the etiology of this increase is not clear, it is likely due to a combination of genetic predisposition, environmental factors, and lifestyle changes, including dietary habits [3–11].

Pediatric asthma has rapidly increased over the past 20 years, particularly in developed countries, and is the most common chronic inflammatory childhood disease. The symptoms of asthma are dyspnea, wheezing in the chest, and repeated coughing episodes. The prevalence of childhood asthma is 7% in France in 1997 [12,13]. In the United States, six million children (8.5%) have asthma [14]. In general, a family history of allergies is an important indication, directing the diagnosis towards allergic asthma in children [15].

Allergic rhinitis is the inflammation of the nasal mucous membrane that appears after exposure to a particular allergen other than an infection. Although it has received less attention than asthma in epidemiological studies, allergic rhinitis is recognized as the most common allergic manifestation in children and it is more prevalent than asthma [16]. For example, the prevalence of allergic rhinitis among 6–12 year old schoolchildren in Budapest was found to be 14.9% [17].

Atopic dermatitis is a chronic skin disease that affects people with a hereditary history of atopy. Its prevalence has increased considerably in recent decades, especially among children in Western countries, affecting up to 30% of preschool children and 15% to 20% of school-age children [18].

Epidemiological studies on the evolution of atopic diseases, most of which have been cross-sectional and longitudinal, have been conducted over the past decade to determine its possible modifiable determinants [19].

Westernization is associated with an increased prevalence of atopy, allergic rhinitis, and asthma [20]. Several studies have been published on the relationship between diet and childhood allergic diseases such as asthma, allergic rhinitis, and atopic dermatitis or eczema. In general, seven allergens are thought to be responsible for around 90% of food allergy: milk, eggs, wheat, peanuts, nuts, soy, and fish [21]. In contrast, the Mediterranean diet seems protective [22].

This paper examines recently published articles dealing with diet, dietary patterns, and nutrition in association with allergic diseases in children. Moreover, it reviews the evidence for maternal dietary consumption during pregnancy and diet during early childhood, and their association with childhood atopic diseases, taking into account the methodology used to assess dietary patterns.

2. Methods

2.1. Data Collection

Studies and trials were identified using the following bibliographic databases from the National Institutes of Health (NIH): MEDLINE/PubMed and Cochrane Database of Systematic Reviews [23].

The articles reviewed in this paper were limited to those published in English or French, in the last 20 years (from 1992 till 2012), among populations aged 0 to 18 years.
All records in PubMed were searched using the following terms: “diet” or “nutrition” or “food” or “dietary patterns” or “antioxidants” or “nutrients” or “polyunsaturated fatty acids” or “lipids” or “Mediterranean diet” AND “asthma” or “rhinitis” or “eczema” or “atopy” or “allergy” and “children”.

In addition, we reviewed reference lists of all available primary studies and review articles to identify and consult other potentially relevant citations. These citations were identified using the same bibliographic databases used to search for the primary studies included in this review.

The most recent search was conducted in March, 2012.

2.2. Inclusion Criteria

We included studies that focused on asthma, allergic rhinitis, and atopic dermatitis as a health outcome related to diet and dietary patterns among population aged 0 to 18 years. We reviewed 101 articles including review articles, cross-sectional, case-control, cohort, and experimental studies (Figures 1 and 2).

We included studies that had at least one of the following outcome measures: (1) Lung function measurements (Forced Expiratory Volume in one second (FEV₁) and/or Forced Expiratory Flow (FEF)); (2) Asthma or asthma symptoms; (3) Wheezing; (4) Rhinitis; (5) Bronchial hyper-responsiveness (BHR); and (6) Eczema or atopic dermatitis.

**Figure 1.** Number of all abstracts consulted, in both adults and children, with the number of excluded and included articles in this review article.
2.3. Exclusion Criteria

Five articles were excluded from the articles reviewed among the population aged 0 to 18 years. One prospective birth cohort study because it was published in 1983, one invited commentary because it was only a commentary and not a full article and three cross sectional studies because after we read the article we found that they were not specifically accurate to our review. Moreover, one cross sectional study was excluded from the adults consulted articles because it was published in 1990 (Figure 1).

3. Results and Discussion

3.1. Assessment of Diet in Epidemiological Studies

3.1.1. Methodological Issues in the Assessment of Diet

Four methods customarily used in adults were used to assess nutrition or diet in children: (1) 24-h recall, (2) dietary record, (3) the food frequency questionnaire (FFQ), and (4) biomarker measures [24]. The FFQ is the most widely used method because it is applicable to large cohorts and provides information on wide ranges of foods. It assesses long-term diet, it is easy to administer, it allows for repeated measurements so it captures changes in diet over time, and it is relatively cheap to analyze and to calculate nutrients. However, its limitation is that the foods studied need to be validated in a particular population to ensure that the main foods are captured.

Twenty-four-hour recall is a relatively precise method using recent memory but it may not reflect long-term diet like the FFQ and its nutrient analysis may be hard to perform [25]. On the other hand, the dietary record gives a precise record of intake over several days so recall errors and bias are reduced. However, it requires a high level of subject knowledge, literacy, and motivation and may not capture long-term diet [26,27]. Finally, biomarkers are the most precise measure of short-term status and may be the only reliable measurement of nutrient exposure [28–31]. Unfortunately, they are more expensive and invasive because biological samples such as blood, hair, nail, etc., are collected, so they are less widely used than the other methods in epidemiological studies.
3.1.2. Methodological Issues in Analysis of Dietary Habits

We identified four different approaches used to analyze dietary habits. Most studies used the simple analysis of each nutrient or food category [32]. Some authors used principal component analysis to extract the dietary patterns in their study population. Others used the nutritional profile of the children to create scores like the KIDMED score in the Mediterranean diet, to evaluate and analyze their dietary habits and their adherence to it [23,33–36]. Moreover, several authors considered the equivalents of food category intake in kilocalories, taking into consideration the metabolic aspect of dietary habits in children and adjusting them to energy intake [27,37,38]. Other authors used more than one approach in evaluating diet in one study [39].

