Relationship of asthma and rhinoconjunctivitis with obesity, exercise and Mediterranean diet in Spanish schoolchildren

Luis Garcia-Marcos, Izaskun Miner Canflanca, Jose Batlles Garrido, Angel Lopez-Silvarrey Varela, Gloria Garcia-Hernandez, Francisco Guillen Grima, Carlos Gonzalez-Diaz, Ignacio Carvajal-Urueña, Alberto Arnedo-Pena, Rosa M Busquets-Monge, Maria Morales Suarez-Varela, Alfredo Blanco-Quiros

Background: Although several studies have investigated the influence of diet on asthma in schoolchildren, none of them has evaluated how obesity can modify this effect. A study was undertaken to evaluate the association of various foods and a Mediterranean diet with the prevalence of asthma and rhinoconjunctivitis, adjusting for obesity and exercise.

Methods: A cross-sectional study was performed in 20 106 schoolchildren aged 6–7 years from eight Spanish cities. Using the ISAAC phase III questionnaire, parents reported chest and nose symptoms, food intake, weight, height and other factors, including exercise. A Mediterranean diet score was developed. A distinction was made between current occasional asthma (COA) and current severe asthma (CSA).

Results: Independent of the amount of exercise, each Mediterranean score unit had a small but protective effect on CSA in girls (adjusted OR 0.90, 95% CI 0.82 to 0.98). Exercise was a protective factor for COA and rhinoconjunctivitis in girls and boys (the more exercise, the more protection). Obesity was a risk factor for CSA in girls (adjusted OR 2.35, 95% CI 1.51 to 3.64). Individually, a more frequent intake (1–2 times/week and ≥3 times/week vs never/occasionally) of seafood (adjusted ORs 0.63 (95% CI 0.44 to 0.91) and 0.53 (95% CI 0.35 to 0.80)) and cereals (adjusted OR 0.56 (95% CI 0.30 to 1.02) and 0.39 (95% CI 0.23 to 0.68)) were protective factors for CSA, while fast food was a risk factor (adjusted ORs 1.64 (95% CI 1.28 to 2.10) and 2.26 (95% CI 1.09 to 4.68)). Seafood (adjusted ORs 0.74 (95% CI 0.60 to 0.92) and 0.67 (95% CI 0.53 to 0.85)) and fruit (adjusted ORs 0.76 (95% CI 0.60 to 0.97) and 0.71 (95% CI 0.57 to 0.88)) were protective factors for rhinoconjunctivitis.

Conclusions: A Mediterranean diet has a potentially protective effect in girls aged 6–7 years with CSA. Obesity is a risk factor for this type of asthma only in girls.

The apparent parallel increase in the prevalence of asthma and obesity has led some authors to hypothesise that changes in diet could be responsible for the increase in the two conditions. Foods that favour obesity could be associated with asthma if the former is a risk factor for the latter. However, the causal relationship between obesity and asthma is debatable. It seems, however, that obesity precedes asthma and is a risk factor for asthma, especially in prepubertal non-allergic boys and in adolescent girls.

Antioxidant nutrients such as vitamin C have been postulated to have a protective role in the development of asthma. Several cross-sectional studies have shown an inverse relationship between the intake of citrus fruit, vegetables, apples and pears and asthma. Fish and fish products have also been associated with a lower prevalence of asthma. Conversely, asthma has been associated with the intake of liver, deep-fried foods and butcher’s meat.

Fatty acids have also been related to the prevalence of asthma. A European ecological study reported that trans-fatty acids, which are found in industrially hydrogenated vegetable fats with widespread use in fast foods, are related to an increase in the prevalence of asthma, rhinoconjunctivitis and eczema. It is possible that diets high in trans-fatty acids are also low in all-cis omega 6 and omega 3 fatty acids, which could down-regulate asthma mediators. On the other hand, the intake of trans-fatty acids changes from north to south Europe, being higher in Iceland and lower in the Mediterranean countries. A somewhat similar north to south gradient in the prevalence of asthma was shown by the International Study of Asthma and Allergies in Childhood (ISAAC), with a lower prevalence in the Mediterranean centres of western Europe which share a classic common diet.

The term “Mediterranean diet” refers to dietary patterns found in olive growing areas of the Mediterranean region. There are several variants of the Mediterranean diet, but some common components can be identified: a high ratio of monounsaturated to saturated fats; a high consumption rate of vegetables, fruits, pulses and grains; and moderate consumption of milk and dairy products.

