MEDITERRANEAN DIET AND CHILDHOOD ASTHMA AND ALLERGIC SENSITIZATION

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INTRODUCTION

The prevalence of asthma and allergic diseases has increased significantly during the last decades, representing a global health burden[1]. In Oslo, Norway, childhood asthma continues to increase, reporting lifetime asthma prevalence of 3.1 % in 1981[2], 8 % in 1993[3], 9.3 % in 1994[4], and 20.2 % in 2004, affecting every fifth 10 – year old child[5]. The rapid changes in prevalence cannot be elucidated by genetic factors alone, environmental causes, such as urbanization, unhealthy diet and less physical activity, have to be considered as possible contributing factors[6].

Many epidemiological studies have investigated possible associations between several dietary factors and asthma, although, the findings are inconsistent. Beneficial effects of fruits and vegetables, which are important antioxidant sources, on wheeze and atopy are shown in various studies[7-10], whereas other studies found no associations[11-13]. Fatty acids have also been postulated to be a protective factor in the development of asthma[14-16], but studies shows conflicting results[17,18]. Recently, there has been some studies suggesting fast food consumption as a contributable factor to the increase of asthma[19]. However, causal relationship between specific nutrients, food types or dietary patterns on asthma prevalence is debatable[20].

Mediterranean dietary pattern is somewhat heterogeneous among Mediterranean countries[21], but several common features can be identified: a high consumption of plant foods such as legumes, cereals, fruits and vegetables, nuts and seeds, low to moderate consumptions of dairy products and egg, a low consumption of meat, and olive oil as the main source of fat[22].

It has been reported by the International Study of Asthma and Allergies in childhood (ISAAC), that the prevalence of asthma in the Mediterranean countries is lower, compared to populations in Northern Europe[23]. The diet is apparently one common factor in these countries besides other lifestyle factors, although it is thought that the Mediterranean dietary pattern could influence the incidence of this disease[7,24,25].

The main objectives of this study were to assess whether Mediterranean diet is positively associated with asthma and allergic sensitization among adolescents in our population.

SUBJECTS AND METHODS

Study design

The present study is a part of the 16-year follow up of the Environment and Childhood Asthma (ECA) study in Oslo. In brief, a cohort of 3.754 newborns was established during 15 months from January 1st, 1992. The ECA study has to date contained three main phases, from birth to two years[26], the 10-year follow-up study [5], and finally a 16 –year follow up completed in 2009.

The present study was conducted between October 2008 and August 2009, and attended by 550 of the 1215 children with lung function measured at birth and/or clinical investigation at two years. The study population (285 boys) had a mean age of 16.7 (standard deviation (±) 0.4) years. The 16-year follow up included blood samples, structured interview of all the subjects including dietary assessment, parental questionnaire, skin prick tests (SPT) for allergic sensitization, exhaled nitric oxide, lung function measurements by flow volume loops, body plethysmography, metacholine challenge test, urine sampling and clinical examination in one day. Dust samples from the children's mattresses were collected by vacuum - cleaners in standardized manner. In addition, they wore an armband activity monitor for four consecutive days.

The Regional Committee of Medical Ethics and Norwegian Data Inspectorate approved the study, and written informed consent was obtained from the parents of all subjects.

Methods

Skin prick tests

Skin prick tests to common inhalant and food allergens were performed in 550 children according to European guidelines[27], using the following 19 allergens: rabbit dander, egg white, peanut, codfish, shrimp, hazelnut (Soluprick®, ALK Abello, Denmark), cockroach, house dust mite (dermatophagoides (D.) pteronnysinus), mugwort pollen (Alyostal, stallergenes, France), cat, dog, grass, mould (Alternaria alternata) (ALK Scherax, Wedel, Germany) birch pollen, aspergillus, hazel, alder, mould (Cladosporium herbarium (Allergopharma, Reinbek, Germany) and cow's milk.

Physician guided interview and parental questionnaire

A paediatrician-guided structured interview of the index subjects as well as a parental questionnaire included modified ISAAC-questions[28] on airway symptoms, in addition to questions concerning environmental exposure and other lifestyle factors such , which may influence the outcomes of interest. Data from the interview was used for the present study.