We can never exclude the fact that our results concerning the approaches used for analyzing dietary habits could be biased by the procedure for inclusion of papers in this manuscript and other approaches would have been used by other authors in studies not included in this review. But from our point of view, these four approaches are the most used in epidemiology studies.

In fact, each approach has its own advantages and limitations. In the simple analysis approach, we can evaluate and analysis each food nutrient apart from the other and therefore, present only the results of the significant associations between the nutrient and the health outcome. However, as a limitation for this approach, is that we cannot evaluate the diet of a person as a whole and see its effect on the health outcome. In contrast, when principal component analysis is used, dietary patterns can be extracted and the whole interaction between food nutrients could be associated with the health outcome. Concerning the score creation, it is a very interesting approach to evaluate dietary habits and the adherence to a specific diet. Finally, the use of the equivalents of food nutrients intake and energy intake is a more specific approach to evaluate each nutrients by itself in a more precise dose than the simple analysis approach, but again it cannot evaluate all nutrients composing a diet all-together.

Often, authors choose the most suitable and valid approach, score or method to assess dietary habits and to present their results and some authors use more than one approach in the same study to include more precisely all associations that could explain their objectives.

3.2. Results and Association between Diet and Atopic Diseases in Recent Childhood Studies

In this section, we report the most important findings with regard to dietary factors and allergic diseases in youths, in recent epidemiological studies performed worldwide (Table 1). The associations shown in these studies are commented, citing the advantages and disadvantages of each methodology.
Table 1. Results and association between diet and allergic diseases in children in recent international epidemiological studies.

| Reference; Country; Study Type | Population | Diet Assessment | Dietary Evaluation | Health Outcome | p-value | aOR   | 95% CI |
|-------------------------------|------------|-----------------|--------------------|----------------|---------|-------|--------|
| Arvaniti et al., (2011) [35]; Greece; Cross-sectional | 700 children, 10–12 years | FFQ and KIDMED score | Adherence to the Mediterranean Diet | Ever had wheezing | 0.001 |  |  |
| | | | | Exercise wheezing | 0.004 |  |  |
| | | | | Night cough | 0.07 |  |  |
| | | | | Ever had diagnosed asthma | 0.002 |  |  |
| | | | | Any asthma symptoms | <0.001 |  |  |
| | | | | Asthma symptoms | <0.001 | 0.86 | 0.75–0.98 |
| Martindale et al., (2005) [40]; UK; Birth cohort | 1924 children followed up to 2 years of age | FFQ during pregnancy at 34 weeks gestation | Maternal vitamin E intake | Wheezing in the absence of a “cold” in the second year of life | 0.009 | 0.49 | 0.26–0.93 |
| | | | | Eczema | 0.016 | 0.42 | 0.22–0.82 |
| | | | | Ever wheezing | 0.01 | 3 | 1.47–6.12 |
| | | | | Eczema | 0.048 | 1.56 | 0.99–2.45 |
| Oh et al. (2010) [30]; Korea; Case-Control | 180 AD and 242 non-AD preschoolers | FFQ and blood samples for fat-soluble vitamins (retinol, α-tocopherol, and β-carotene) and vitamin C | β-carotene | Atopic dermatitis | 0.03 | 0.44 | 0.22–0.88 |
| | | | | Vitamin E | <0.001 | 0.33 | 0.16–0.67 |
| | | | | Folic acid | <0.001 | 0.37 | 0.18–0.73 |
| | | | | Iron | 0.01 | 0.39 | 0.19–0.79 |
| | | | | α-tocopherol | 0.037 | 0.64 | 0.41–0.98 |
| | | | | Retinol (vitamin A) | 0.022 | 0.74 | 0.58–0.96 |
| | | | | Vitamin C | 0.559 | 0.94 | 0.76–1.17 |
| Hijazi et al., (2000) [41]; Saudi Arabia; Case-Control | 114 cases and 202 controls | FFQ and SPTs | Fast food | Asthma and wheezing | 0.008 |  |  |
| | | | | Animal fat for cooking | 0.062 |  |  |
| | | | | Eating fish | 0.073 |  |  |
| | | | | Milk daily | 0.04 | 2.4 | 1.21–4.75 |
| | | | | Vegetables Fiber | 0.01 | 2.83 | 0.98–8.09 |
| | | | | Vitamin E | 0.009 |  |  |
| | | | | Magnesium | 0.005 | 3 | 1.38–6.50 |
| | | | | Calcium | 0.001 |  |  |
| | | | | Sodium | <0.001 | 2.88 | 1.42–5.87 |
| | | | | Potassium | 0.002 |  |  |
| Source | Country | Study Type | Sample Size | Dietary Assessment | Outcomes | Odds Ratio (95% CI) |
|--------|---------|------------|-------------|-------------------|----------|------------------|
| Miyake et al., (2010) [42]; Japan; Birth cohort | 763 mother-child pairs | Diet history questionnaire and 16-days dietary records | Total vegetables | Wheezing | 0.23 0.69 0.41–1.15 |
| | | | Total fruit | | 0.11 1.51 0.90–2.57 |
| | | | Total vegetables | | 0.22 0.7 0.41–1.19 |
| | | | Green and yellow vegetables | Eczema | 0.01 0.41 0.24–0.71 |
| | | | Total fruit | | 0.34 0.78 0.45–1.35 |
| | | | Citrus fruit | | 0.03 0.53 0.30–0.93 |
| | | | Vitamin E | | 0.04 0.54 0.32–0.90 |
| | | | Zinc | | 0.06 0.69 0.41–1.17 |
| | | | β-carotene | | 0.04 0.52 0.30–0.89 |
| | | | Vitamin E | | 0.15 0.59 0.34–1.02 |
| Palmer et al., (2012) [43]; South Australia; Randomized controlled trial | 706 infants at high hereditary risk of having allergic disease. | Intervention group (n = 368); Control group (n = 338) | n-3 (LCPUFA) | Egg sensitization | 0.02 0.62 0.41–0.93 |
| | | | Ig E associated allergic disease at 1 year of age; SPTs | n-3 LCPUFA | Eczema with sensitization | 0.06 0.64 0.40–1.03 |
| Nwaru et al., (2011) [44]; Finland; Birth cohort study with 5-year follow-up | 2441 children | Maternal FFQ data | Magnesium | Eczema | 0.78 0.62–0.97 |
| Miyake et al., (2011) [45]; Japan; Cross-sectional | 23,388 schoolchildren 6–15 years | Diet history questionnaire for children and adolescents | PUFA | | |
| | | | n-3 Long Chain PUFA | | 0.04 1.26 1.07–1.48 |
| | | | α-linoleic acid | Eczema | 0.009 1.31 1.11–1.54 |
| | | | n-6 PUFAs | | 0.003 1.31 1.12–1.55 |
| | | | Linoleic acid | | 0.01 1.26 1.07–1.48 |
| | | | Arachidonic acid | Eczema | <0.001 0.81 0.69–0.95 |
| | | | Arachidonic acid | Rhinocconjunctivitis | 0.03 0.86 0.74–0.99 |
| Emmanouil et al., (2010) [26]; Greece; Cross-sectional study | 1964 children, 24–72 months | 3 days diet records | Vitamin C | Ever wheeze | 0.997 0.99–1.00 |
| | | | Vitamin C | Current wheezing | 0.996 0.99–0.99 |
| | | | Calcium | Current wheezing | 0.999 0.99–0.99 |
| | | | Magnesium | Current wheezing | 1.005 1.00–1.00 |
| | | | MUFA | Ever wheezing | 1.023 1.00–1.04 |
| | | | MUFA | Current wheezing | 1.02 1.00–1.03 |
| | | | Magnesium | Diagnosed asthma | 1.006 1.00–1.01 |
Table 1. Cont.