The present study focuses on the association between asthma (current occasional asthma (COA) and current severe asthma (CSA)) and rhinoconjunctivitis and the individual intake of several foods and of a Mediterranean diet, controlling for obesity and exercise.

METHODS

Using the ISAAC phase III questionnaire (core and environmental questionnaires) (http://isaac.auckland.ac.nz), parents of children aged 6–7 years in the school setting from eight Spanish centres (Cartagena, Barcelona, Bilbao, Valencia, Madrid, Asturias, San Sebastián and La Coruña) were surveyed. Except for Barcelona, Madrid and Asturias, the centres were...
included all schools or a random sample of schools within the city district which had children of the targeted age range. In Madrid all schools within the health area of the Hospital 12 de Octubre were included, and in Barcelona all the schools in the Hospital del Mar health area were included. In Asturias schools were randomly sampled from the entire province. The questionnaires were translated into Spanish and translated back into English according to the ISAAC protocol and were validated later. The questionnaires were given to the children by their teachers, filled in by the parents at home and returned to the school within 1 week.

The core questionnaire included questions on asthma and rhinoconjunctivitis symptoms. The environmental questionnaire included questions on food consumption (never or occasionally, 1–2 times/week and ≥3 times/week).

For the purpose of this study, current asthma was defined as a positive answer to the question: “Has your child had wheezing or whistling in the chest during the last 12 months?” CSA was defined using a combination of the following three questions to assess the severity of asthma:

- “How many attacks of wheeze has your child had during the last 12 months (none, 1–3, 4–12, >12)?”
- “In the last 12 months, how often on average has your child’s sleep been disturbed due to wheezing (never, <1 night/week, ≥1 nights/week)?”
- “In the last 12 months, has wheezing been severe enough to limit your child’s speech to only one or two words at a time between breaths?”

Children were considered to have CSA when there were ≥4 asthma attacks or when sleep was disturbed ≥1 nights/week or when there had been an episode of speech limitation. Children with “current asthma” that was not ‘clinically significant’ were considered to have COA.

Rhinoconjunctivitis was defined as a positive answer to the following two questions:

- “In the past 12 months, has your child had a problem with sneezing or a runny or blocked nose when he/she did not have a cold or the flu?”
- “In the past 12 months, has your child’s sleep been disturbed due to sneezing (never, <1 night/night/week, ≥1 nights/night/week)?”

The regional ethics committee of Asturias approved this study for all ISAAC III centres in Spain.

RESULTS

The mean participation rate was 78.7%. The number of children included in the analysis after exclusion of those not born in Spain (n = 1249) and those who were outside the target age range (n = 683) was 20 106. Table 1 shows the frequency of intake of the surveyed foods among these children.

Those with no available data on weight and/or height (n = 2961) and/or consumption of a specific food were not used in the analyses where individual foods were included as variables. Consequently, the maximum possible number of children included in the analysis of a given individual food was 17 145. The number of children suffering from COA, CSA and rhinoconjunctivitis in this group were 1379 (8.0%; 95% CI 7.6% to 8.4%), 390 (2.3%; 95% CI 2.0% to 2.5%) and 1446 (8.4%; 95% CI 8.0% to 8.8%), respectively. The number of children with COA, CSA and rhinoconjunctivitis among those who had missing data on weight and height were 260 (8.7%; 95% CI 7.7 to 9.8), 94 (3.2%; 95% CI 2.5% to 3.8%) and 272 (9.1%; 95% CI 8.1% to 10.2%). There were no statistical differences in the Mediterranean score between children included in the analysis and those excluded.

Children with at least one missing answer in the food questionnaire (n = 1622) could not be used to calculate the Mediterranean diet score and were not included in the analyses in which this variable was included. The frequency of the intake of the various foods is shown in table 1. The odds ratios (ORs, adjusted for sex, obesity, maternal smoking, older or younger siblings and exercise) of the intake of different foods for suffering from COA, CSA and rhinoconjunctivitis are shown in tables 2, 3 and 4 respectively.

The food with a most consistent protective effect on COA was nuts, although the intake of seafood, fruit, vegetables and margarine showed a significant protective trend (table 2). For CSA, seafood and cereals were clearly protective whereas fast food was a risk factor (table 3). Meat, fruit, vegetables and milk were not consistent protective factors but showed a significant protective trend (table 3).
Seafood and fruit were clear protective factors for rhinoconjunctivitis and a significant protective trend was found for meat, cereals and milk (table 4). Eating eggs with more frequency than never or occasionally was a protective factor for CSA and for rhinoconjunctivitis in the last year (Tables 3 and 4).