Assessment of diet

Dietary information was collected using a semi structured food frequency interview containing 21 food items and 14 beverages, asking about how often the item was eaten. To asses the accurate amount of intake, the interview had 8 possible responses for the food items ranging from “never or rare” to “4 or more per day, and 7 possible responses for beverages ranging from “never or rare” to “7 glasses or more per day. The collected information was further converted into monthly consumption frequencies as follows: For food items: Never/Rare, twice a month, 6 times a month, 20 times a month, 30 times a month, 60 times a month, 90 times a month, and 120 times a month. For beverages: Never/rare, 2 glasses a month, 6 glasses a month, 20 glasses a month, 60 glasses a month, 150 glasses a month and 210 glasses a month. Foods were categorized into eight major groups: 1.Vegetables (potatoes, carrot, tomatoes, cauliflower, broccoli), 2.Legumes (kidney beans, green peas), 3.Fruits and Nuts (apple, orange, banana, peach, watermelon, grapes, pear, pineapple, kiwi, strawberry, almonds, walnuts, hazelnuts, peanuts), 4.Dairy products (milk), 5.Cereals (cereals, pasta, rice, bread), 6.Fish (Fish, seafood), 7.Meat , 8.Junk food and Fat (fast food, chips, French fries, candy, chocolate).

To further evaluate the degree of adherence to Mediterranean diet, a dietary score was developed, based on the score originally developed by Trichopoulou et al [29] and minor adaptations was made as follows: a) The ratio of monounsaturated lipids to saturated lipids could not be calculated due to lack of applicable data, b) The ethanol consumption component was not included in the diet score, and c) a new food group, junk food and fat, was established and included in the diet score, as done by de, Batlle J et al [24] . Furthermore, we did not have separate data on cheese and yoghurt consumption, which are components included in one of the major food groups, Dairy products, in the original score.

For the purpose of the present study, the Mediterranean diet score included eight major food groups as described previously, and a value of 0 or 1 was assigned for each of them, using the median consumption as the cut-off point. For components positively associated with the Mediterranean diet (Vegetables, Legumes, Fruits and Nuts, Cereal, and fish) subjects whose consumption was at or above the median were assigned a value of 1, and subjects whose consumption was below the median were assigned a value of 0. For components potentially unfavourable (Meat, Dairy Products and Junk food and Fat), subjects whose consumption was at or above the median were assigned a value of 0, and subjects whose consumption was below the median were assigned a value of 1. Finally, the total Mediterranean diet score ranged from 0 – 8, representing minimal to maximal adherence to Mediterranean diet.

Anthropometric measurements

Subjects were weighed wearing light clothing and without shoes to the nearest 1.0 kg. Height was measured to the nearest 1.0 cm by using a stadiometer. Body mass index was calculated for all subjects. Obesity and overweight was defined according to the cut-off points reported by Cole et al[30], for each age group and sex.

Outcomes and explanatory variables

The main outcomes were current asthma and allergic sensitization at 16 years of age. Current asthma was defined as a doctor's diagnosis of asthma ever and wheeze and/or chest tightness in the last 12 months and/or use of asthma medication in the last 12 months. Allergic sensitization was regarded as positive with a wheal diameter ≥3 mm larger than the negative control (NaCl) to one or more of the 19 allergens.

The main explanatory variable was the Mediterranean score (0-8, eight being complete adherence to the score).

Statistical Analysis

To compare group for continuous variables a two-sample t-test was applied, whereas Pearson's Chi-square test was applied for categorical variables. To assess the importance of predictor variables, multiple binary logistic regression analysis was applied for binary outcome and multiple regression analysis for continuous outcome. The assumptions for the regression models were tested using: Jacknife residuals, Cook's d and variance inflation

factors (VIF). For the logistic models we used the Pearsons and Deviance residuals as well as the DFBetas, the difdeviance and the difpearson to assess the fit and the validity of the model. In the regression analysis, we applied Hosmer's step down procedure [31], testing for confounding. In the final model, we tested for interactions. All p-values ≤ 0.05 were considered significant. A logistic regression of a binary response variable on a continuous, variable with a sample size of 550 observations achieves 88% power at a 0.05 significance level to detect an odds ratio of 0.67. An adjustment was made since a multiple regression of the independent variable of interest on the other independent variables in the logistic regression obtained an R-Squared of 0.250. The analysis was performed using Statistical Analysis System (SAS, version 9.2, SAS Institute Inc., Cary, NC, USA)