| Study | Sample Size | Dietary Assessment | Outcomes | Odds Ratio (95% CI) |
|-------|-------------|--------------------|----------|--------------------|
| Miyake et al., 2010 [46]; Japan; Birth cohort 763 mother-child (16–24 months) pairs | Diet history questionnaire during pregnancy | Dairy products | Wheezing | 0.007 (0.25–0.79) |
| | | | Milk | 0.02 (0.28–0.87) |
| | | | Cheese | 0.02 (0.31–0.85) |
| | | | Calcium | 0.04 (0.32–0.99) |
| | | | Vitamin D | 0.04 (0.43–0.97) |
| | | | Eczema | 0.03 (0.41–0.98) |
| Suárez-Varela et al., 2010 [23]; Spain; Cross-sectional 13,153 schoolchildren 6–7 years | FFQ and a Mediterranean diet score | Butter | Atopic Dermatitis | 0.04 (0.50–0.97) |
| | | Nuts | | 0.003 (0.33–0.80) |
| | | Milk (once or twice a week) | | 0.007 (0.22–0.79) |
| | | Milk (3 or more times a week) | | 0.001 (0.33–0.75) |
| | | Mediterranean diet score | | 0.071 (0.99–1.08) |
| Nagel et al., 2010 [47]; 29 centers in 20 countries; Multicenter cross-sectional studies 50,004 schoolchildren 8–12 years, (29,579 with skin prick testing) | FFQ and a Mediterranean diet score | Fruit intake | Current wheezing in affluent countries | 0.168 (0.73–1.02) |
| | | | Current wheezing in non-affluent countries | 0.168 (0.57–0.88) |
| | | | Fish | 0.04 (0.78–1.08) |
| | | | Current wheezing in non-affluent countries | 0.018 (0.65–0.95) |
| | | | Current wheezing | 0.05 (0.86–1.45) |
| | | | Asthma ever | 0.03 (0.90–1.35) |
| | | | | 0.03 (1.11) |

aOR: Adjusted Odds Ratio; CI: Confidence Interval; FFQ: Food Frequency Questionnaire; KIDMED: Score for adherence to the Mediterranean diet in children; SPTs: Skin Prick Tests; IgE: Immunoglobulin E; LCPUFA: Long Chain Polyunsaturated Fatty Acids; PUFA: Polyunsaturated Fatty Acids; MUFA: Monounsaturated Fatty Acids.

3.2.1. The Mediterranean Diet

Studies on adherence to the Mediterranean diet are numerous. In fact, it is now considered as a healthy diet and has been proven as a protective factor against allergic diseases in most of the studies performed in children.

We reviewed five cross-sectional studies and one review article which all found that the adherence to the Mediterranean diet was inversely related with atopy in children (Table 2). Adherence to the Mediterranean diet, and following a healthy dietary pattern by eating more fruits and vegetables, for example, has been shown to be a protective factor for atopic diseases in children in many countries such as Sweden, Greece, and Mexico [39,48,49]. In addition, a high level of adherence to the Mediterranean diet was a protective factor for current wheezing in children [47,50]. One study found no association between the Mediterranean diet and atopic dermatitis (adjusted odds ratio (aOR) = 1.03, 95% confidence interval (CI) = 0.99–1.08) [22].

In Athens, Arvaniti et al. studied adherence to the Mediterranean diet in children aged 10–12 years in relation to wheezing and asthma symptoms. They found that a high level of adherence to the Mediterranean diet had a protective effect on asthma symptoms (aOR = 0.86; 95% CI = 0.75–0.98) [35]. In
this study, dietary habits were evaluated by an FFQ completed by the children and their parents through face-to-face interviews, and a special diet score, the KIDMED score, was calculated to evaluate adherence to the Mediterranean diet. Higher KIDMED scores corresponded to greater adherence to the diet. There was a lack of association between single foods and asthma prevalence, probably due to a recall bias because information about the diet was provided by the parents, but the overall results suggested a protective effect of a high level of adherence to the Mediterranean diet on asthma symptoms.