The Mediterranean diet score had a median of 13 points (minimum 4, maximum 20, interquartile range 2). There was a statistically significant difference in this score between obese and non-obese children both for boys ($Z = 3.73$, $p < 0.001$) and girls ($Z = 4.13$, $p < 0.001$). However, this difference was very small with a median value of 13 for both groups. There was a small but significant association ($OR 1.14$, 95% CI 1.02 to 1.28, $p = 0.017$) between being obese and exercising less frequently (1–2 times/week vs $>3$ times/week).

Table 5 shows the effect of obesity, Mediterranean score and exercise together with maternal smoking and number of siblings on COA, CSA and rhinoconjunctivitis (ORs adjusted for all the variables in the table). Obesity seems to be a risk factor for the three outcome variables in both girls and boys at this age; however, the effect was greatest for CSA in girls (10% protection per each score unit). Since this diet is rich in both antioxidants and cis-monounsaturated fatty acids, this is not an unexpected finding. Individual foods seem to influence the prevalence of asthma in different ways according to the type of asthma (Tables 2 and 3). Whereas nuts were the only protective factor for COA, seafood and cereals were protective for CSA and fast food was a risk factor for CSA. It is possible that the apparent protective effect of nuts on COA is a result of reverse causation bias. The individual effect of seafood and cereals is in agreement with a recent report from the Netherlands in children in phase II of the ISAAC study which showed a protective effect of whole grain products and fish.

Seafood and—to a lesser extent—cereals have a protective effect on rhinoconjunctivitis. This could indicate that their protective effect on more severe asthma is mediated by protection from atopy, which is a very important risk factor for more severe asthma in children aged 8–10 years.

Fruit showed a clear protective effect on rhinoconjunctivitis and a trend for a protective effect on more severe asthma. In a
cross-sectional study on a large sample of children aged 6–7 years using the ISAAC questionnaire, Forastiere et al7 found an association between consumption of citrus/kiwi fruit during the winter and a lower prevalence of several asthma symptoms and also of rhinitis during the last year. In this study consumption of citrus fruit during the winter was specifically examined, whereas in the present study the season of the year was not considered. More recently, Farchi et al29 have reported their findings on the intake of several foods in the same Italian population of children that was surveyed again 1 year later. Although there seemed to be a protective trend, they did not find any significant association between the intake of fruit and the prevalence of wheeze in the last year. In contrast, as in the present study, the protective effect on rhinoconjunctivitis (same definition as in the current survey) was significant.

In the present study there was a certain trend in the association of the intake of vegetables with a lower prevalence of the three outcome variables, although this did not reach full statistical significance in any instance. In a study by the ISAAC group, an inverse relationship was found between the prevalence rates of asthma, allergic rhinoconjunctivitis and atopic eczema and the intake of vegetables.9 Farchi et al19 showed a trend between the intake of cooked vegetables and the protective effect on wheeze in the last year, but there was no effect on rhinoconjunctivitis.

The Mediterranean diet seems to offer some protection from asthma, especially from CSA. This is probably due to a mixed effect of taking “protective” foods and avoiding “risky” foods. For example, in the present study and consistent with others,17 30 fast food was associated with a higher prevalence of CSA.

The association between obesity and asthma is still a controversial issue, especially the temporal relationship between the two. The prospective longitudinal study by Gilliland et al7 on children aged 4–11 years has recently shown that the incidence rate of doctor-diagnosed asthma is significantly higher in overweight (>85th percentile) and obese (>95th percentile) children (both girls and boys). When stratified by atopy, they found that the risk was higher among non-allergic children. Previously, Castro-Rodriguez et al found in the Tucson cohort that there was no relationship between BMI and asthma at the age of 6 years, but there was an association between overweight and obesity and asthma at the age of 11, especially in girls. They concluded that girls who became obese between 6 and 11 years of age were seven times more likely to develop asthma symptoms at the age of 11 or

