

Adherence to the Mediterranean type of diet is associated with lower prevalence of asthma symptoms, among 10–12 years old children: the PANACEA study

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Epidemiological studies have shown several associations between asthma symptoms and dietary factors. The aim of this work was to evaluate the relationship between adherence to the Mediterranean diet and childhood asthma. A cross-sectional analysis was performed on 700 children (323 boys), 10–12 yr old, selected from 18 schools located in Athens greater area. Children and their parents completed questionnaires, which evaluated, among others, dietary habits. Asthma was defined according to ISAAC II criteria. Adherence to the Mediterranean diet was evaluated using the KIDMED score (theoretical range 0–12). Higher KIDMED score corresponds to greater adherence to the Mediterranean diet. Greater adherence to the Mediterranean diet was inversely associated with ever had wheeze ($p = 0.001$), exercise wheeze ($p = 0.004$), ever had diagnosed asthma ($p = 0.002$) and with any asthma symptoms ($p < 0.001$). One-unit increase in the KIDMED score was associated with 14% lower likelihood of having asthma symptoms (odds ratio = 0.86, 95% confidence interval 0.75–0.98), after adjusting for various confounders. No significant associations were found between asthma symptoms and consumption of fruits ($p = 0.25$), vegetables ($p = 0.97$), legumes ($p = 0.76$), cereals ($p = 0.71$), dairy ($p = 0.61$), salty snacks ($p = 0.53$), or margarine/butter ($p = 0.42$) consumption, while increased fish and meat intake was associated with less asthma symptoms ($p = 0.04$ and $p = 0.01$, respectively). Our findings suggest an inverse relationship between level of adherence to the Mediterranean diet and prevalence of asthma in school-aged children.

Dietary and other lifestyle factors in western society have been changing over recent decades, particularly in children, while asthma prevalence has been increasing (1). The majority of studies in the field of nutrition epidemiology have evaluated the role of specific nutrients on asthma prevalence; however, the dietary pattern analysis seems to receive much attention during the last years. Under this overall concept of dietary assessment, an association between adherence to Mediterranean diet and asthma prevalence in children has been revealed (2–4).

The Mediterranean diet, a cultural model for healthy eating, has been associated with low incidence of mortality and morbidity from chronic diseases in Mediterranean populations, compared to populations in the US or Northern Europe (5). A similar north–south gradient has been observed for asthma, with some Southern Mediterranean countries such as Greece or Albania, presenting the lowest prevalence (6). The traditional Mediterranean diet is characterized by a high intake of vegetables, legumes, fruits, and cereals (in the past largely unrefined); a moderate to high intake of fish, a

low intake of saturated lipids but high intake of unsaturated lipids, particularly olive oil; a low to moderate intake of dairy products, mostly cheese and yogurt; and a low intake of meat. The high content in the diet of vegetables, fresh fruits, and cereals, and the liberal use of olive oil guarantee an adequate intake of β -carotene, vitamin C, tocopherols, a linolenic acid, various important minerals, and several possibly beneficial bioactive compounds like polyphenols and antioxidants (7). Several epidemiological studies in children have demonstrated a reduced risk of asthma in relation to a high fruit and vegetable and fish intake (8–12).

In this work, the association of adherence to the traditional Mediterranean diet on asthma in boys and girls aged 10–12 yr from the greater area of Athens, Greece, was evaluated.

Materials and methods

Study sample

The PANACEA study (Physical Activity, Nutrition and Allergies in Children Examined in Athens) took place in Athens during 2005–2006. The survey enrollment was 700 students (323 boys, 377 girls) aged from 10 to 12 yr (fourth to sixth school grade) who were selected from 18 schools located in several areas of Athens. Schools were randomly selected from a list of schools provided by the regional education offices. The overall participation rate was 83.5%. Only pre-menstrual girls were included. To include a subject in the study, children's parents or guardians were fully informed about the objectives and methods of the study, and an informed consent was signed. The number of enrolled children was adequate enough to provide us with statistical power 80% to evaluate standardized differences between various groups greater than 0.5 at probability level <0.05 .

Measurements

A composite questionnaire, developed for the purposes of the study, was applied to retrieve information about age, sex, school class, dietary habits, and physical activity status of the children, as well as asthma symptoms. The questionnaire was completed by the enrolled children with the assistance of their parents through face-to-face interviews. The questionnaire also included information regarding the social and economic status of the family as assessed from the educational level of the parents (i.e., none, basic education, high school, academic), the number of cars within the family, the availability of child's own room, and the number of siblings), as well as information on hospitalizations of the children. Details about the measurements used have been presented elsewhere (13).

Evaluation of asthma symptoms

To evaluate asthma symptoms, the parents responded to seven questions according to the ISAAC protocol (14). In particular, the duration and the evaluation of the presence of asthma symptoms was assessed by four questions: if the child (i) ever had wheezing, (ii) ever had disturbed sleep because of

wheezing, (iii) ever had asthma and (iv) ever had dry cough at night, except in cases of cold or chest infection. The severity of asthma symptoms was evaluated by three questions that asked about specific details of the above symptoms in the past 12 months: (i) the number of attacks of wheezing, (ii) if their sleep was disturbed because of wheezing, and (iii) if wheezing was so severe to cause limitation of speech to one or two words at the time between breaths.