Although there have been several nutritional studies assessing single nutrients instead of assessing dietary patterns, the single food approach may fail to account for interactions between nutrients. Indeed, people eat meals consisting of a variety of foods with combined nutrients, not just isolated foods [51]. Furthermore, Nagel et al. studied food categories in relation with asthma and wheezing in a multicenter study (ISAAC phase 2) of more than 50,000 schoolchildren aged 8–12 years old. Fruit intake was associated with a low prevalence of current wheezing in both affluent and non-affluent countries (p = 0.168). Consumption of fish in affluent countries (aOR = 0.92, 95% CI = 0.78–1.08) and of cooked green vegetables in non-affluent countries (aOR = 0.78, 95% CI = 0.65–0.95) was associated with a lower prevalence of current wheezing and asthma [47].

An FFQ was used to collect information retrospectively by parents about the usual diet consumed by their children and then a Mediterranean dietary pattern was derived according to the consumption frequency of food items. The data collected retrospectively may have also introduced a recall bias, but it gave the exact recent consumption. Moreover, the authors in this study could not adjust for total energy intake and body mass index because it was based on the ISAAC questionnaire [35].

Despite the limitations of the cited studies, the consistency of the findings pleads in favor of the inverse relationship between the Mediterranean diet and allergic diseases.

3.2.2. Antioxidant Nutrient Intake

Evidence is accruing of the protective effect of antioxidants and vitamins for health problems such as asthma, allergic rhinitis, and atopic dermatitis. Our knowledge of the health effects of these antioxidant nutrients is far from complete owing to the inconsistent or even contradictory epidemiological studies undertaken on this subject, especially in children.

We reviewed a total of 13 articles in relation to fruit and vegetable consumption, antioxidant, and vitamin intake, in the association with health outcomes such as allergic diseases, atopy, lung function levels and respiratory symptoms, childhood asthma, asthma symptoms, wheezing, atopic dermatitis or eczema, allergic sensitization, and allergic rhinitis. The majority of these studies were cross-sectional (n = 8), three were birth cohort studies, and there was one case-control study on atopic dermatitis, and one review article (Table 2). In general, antioxidant intake including fruit, vegetables, and vitamins may be considered as protective against allergic diseases in children.
Table 2. Reviewed studies on antioxidant nutrients, vitamins, and Mediterranean diet in children and adolescents and their association with allergic diseases.

| Reference; Country; Study Type | Population | Significant Food Association | Health Outcome Measured | Association |
|--------------------------------|------------|------------------------------|-------------------------|-------------|
| Cook et al., 1997 [52]; UK; Cross-sectional | 2650 children | Fresh fruit (vitamin C) | Lung function (FEV₁ and wheezing) | Fresh fruit intake was associated positively with lung function. |
| Forastiere et al., 2000 [53]; Italy; Cross-sectional | 18,737 children, 6–7 years | Fruit rich in vitamin C | Wheezing symptoms | Consumption of fruit rich in vitamin C may reduce wheezing symptoms in childhood. |
| Gilliland et al., 2003 [54]; California; Cross-sectional | 2566 children | Dietary antioxidants and vitamin A | Lung function levels (FEV₁ and FEF₂₅₋₇₅) | An inadequate dietary antioxidant vitamin intake is associated with reduced lung function levels in children. |
| Kalantar-Zadeh et al., 2004 [55]; Review article | In children | Dietary antioxidants | Childhood asthma | Most studies indicate a higher prevalence of dietary antioxidant deficiency among asthmatic patients; But results seem to be contradictory; More epidemiological studies are needed. |
| Rubin et al., 2004 [56]; New York; Cross-sectional | 7505 children, 4–16 years | Serum antioxidants | Childhood asthma | No association of vitamin E with asthma; High β-carotene, vitamin C and selenium intake was associated with a reduction in asthma. |
| Harik-Khan et al., 2004 [57]; New York; Cross-sectional | 4,093 children, 6–17 years | Vitamin C and α-carotene | Asthma | Low vitamin C and α-carotene intake are associated with asthma risk. |
| Chatzi et al., 2007 [33]; Greece; Cross-sectional | 690 children, 7–18 years | Mediterranean diet | Allergic rhinitis, asthma and atopy | High dietary intake of fruits, vegetables and nuts may have a protective role on the prevalence of asthma symptoms and allergic rhinitis. |
| Okoko et al., 2007 [58]; UK; Cross-sectional | 2560 children, 5–10 years | Fruits | Asthma, asthma symptoms and wheezing | Banana consumption and drinking apple juice were negatively associated with wheezing but not asthma. |
| Chatzi et al., 2007 [59]; Spain; Cross-sectional | 460 school children, 6.5 years | Fruits and vegetables | Wheezing, atopic wheezing and atopy | Fruit and vegetable intake was inversely associated with current and atopic wheezing. |
| Burns et al., 2007 [60]; United States and Canada; Cross-sectional | 2112 students, 16–19 years | Fruits, antioxidants, nutrients and n-3 fatty acids | Pulmonary function and respiratory symptoms | Adolescents with the lowest dietary intake of antioxidant had lower pulmonary function and increased respiratory symptoms, especially among smokers. |
| De Batlle et al., 2008 [49]; Mexico; Cross-sectional | 1476 children aged 6–7 years old | Mediterranean diet | Asthma and rhinitis | Mediterranean diet has a protective effect on asthma and allergic rhinitis in children. |
| Castro-Rodriguez et al., 2008 [50]; Spain; Cross-sectional | 1784 preschoolers ages 4 years old | Mediterranean diet | Current wheezing | Mediterranean diet was shown as a protective factor for current wheezing. |
Table 2. Cont.