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Adjusted odds ratio (aOR) of current severe asthma in last year for different frequencies of food consumption relative to consuming that food never or occasionally among children aged 6–7 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Once or twice per week</strong></td>
</tr>
<tr>
<td></td>
<td>aOR (95% CI)</td>
</tr>
<tr>
<td>Meat</td>
<td>0.56 (0.20 to 1.58)</td>
</tr>
<tr>
<td>Seafood</td>
<td>0.63 (0.44 to 0.91)</td>
</tr>
<tr>
<td>Fruit</td>
<td>0.87 (0.55 to 1.35)</td>
</tr>
<tr>
<td>Vegetables</td>
<td>0.87 (0.63 to 1.21)</td>
</tr>
<tr>
<td>Fruits</td>
<td>0.84 (0.52 to 1.35)</td>
</tr>
<tr>
<td>Cereals</td>
<td>0.56 (0.30 to 1.02)</td>
</tr>
<tr>
<td>Pasta</td>
<td>0.58 (0.32 to 1.05)</td>
</tr>
<tr>
<td>Rice</td>
<td>0.80 (0.51 to 1.27)</td>
</tr>
<tr>
<td>Butter</td>
<td>1.15 (0.89 to 1.49)</td>
</tr>
<tr>
<td>Margarine</td>
<td>1.02 (0.77 to 1.35)</td>
</tr>
<tr>
<td>Nuts</td>
<td>0.96 (0.77 to 1.22)</td>
</tr>
<tr>
<td>Potato</td>
<td>0.47 (0.28 to 0.81)</td>
</tr>
<tr>
<td>Milk</td>
<td>0.65 (0.31 to 1.40)</td>
</tr>
<tr>
<td>Eggs</td>
<td>0.57 (0.38 to 0.84)</td>
</tr>
<tr>
<td>Fast food</td>
<td>1.64 (1.28 to 2.10)</td>
</tr>
</tbody>
</table>

Odds ratio adjusted for sex, obesity, maternal smoking, siblings and exercise.

<table>
<thead>
<tr>
<th>Table 4</th>
<th>Adjusted odds ratio (aOR) of rhinoconjunctivitis symptoms in last year for different frequencies of food consumption relative to consuming that food never or occasionally</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Once or twice per week</strong></td>
</tr>
<tr>
<td></td>
<td>aOR (95% CI)</td>
</tr>
<tr>
<td>Meat</td>
<td>0.61 (0.34 to 1.13)</td>
</tr>
<tr>
<td>Seafood</td>
<td>0.74 (0.60 to 0.92)</td>
</tr>
<tr>
<td>Fruit</td>
<td>0.76 (0.60 to 0.97)</td>
</tr>
<tr>
<td>Vegetables</td>
<td>0.87 (0.73 to 1.05)</td>
</tr>
<tr>
<td>Fruits</td>
<td>0.72 (0.57 to 0.93)</td>
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<tr>
<td>Cereals</td>
<td>0.76 (0.50 to 1.14)</td>
</tr>
<tr>
<td>Pasta</td>
<td>0.83 (0.57 to 1.20)</td>
</tr>
<tr>
<td>Rice</td>
<td>0.81 (0.64 to 1.04)</td>
</tr>
<tr>
<td>Butter</td>
<td>0.91 (0.79 to 1.05)</td>
</tr>
<tr>
<td>Margarine</td>
<td>1.01 (0.86 to 1.17)</td>
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<tr>
<td>Nuts</td>
<td>1.06 (0.94 to 1.20)</td>
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<tr>
<td>Potato</td>
<td>0.72 (0.52 to 0.99)</td>
</tr>
<tr>
<td>Milk</td>
<td>0.60 (0.37 to 0.96)</td>
</tr>
<tr>
<td>Eggs</td>
<td>0.76 (0.60 to 0.93)</td>
</tr>
<tr>
<td>Fast food</td>
<td>1.07 (0.93 to 1.24)</td>
</tr>
</tbody>
</table>

Odds ratio adjusted for sex, obesity, maternal smoking, siblings and exercise.
13 years. However, a recent cross-sectional study on 11 199 Canadian children aged 4–11 years failed to show any relationship between being overweight or obese (>85th percentile) and suffering from asthma as reported by the mother.\(^1\) Previously, a similar German study\(^2\) on 9357 children aged 5–6 years found an association of overweight/obesity (>90th percentile/ >97th percentile) in girls but not in boys. In our study in children aged 6–7 years, there was a strong association between obesity and CSA in girls after adjusting for the intake of a Mediterranean diet and exercise.