RESULTS

The general characteristics of the study population are shown in table 1. Current asthma and allergic sensitization were defined in 17.5 % and 48.4 % of subjects, respectively. Among the adolescents 2.5 % were obese, 12.2 % were overweight, 3.8 % smoked daily, while 8.8 % smoked weekly, sometimes or previously. Complete data for the diet score was obtained in 549 (99.8 %) of the subjects. The mean Mediterranean diet score was 4.0 standard deviation ± 1.6, which indicates a moderate adherence to the Mediterranean dietary pattern in our study population.

The Mediterranean diet tended to be inversely association with current asthma (OR 0.88 95 % CI 0.77-1.02), although it was not statistically significant. When adjusting for gender, age, BMI, socio-economic status, smoking and physical activity, the point estimates remained generally unchanged (OR 0.85 95 % CI 0.63-1.15). No associations were found between Mediterranean diet score and allergic sensitization in the crude (OR 0.89, 95 % CI 0.71-1.12) or the adjusted (OR 0.86, 95 % CI 0.67-1.09) analyses.

The average monthly consumption (times/month) for food components included in the Mediterranean diet score in addition to cod liver oil supplements, is summarized in table 2.

Table 3 presents the independent associations between each of the score components and the outcomes of interest. Intake of fruits and nuts were significantly associated with current asthma (OR 0.99, 95 % CI 0.99-1.00). However, this very small effect did not remain significant in the multivariate analyses. For the other score components we did not observe any significant associations with current asthma or allergic sensitization.

DISCUSSION

Adherence to Mediterranean diet was not significantly associated with the presence of current asthma and allergic sensitization, although a trend toward an inverse association was noted. Nor were the individual food item groups significantly associated with current asthma or allergic sensitization.

The lack of significant associations between Mediterranean diet and current asthma are in line with some[12]), but not all[24,32] studies, highlighting the inconsistent findings of the postulated protective effect of the Mediterranean diet on the prevalence of asthma. In 6-7 year old girls Marcos et al observed a protective effect [33] and Barcala et al[12] an increased risk of current severe asthma of a Mediterranean diet and no significant associations between Mediterranean diet and other asthma categories, consistent with our findings. In Crete a protective effect of Mediterranean diet has been found on nocturnal cough, but not for wheezing[7] in children aged between 7 and 18 years.

We found no significant associations between Mediterranean diet and allergic sensitization, in line with the few other studies we are aware of assessing this hypothesis [7,32].

The definition of Mediterranean diet is not consensual, although it is considered as one of the healthiest dietary models. A great adherence to the Mediterranean diet, which is characterized by high consumption of fish, vegetables, fruits, nuts, legumes and olive oil, is associated with a significant reduction in total mortality[29]. Several hypotheses have evolved, indicating that nutritional components may prevent or limit inflammatory airway response, though no clear answers has emerged[20].

The lack of convincing documentation in our and other groups of specific food groups or single nutrients having a role in the development of asthma has shifted to evaluate if entire dietary patterns alterations may influence asthma and atopic disease devlopment[34]. The lack of observed beneficial effect from nutrients considered as promediterranean on asthma such as polyunsaturated fatty acids[35] and vitamin C[36] and E[13] are nevertheless challenged by the observed inverse association between fish consumption and asthma[11,16,32], as well as potential protective effect of fruits and vegetables on asthma prevalence[10,37,38].

Strengths and limitations

The present study had sufficient statistical power to detect a risk reduction of 33% and insufficient population size is therefore unlikely to explain our lack of association between the diet and current asthma or allergic sensitization. On the other hand a reverse causation effect cannot be ruled out, in that adolescents with an asthma diagnosis may attempt dietary modifications to improve asthma control[39].