| Study          | Sample Size | Intervention/Outcome | Findings                                                                 |
|----------------|-------------|----------------------|--------------------------------------------------------------------------|
| Bacopoulou et al., 2009 [61]; Greece; Birth cohort (18 years follow-up) | 2133 children, 7- and 18- years | Fruits and vegetables | Asthma | Daily consumption of fruits and vegetables was negatively associated with current asthma. |
| Patel et al., 2009 [62]; UK; Birth cohort (8 years follow-up) | 861 children, 5- and 8-years | Dietary antioxidant | Wheezing or eczema, allergic sensitization and immunoglobulin E levels | No association between antioxidant intakes and wheezing or eczema; Increased beta-carotene intake was associated with a reduced risk of allergic sensitization and lower immunoglobulin E levels. |
| Chatzi and Kogevinas, 2009 [63]; Review article | In children | Mediterranean diet | Asthma and atopy | High level of adherence to Mediterranean diet in early life protects against development of asthma and atopy in children. |
| Oh et al., 2010 [30]; Korea; Case-control | Children, 5–6 years (180 cases and 242 controls) | Antioxidant nutrients | Atopic dermatitis | Higher antioxidant intake reduces risk of atopic dermatitis (AD); No relationship of AD with vitamin C. |
| Nagel et al., 2010 [47]; in 20 countries; Cross-sectional | 50,004 school children, 8–12 years | Mediterranean diet | Wheeze and asthma | Adherence to Mediterranean diet may provide protection against wheeze and asthma. |
| Gonzalez Barcala et al., 2010 [36]; Spain; Cross-sectional | 14,700 children and adolescents | Mediterranean diet | Asthma | Greater adherence to the Mediterranean Diet (MD) is associated with a higher risk of severe asthma in girls of 6–7 years; The results of the study do not support a protective effect of MD on prevalence or severity of asthma. |
| Rosenlund et al., 2011 [39]; Sweden; Birth cohort (8 years follow-up) | 2447 children | Fruit intake | Allergic disease | Inverse association between fruit intake and allergic disease in children. |

FEV₁: Force expiratory volume in 1 second; FEF 25–75: Forced expiratory flow between 25% and 75% of forced vital capacity.

3.2.2.1. Fruit and Vegetables

A diet high in antioxidants may prevent the expression of allergic diseases. Furthermore, a diet rich in fruit, vegetables and antioxidants may contribute to optimal respiratory health [33,59,60].

Hijazi et al. suggested that lower intake of vegetables (aOR = 2.83, 95% CI = 0.98–8.09) was negatively associated with asthma [41]. In fact, an FFQ was used in this study performed in Saudi Arabia that included the main foods present in the Saudi diet, i.e., vegetables and local fruit, such as dates. These results provide information about the dietary intake in Arab groups rather individuals so the food studied need to be validated in this particular population to ensure that the main foods are captured.
Forastiere *et al.* concluded that the consumption of fruit rich in vitamin C may reduce wheezing symptoms in childhood [53]. This could be due to the fact that vitamin C may protect airways against oxidant attack [64], thus reducing asthma symptoms. An information bias is possible in this study, since a parental questionnaire was used to evaluate both dietary factors and health outcomes. However, questionnaire data on dietary intake completed by parents are generally considered to be reliable, especially regarding vitamin C intake [65]. Moreover, an infrequent consumption of fresh fruit may be an indicator of a poor diet, which may lack vitamins other than vitamin C, such as A and E, that may also have a protective effect on respiratory symptoms [64,66]. Intake of vitamins C and E is usually correlated [67] and both are likely to play a synergistic role in the antioxidant defense mechanism [64].

In contrast, Cook and coworkers found no association between vitamin C levels in fresh fruit and lung function in children [52]. The lack of statistical significance in that study could be due to the small number of subjects with symptoms. The lack of a relationship between wheezing and fresh fruit consumption could be due to protection against bronchoconstriction in susceptible individuals, which is in accordance with a recent study in adults [68]. Moreover, Oh *et al.* found no relationship between atopic dermatitis risk and plasma vitamin C (aOR = 0.94, 95% CI = 0.76–1.17) [30].

In Greece, Emmanouil *et al.* found that vitamin C intake was negatively associated with the prevalence of ever wheezing (aOR = 0.99, 95% CI = 0.99–1.00) and current wheezing (aOR = 0.99, 95% CI = 0.99–0.99) in children [26]. Dietary intake was assessed with a three-day dietary record. Therefore, over- or under-reporting of dietary intake may have confounded the results. Another limitation of this study was that it focused on isolated nutrients by using a simple analysis of each nutrient and did not take into account food groups or specific food items.

3.2.2.2. Dairy Products

Regarding the consumption of dairy products, including milk consumption, we reviewed three articles: two cross-sectional studies and one case-control study. These studies suggested that milk consumption could be associated with a protective effect on atopic eczema and asthma symptoms.

In Spain, Suárez-Varela *et al.* used a FFQ and a Mediterranean diet score to show that milk was negatively associated with atopic dermatitis in children aged six to seven years old, if consumed once or twice a week (aOR = 0.42, 95% CI = 0.22–0.79) [22]. In fact, milk is a source of saturated fats that has been associated with a protective effect on atopic disease [69].

In Saudi Arabia, Hijazi *et al.* suggested that a lower consumption of milk (aOR = 2.4, 95% CI = 1.21–4.75) is associated with a higher prevalence of asthma symptoms and allergy [41].

3.2.2.3. Other Vitamins and Nutrients

The total articles reviewed with their study designs regarding vitamins and nutrients are cited in the beginning of the section “Antioxidant nutrient intake”.