It is interesting that exercise was associated with a lower prevalence of COA and rhinoconjunctivitis (the more exercise the more “protection”) but had no effect on CSA. If this was due to a reverse causation effect, it would be expected to result in greater “protection” in patients with more severe asthma. It might therefore be hypothesised that patients with mild asthma benefit from exercise while those with severe asthma do not. However, it is more likely that severe asthma is related to less intense exercise than mild asthma, thus blunting the beneficial effect of strong exercise (there was in fact a trend towards a protective effect of more frequent exercise in the CSA group). This lack of exercise can make the effect of diet and obesity more obvious in those with CSA, at least in girls.

One limitation of the present study is information bias on food intake and on reported height and weight. It has been shown that parents are reliable when reporting the food intake of their children, especially fruit and vegetables;\(^3\) however, the ISAAC food questionnaire does not allow correction for energy intake. Nevertheless, most studies on diet and asthma in children do not adjust for this parameter. On the other hand, the height and weight reported by parents have been shown to be reliable for defining obesity in our environment.\(^4\)

A further possible limitation is that, as the family history of asthma and allergy is not recorded in the ISAAC phase III questionnaire, we could not control for this factor. It is possible that parents with asthma or allergy change their children’s diet to a “less allergenic” one (whatever this means at the age of 6–7 years). However, our own results of the ISAAC phase II study in children aged 10–11 years (data not shown) reveal a higher consumption of fruits in children whose mothers did not have asthma than in those whose mothers had asthma. Also, and contrary to what would be expected in a healthy worker effect, children whose mothers had asthma had a higher intake of hamburgers and fizzy drinks. These findings suggest that the way mothers approach their children’s diet is probably largely influenced by their own, and having a child with asthma does not change it greatly. We therefore do not think it likely that including the family history in our model would have had a substantial effect on the results.

As with all cross-sectional studies, our study has the limitation of not being able to show the time relationships of the associations found, so it is not possible to reach causal conclusions. For all these reasons, the results of the present study must be taken with caution: the present findings need to be confirmed by interventional or prospective studies before the intake of the Mediterranean diet is recommended as part of the environmental management of asthma.

In summary, the results of the present study suggest that the Mediterranean diet has a potential protective effect in girls aged 6–7 years with CSA. In contrast, after adjusting for this type of diet, obesity is a risk factor for CSA only in girls.

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**Table 5** Summary logistic regression of the main factors under study

<table>
<thead>
<tr>
<th></th>
<th>Current occasional asthma</th>
<th></th>
<th>Current severe asthma</th>
<th></th>
<th>Rhinoconjunctivitis</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Girls</td>
<td>Boys</td>
<td>aOR (95% CI)</td>
<td>Girls</td>
<td>Boys</td>
<td>aOR (95% CI)</td>
</tr>
<tr>
<td>Mediterranean diet (per score unit)</td>
<td>0.97 (0.92 to 1.01)</td>
<td>0.98 (0.93 to 1.04)</td>
<td>0.90 (0.82 to 0.98)</td>
<td>0.98 (0.91 to 1.06)</td>
<td>0.98 (0.93 to 1.03)</td>
<td>0.99 (0.95 to 1.03)</td>
</tr>
<tr>
<td>Obesity</td>
<td>1.10 (0.82 to 1.48)</td>
<td>1.40 (1.11 to 1.78)</td>
<td>2.35 (1.51 to 3.64)</td>
<td>1.30 (0.84 to 2.01)</td>
<td>1.22 (0.91 to 1.62)</td>
<td>1.18 (0.92 to 1.51)</td>
</tr>
<tr>
<td>Exercise</td>
<td>Never/occasionally</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>1–2 times/week</td>
<td>0.74 (0.59 to 0.93)</td>
<td>0.68 (0.54 to 0.86)</td>
<td>1.07 (0.67 to 1.70)</td>
<td>1.05 (0.66 to 1.65)</td>
<td>0.75 (0.60 to 0.95)</td>
</tr>
<tr>
<td></td>
<td>&gt;3 times/week</td>
<td>0.53 (0.43 to 0.70)</td>
<td>0.56 (0.45 to 0.70)</td>
<td>0.79 (0.48 to 1.30)</td>
<td>0.77 (0.49 to 1.22)</td>
<td>0.60 (0.47 to 0.76)</td>
</tr>
</tbody>
</table>

aOR, adjusted odds ratio (adjusted for younger and older siblings and maternal smoking).
REFERENCES

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