The Mediterranean diet score based upon detailed dietary information was a regional modification of validated score developed by Trichopolou[29] to investigate the adherence to Mediterranean diet and survival in an adult Greek population. By using the Mediterranean diet score, we could identify the dietary pattern without calculating grams of consumption of each food, as done by other scores[40]. The height and weight was measured using the same instrument in all subjects, in contrast to other studies, which calculates BMI based on self-reported measurments[25,33]. Finally, the definition of current asthma included doctor's diagnosis, although other studies mostly define current asthma by the severity of symptoms alone[12,33].

The dietary data assessed the present dietary habit, and did consequently not account for previous dietary habits. Thus, a potential causal relationship could not be assessed in the present study. Moreover, adjustments for total energy intake could not be calculated due to lack of available data.

In conclusion, our findings do not support a potential protective effect of the Mediterranean diet on the prevalence of asthma and allergic sensitization.

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Tabel 1. Main characteristics of the study population

	n	%	Mean ± S.D
Age			16.7 ± .4
Sex			
Boys	285	51.8	
Girls	265	48.2	
Height (cm)			172.9 ± 8.4
Weight (kg)			65.8 ± 11.2
BMI			
Underweight	24	5.3	
Normal weight	440	80.0	
Overweight	67	12.2	
Obesity	19	2.5	
Organized physical activity (hours/week)	424/550		4.9 ± 5.2
Smoking	69/548		
Daily	21	3.8	
Not daily	48	8.8	
Maternal education	538		
No education			
Elementary	30	5.6	
High school	178	33.1	
University	330	61.3	
Paternal education	536		
No education	1	.2	
Elementary	41	7.6	
High School	143	26.7	
University	351	65.5	
Current Asthma	96/550	17.5	
Allergic sensitization	548		
No positive SPT	282	51.3	
At least one positive SPT	266	48.4	

BMI: Body mass index
SPT: Skin prick test
S.D: Standard deviation

Table 2. Description of monthly food consumption (times/month)

Food Groups	Mean (S.D)
Vegetables	27.5 (18.1)
Legumes	2.3 (5.1)
Fruits and Nuts	35.6 (32.6)
Cereals	78.3 (38.3)
Meat	18.3 (14.7)
Fish	6.8 (8.8)
Dairy products	47.9 (49.2)
Junk food and fat	24.1 (24.4)
Cod liver oil	8.7 (12.8)

Table 3. Independent associations between each of the score components and the outcomes of interest

Current asthma

	Crude OR	Adjusted OR
Vegetables	0.99 (0.98-1.01)	1.02 (0.99-1.05)
Legumes	1.01 (0.98-1.05)	1.04 (0.99-1.10)
Fruits and Nuts	0.99 (0.99-1.00)	1.01 (0.99-1.02)
Cereals	1.00 (1.00-1.01)	1.01 (0.99-1.01)
Dairy products	1.00 (1.00-1.01)	1.00 (0.99-1.01)
Fish	1.00 (0.98-1.03)	0.95 (0.84-1.06)
Meat	0.99 (0.97-1.01)	0.99 (0.96-1.02)
Junk food and Fat	1.00 (0.99-1.01)	0.99 (0.96-1.01)
Cod liver oil	1.00 (0.98-1.02)	1.56 (0.54-4.51)

OR: Odds Ratio, CI: Confidence Interval
Adjusted for: Gender, age, smoking, BMI and Physical activity

Allergic sensitization

	Crude OR	Adjusted OR
Vegetables	1.01 (1.00-1.02)	1.02 (0.99-1.04)
Legumes	1.01 (0.98-1.05)	1.01 (0.97-1.07)
Fruits and Nuts	1.00 (1.00-1.01)	1.01 (0.99-1.01)
Cereals	1.00 (0.99-1.01)	1.01 (0.99-1.01)
Dairy products	1.00 (1.00-1.01)	1.00 (0.99-1.01)
Fish	1.01 (0.99-1.03)	1.03 (0.95-1.11)
Meat	1.01 (1.00-1.02)	1.01 (0.98-1.03)
Junk food and Fat	1.00 (0.99-1.01)	1.00 (0.99-1.02)
Cod liver oil	1.00 (0.99-1.02)	0.85 (0.39-1.88)

OR: Odds Ratio, CI: Confidence Interval
Adjusted for: Gender, age, smoking, BMI and Physical activity