In Korea, Oh *et al.* showed in a case-control study that atopic dermatitis was negatively associated with intake of antioxidant nutrients [β-carotene (aOR = 0.44, 95% CI = 0.22–0.88), vitamin E (aOR = 0.33, 95% CI = 0.16–0.67), folic acid (aOR = 0.37, 95% CI = 0.18–0.73), and iron (aOR = 0.39, 95% CI = 0.19–0.79)]. Reduced atopic dermatitis risk was found with the increase in α-tocopherol (aOR = 0.64, 95% CI = 0.41–0.98) and retinol concentrations (aOR = 0.74, 95% CI = 0.58–0.96) [30].
Diet was assessed using a validated semi-quantitative FFQ. Fasting blood samples were used to analyze fat-soluble vitamins (retinol, α-tocopherol, and β-carotene) and vitamin C. The authors assessed antioxidant nutrient intake by FFQ in the previous 12 months, which provided long-term regular intake. In contrast, serum antioxidant nutrients are indices of short-term nutritional status [70]. These findings suggest that long-term antioxidant nutritional status measures would be more sensitive markers for atopic dermatitis than recent ones. Furthermore, the unavailability of supplementary intake of vitamins and minerals in this study may have underestimated the true association between some nutrients and atopic dermatitis.

In Finland, Nwaru et al. showed that dietary intake of magnesium was negatively associated with eczema in children (aOR = 0.78, 95% CI = 0.62–0.97) [44]. An FFQ for maternal intake was used but it had the same limitations as every FFQ, i.e., it has to be used in a specific population, in this study, the Finnish population, and the food studied needs to be validated in that population to ensure that the main foods are captured.

In Saudi Arabia, Hijazi et al. suggested that fiber (p = 0.009), vitamin E (aOR = 3, 95% CI = 1.38–6.50), magnesium (p < 0.001), calcium (p < 0.001), sodium (aOR = 2.88, 95% CI = 1.42–5.87), and potassium (p = 0.002) were negatively associated with asthma after adjustment for energy intake [41]. In this study, diet and risk factors for allergies were evaluated by the ISAAC questionnaire translated into Arabic and atopy was assessed by skin prick testing. The FFQ may provide useful information on intake only in groups rather than individuals and may be used for comparisons between these groups. Moreover, the FFQ used in this study may be an inappropriate method to demonstrate the intake of some nutrients like salt because of the geographical setting of the Saudi Arabia compared to western countries.

3.2.3. Fat and Fish Studies

Fat and fish intake have been correlated with allergic diseases in children. We reviewed a total of 11 articles that studied the relationship between fish consumption and fat intake and allergic diseases in children. The majority of these studies were cross-sectional (n = 8), in addition to one cohort study, one nested case-control study, and one randomized controlled trial (Table 3). Epidemiological studies have shown that fish intake, monosaturated fats and omega-3 polyunsaturated fatty acids have a protective effect on asthma, respiratory health, and atopic dermatitis [28,71–74]. Other studies were contradictory and showed that n-3 and n-6 polyunsaturated fatty acids may be risk factors for asthma symptoms and eczema [45,75]. On the other hand, fatty foods of animal origin and saturated fatty acids were a risk factor for asthma in children [27,38].
Table 3. Reviewed studies on fish and fat intake in infants and children and their association with allergic diseases.

| Reference; Country; Type of Study | Population | Significant Food Association | Health Outcome Measured | Association |
|-----------------------------------|------------|------------------------------|-------------------------|-------------|
| Peat et al., 1992 [73]; Australia; Cross-sectional Hodge et al., 1996 [72]; Australia; Cross-sectional | 4366 children | Fish | Bronchial hyper responsiveness | Protective effect of fish on bronchial hyper responsiveness in children. |
| Yu et al., 1996 [28]; Sweden; Birth cohort | 574 children | Oily fish | Asthma | Consumption of oily fish may protect against asthma in childhood. |
| Hodge et al., 1996 [72]; Australia; Cross-sectional | 68 infants | n-3 and n-6 fatty acids | Allergic dermatitis and asthma | Significant correlations found between n-3 and n-6 fatty acids in the cord blood of children who did not develop allergic dermatitis or asthma by 6 years of age. |
| Yu et al., 1996 [28]; Sweden; Birth cohort | 1166 children, 13–17 years | Fat-rich foods; saturated fats and monounsaturated fats | Asthma | A higher prevalence of asthma was related to fat-rich foods of animal origin; Saturated fats were associated with increased risk of asthma. Monounsaturated fats were inversely associated with asthma. |
| Huang et al., 2001 [38]; Taiwan; Cross-sectional | Schoolchildren, 6–15 years | Fish | Respiratory health | Higher fish intake was positively related to prevalence of asthma. |
| Antova et al., 2003 [74]; Six European countries; Cross-sectional | 20,271 children, 7–11 years | Fish | Asthma | Low fish intake was a consistent predictor of poor respiratory health. |
| Miyake et al., 2008 [75]; Japan; Cross-sectional | 541 children, 3 years old | Polyunsaturated fat | Atopy and wheezing | Sensitized wheezy children had a higher total polyunsaturated fat intake compared with non-sensitized non-wheezy children. |
| Al Biltagi et al., 2009 [71]; Egypt; Randomized Controlled Trial Rodri’guez et al., 2010 [27]; Spain; Cross-sectional | 60 children, 7–10 years | Omega-3 fatty acids | Asthma and pulmonary function | Both n-3 and n-6 polyunsaturated fatty acids may be associated with an increased prevalence of wheezing. |
| Miyake et al., 2011 [45]; Japan; Cross-sectional | 638 school children, 8–13 years | Saturated fatty acids (SFAs) | Current asthma | Diet supplementation with omega-3 fatty acids significantly improved asthma control and pulmonary functions. |
| Miyake et al., 2011 [45]; Japan; Cross-sectional | 23,388 schoolchildren, 6–15 years | n-3 and n-6 PUFAs | Eczema and rhino conjunctivitis | Increased intakes of SFAs, especially butter, seem to be related to current asthma. |

PUFAs: Polyunsaturated Fatty Acids.
3.2.3.1. Fat Intake

Several studies have shown that diet supplementation with omega-3 polyunsaturated fatty acids significantly improved pulmonary function tests, thus childhood asthma, as well as having a protective effect against allergic dermatitis [28,71]. On the other hand, increased consumption of n-6 polyunsaturated fatty acids (PUFAs) reportedly contributed to the recent increased prevalence of asthma and may be associated with an increased prevalence of wheezing in children [75].

A more recent study by Miyake et al. in Japan on more than 23,000 schoolchildren 6–15 years old showed that consumption of both n-3 and n-6 polyunsaturated fatty acids was positively associated with the prevalence of eczema (aOR = 1.31, 95% CI = 1.11–1.54 and aOR = 1.26, 95% CI = 1.07–1.48, respectively). In contrast, polyunsaturated omega-6 fatty acid (arachidonic acid) may be negatively associated with eczema (aOR = 0.81, 95% CI = 0.69–0.95) and rhino-conjunctivitis (aOR = 0.86, 95% CI = 0.74–0.997) [70]. Both n-3 and n-6 polyunsaturated fatty acids may be associated with an increased prevalence of wheezing [75]. A self-administered diet history questionnaire was used to assess children’s dietary intakes in the Miyake et al. study [45]. This method should be interpreted with caution as it might not reflect long-term intake by children and may underestimate the results. Moreover, the authors did not include intake of dietary supplements in this study because their use is uncommon in Japan.

In South Australia, Palmer et al. showed in their randomized controlled trial (RCT) that n-3 long chain polyunsaturated fatty acid supplementation in pregnancy did not reduce the overall incidence of immunoglobulin E-associated allergies in the first year of life, although atopic eczema was decreased (aOR = 0.64, 95% CI = 0.40–1.03) [43]. In this RCT, the concentration of long chain polyunsaturated fatty acids (LCPUFA) in plasma phospholipids from cord blood was evaluated as an independent biomarker of adherence to the protocol supplementation of the women in the n-3 LCPUFA and in the control group. The calculation of the concentration of LCPUFA in this RCT is a precise measure of short-term status and may be the only reliable measurement of LCPUFA intake.

3.2.3.2. Fish Intake

Concerning fish intake, results of studies in children seem contradictory. Consumption of oily fish may protect against asthma in childhood [72] and eating fish more than once a week has a protective effect on bronchial hyper-responsiveness and asthma in children [73,78]. On the other hand, frequency of fish intake was positively related to the prevalence of asthma in a cross-sectional study done in Japan [78]. In contrast, Hijazi et al. in Saudi Arabian study suggested that eating fish (p = 0.073) was not significantly related to asthma and wheezing [41]. These discrepancies could be explained by the differences in diet between countries. In fact, the Japanese often eat fish cooked with salt, which could lead to the positive association between fish and asthma in this study [78]. In contrast, the absence of relationship observed between fish intake and asthma in the Saudi population could be due to their lower consumption of fish and frequent consumption of lamb and chicken.
3.2.4. Fast Food and Soft Drinks

Fast food consumption is considered unhealthy especially for children. It contributes to increasing obesity and can also increase the prevalence of chronic diseases like asthma in children [79]. We reviewed six articles regarding fast food and/or soft drinks consumption and allergic diseases in childhood: one case-control study and five cross-sectional studies. Recently, respiratory allergic diseases in children such as asthma, wheezing and bronchial hyper-responsiveness have been correlated with the high consumption of fast food, like the frequent consumption of hamburgers, salty-snack eating, and frequent takeaway consumption [41,80]. These associations were more significant in children with a higher sedentary lifestyle such as watching television or playing video games for more than two hours a day [81]. An FFQ was completed by parents in the latter study, so the results could be subject to recall bias and the behaviors of the children could be either under- or over-estimated. In fact, a child who is already asthmatic may change his behaviors by staying indoors more often in order to avoid outdoor allergens. Therefore, he will increase his television-watching and will lead a more sedentary life, which in turn may lead to obesity and increase asthma symptoms [82].

Moreover, the consumption of soft drinks containing preservatives or colorants increased significantly the risk of allergic rhinitis symptoms in children [17]. All these studies used the FFQ to evaluate fast food intake [17,41,79–82]. Future research into the effects of diet on allergic disease should focus on these unhealthy foods whose consumption has increased in recent years, and include further analysis of food intake based on daily diaries.

3.2.5. Antenatal and Postnatal Dietary Intake

The increased prevalence of allergic diseases over the last few decades may result from changes in prenatal or early-life environment, including maternal diet during pregnancy and dietary patterns during early childhood. Therefore, prevention of asthma by early allergen avoidance is essential in high-risk children, because early allergic sensitization is a significant risk factor for later development of asthma and atopic diseases [83]. Moreover, a recent review article suggested that antioxidant intake in prenatal and early life could protect against the development of atopic diseases [84]. Furthermore, recent studies of vitamin D intake suggest that it may be protective for atopy, although this still remains controversial [84]. In addition, early fish consumption could reduce significantly the risk of allergic diseases in children [85].

On the other hand, prolonged breastfeeding during the first year of life has been found to be protective against the development of atopy and asthma in children [86]. In contrast, a recent systematic review and meta-analysis showed that there was no association between breastfeeding and wheezing and asthma in children [87].

For this section, we reviewed in total 15 articles: seven review articles, one cross-sectional study, six cohort studies, and one systematic review and meta-analysis.

3.2.5.1. Maternal Intake during Pregnancy

In the United Kingdom, Martindale et al. investigated maternal antioxidant intake during pregnancy and its relationship with asthma and atopic dermatitis [40]. There were no statistically significant
associations between wheezing symptoms in the first two years of life and total maternal intake of β-carotene, selenium, magnesium, manganese, copper, and zinc. In the second year of life, there were significant negative associations with maternal total vitamin E intake (aOR = 0.49, 95% CI = 0.26–0.93) and maternal vitamin C intake was positively associated with wheezing (aOR = 3, 95% CI = 1.47–6.12) and eczema (aOR = 1.56, 95% CI = 0.99–2.45) [40]. An FFQ administered at 34 weeks gestation was used to assess diet during pregnancy. Despite its effectiveness to elicit accurate data on the dietary intake of foods containing antioxidant vitamins and minerals, FFQ estimates of dietary nutrient intake are dependent on subject recall of the foods consumed and of their quantities [24].

Previous studies that have investigated associations between dietary vitamin C, fruit, asthma, and respiratory symptoms have reported beneficial associations [52,54]. However, Martindale et al. unexpectedly found a positive association between maternal vitamin C intake and wheezing in children in the second year of life [40]. A possible explanation is that at high vitamin C concentrations might have a pro-oxidant effect, which could lead to respiratory symptoms [88]. Another possibility is that other added constituents of foods containing vitamin C might promote the development of wheezing in early life. Sulfites added as preservative to fruit drinks have been shown to cause wheezing in susceptible individuals [89]. No associations were found in that study between maternal dietary intake of selenium and wheezing or eczema in the first two years of life due to the reduced effectiveness of the FFQ in quantifying selenium intake because the correlation coefficient for selenium was weaker than that of vitamins E and C [40].

In Japan, Miyake et al. found that higher maternal consumption of green and yellow vegetables (aOR = 0.41, 95% CI = 0.24–0.71), citrus fruit (aOR = 0.53, 95% CI = 0.30–0.93), and β-carotene (aOR = 0.52, 95% CI = 0.30–0.89) during pregnancy may be protective against the development of eczema in infants [85]. Moreover, higher maternal vitamin E intake may reduce the risk of wheezing in infants (aOR = 0.54, 95% CI = 0.32–0.90). They also showed that higher maternal intake of total dairy products (aOR = 0.45, 95% CI = 0.25–0.79), milk (aOR = 0.5, 95% CI = 0.28–0.87), cheese (aOR = 0.51, 95% CI = 0.31–0.85), and calcium (aOR = 0.57, 95% CI = 0.32–0.99) was negatively associated with infantile wheezing but not with eczema (aOR = 0.54, 95% CI = 0.32–0.90). In contrast, higher maternal vitamin D intake might reduce childhood wheezing (aOR = 0.64, 95% CI = 0.43–0.97) and eczema (aOR = 0.63, 95% CI = 0.41–0.98), and a higher consumption of calcium and dairy foods during pregnancy may reduce the risk of childhood wheezing [46,90]. Data on maternal intake during pregnancy was evaluated by a diet history questionnaire that could only approximate consumption, so this would bias the estimates of the association toward the null. The diet history questionnaire was also designed to assess only recent dietary intake, so the data collected should only be taken as suggestive owing to the changing dietary habits of pregnant women due to the nausea they may experience during pregnancy.

Furthermore, studies have shown that vitamin D has many beneficial effects other than bone maintenance. The effect of vitamin D on surfactant production and in lung maturation has been confirmed in human studies [67]. Vitamin D is known to affect the immune system and lung development and function in children, so it might be protective for asthma [91].

In 2007, Devereux et al. showed that maternal intake of vitamin D was negatively associated with wheezing in five-year-old children [92]. Camargo et al. found that maternal intake of vitamin D was...
negatively associated with recurrent wheezing in children aged three years but no association with eczema was evidenced [93].

3.2.5.2. Dietary Patterns in Early Childhood

One of the major modifiable dietary environmental risk factors for childhood asthma is the lack of breastfeeding [94]. A prospective birth cohort study in West Australia showed that the risk of childhood asthma aged six years was significantly reduced if exclusive breastfeeding was continued for at least the first four months of life [95].

A systematic literature review showed that avoidance of cow’s milk protein prevents the development of wheezing in atopic children [96] and that breast-milk should be the food of choice for all babies, except in some high-risk babies in whom hydrolyzed milk formula helps reduce the risk of developing asthma [97]. Moreover, frequent consumption of products containing milk fat in pre-school children was associated with a reduced risk of asthma symptoms [98]. A recent review article concluded that exclusive breastfeeding for four to six months and the postponement of solid food until four months of age are the main measures considered effective in the prevention of allergy in children [99].

4. Conclusions

In conclusion, various methodologies have been used to evaluate dietary factors in relation with asthma, allergic rhinitis and atopic dermatitis. Although the association of diet with allergic diseases has been studied worldwide, their findings are contradictory and sometimes barely significant. While the methods are all effective and useful in determining dietary factors, they seem less specific and sensitive for evaluating the quality of diet in childhood. Moreover, a child’s diet is not based on a single food item but is rather a complex of nutrients eaten together, which involves food interactions. For these reasons, the most suitable methodology for evaluating diet is one that evaluates long-term and short-term evaluation of dietary intake plus one to assess dietary patterns and quality of diet in relation with allergic diseases. Therefore, validation methods for assessing dietary habits, especially in epidemiology, should be developed because of it is not possible to use biological samples and biomarkers in all studies due to their high costs.

Moreover, we cannot exclude the possibility of a selection bias regarding the papers chosen to be included in this review; this is one limitation of our work. Hence, we suggested a future systematic and exhaustive review to be done on this large domain that would include all articles that dealt with diet and allergies. However, even if we can’t draw any final and definite conclusion based on this review, recommendations can be made on the main results that we have obtained from very large studies included in this work that could have a positive effect on limiting the rising of allergies in our time.

Despite these limitations, a major finding is that diet and allergic diseases are reality after all, they are not some myth or rumor that we are talking about more recently. Dietary factors may be an etiology of atopic diseases, especially in children. A healthy diet rich in antioxidants and omega-3 fatty acids consumed by the mother during pregnancy and by the child during childhood may reduce significantly the prevalence and incidence of asthma, allergic rhinitis, and atopic dermatitis, even in children with a hereditary predisposition for atopy. More prospective and interventional studies need to be performed on food groups and food items rather than on single nutrients to support the available
results and widen the possibility of making generalizations. This could lead to recommendations for a special diet to be followed during pregnancy and in childhood, at least until adolescence. The “allergy epidemic” that the world is currently undergoing might thus be reduced.

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Conflicts of Interest

The authors declare no conflict of interest.

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