Evaluation of dietary habits and adherence to the Mediterranean diet

As mentioned earlier, the questionnaire also used a semi-quantitative Food Frequency Questionnaire (FFQ), which gathered information on daily or weekly basis on 63 foods and beverages usually consumed in Greece and on the habits pertaining to mealtime behaviors (15). In particular, daily consumption of various meals, the frequency of consumption of foods outside the home (including school canteens and non-home-made meals), the cooking method usually used, the type of oils/fat consumed, the frequency of snacks consumed and the frequency of consumption of various foods, such as fish, poultry, meat and meat products, eggs, various types of bread, potatoes, rice, fruits, fruit juices, vegetables, soft drinks and beverages, as well as the intake of traditional Greek cooked meals. Especially for the assessment of diet pattern of breakfast, there was a question about the frequency of breakfast consumption during a week (in times per week) and another question assessing the food most frequently that children consume for breakfast (close-type question with one out of eight possible answers: 'milk, yogurt, cereals, fruit juice, honey/marmalade, bread/toast, butter/margarine, cake'). Cereals for breakfast were defined as the commercially available ready-to-eat cereals of any type (plain ready-to-eat cereals, whole-grain cereals, etc.). Regarding the other foods and beverages that were assessed by the FFQ questionnaire were included in the following categories: (i) 'dairy products' that included all kinds of milk, yoghurt, and cheese; (ii) snacks that were categorized into two main types: 'salty' snacks (such as hamburger, pizza, hot-dog, toast, cheese pie, spinach pie, all kind of crisps, popcorn) and 'sweet' snacks (such as ice-cream, milk shake, all kinds of chocolate, croissant, cakes, biscuits); (iii) any type of soda drink; (iv) fruit juices (fresh or ready-made); (v) other beverages (such as tea, chamomile, etc.); and (vi) traditional Greek cooked foods. Typical serving sizes of the above food and beverages used as units for measurements and were clearly described in the FFQ (e.g., a can of soft drink, one hamburger, one portion of chicken approximately 150 g, a bag of crisps, etc.). The FFQ questionnaire was administered to all the children who participated in the study and completed by their parents during face-to-face interviews. The FFQ questionnaire has been found reliable and valid in previous analyses (15).

Children's adherence to the Mediterranean diet was evaluated using the KIDMED index (Mediterranean Diet Quality Index for children and adolescents). The index is derived from 16 components, which summarize the inherent characteristics of the Mediterranean diet. The theoretical score ranges from 0–12 (score of 0–3 reflects poor adherence to the

Mediterranean diet, score between 4–7 and 8–12, indicate average and good adherence to the Mediterranean diet) (16). Specifically, the KIDMED index presumes a daily consumption of at least one serving of fruit and vegetables, while consumption of at least two servings of each group is preferable. The recommended level of consumption of dairy products is at least three servings daily: one dairy product for breakfast and at least two servings of yogurt and/or cheese during the rest of the day. Consumption of grains and cereals is recommended daily for breakfast, while pasta or rice should be consumed at least five times per week. A weekly consumption of at least 2–3 servings of nuts and fish and two servings of pulses are advisable. Olive oil is recommended for culinary use, but no frequency is suggested. Dietary behaviors that are viewed as detrimental and alien to the principles of the Mediterranean diet include the frequent intake of sweets and candies (we defined this as more than twice daily), the use of commercially baked goods and pastries for breakfast, consumption of fast-foods, and non-consumption of breakfast.

Evaluation of physical activity and anthropometric characteristics

The study's questionnaires also included a physical activity and lifestyle assessment tool (i.e., the Physical Activity Lifestyle Questionnaire, PALQ) on the frequency and duration of several sports (brisk walking, running, swimming, and cycling), non-sports (going out with friends, social visits, going to the movies or theater) and sedentary activities such as watching television, working on a computer, or playing video games (17). The PALQ has been previously validated in metabolic equivalence (MET, 1 MET is equivalent to a metabolic rate consuming 3.5 ml of oxygen per kg of body weight per min [3.5 ml/kg/min]) by the Department of Sports Science, of the Democritus University of Thrace, Greece and has been found to be a reliable and valid estimating instrument of physical activity in children for use in epidemiological studies, compared with other physical activity questionnaires and accelerometer measurements. Children whose activities reported were equivalent to at least 2 MET/min per day were defined physically active. Moreover, total hours of physical activities during school as well as outdoor were evaluated.

Standing height to the nearest 0.1 cm after children had removed their shoes and body weight to the nearest 0.1 kg on calibrated digital scales were also measured. Children's body mass index (BMI) was calculated to classify them as overweight and obese, using the International Obesity Task Force (IOTF) classification (18). These cut-off points are based on health-related adult definitions of overweight (≥ 25 kg/m²) and obesity (≥ 30 kg/m²) but are adjusted to specific age and sex categories for children.

Bioethics

The study has been designed according to the principles of the declaration of Helsinki (1989). The protocol of the study was approved by the Research Department of the Education Institute of the Hellenic Ministry of Education, which is responsible

to attribute ethical approval to any study that takes place in school settings (approval number 29712/G7/2006).

Statistical analysis

All the continuous variables are presented as mean $\pm$ standard deviation (s.d.) and the categorical variables presented as absolute and relative frequencies. Associations between categorical variables were tested using the chi-square test, while comparisons between proportions was evaluated using the Z-test. Comparisons between mean values were evaluated using the *t*-test, after checking for the normality of the distributions. To assess the relationship between asthma symptoms and adherence to the Mediterranean diet, we applied multiple logistic regression analysis, after adjusting for various factors that were considered as potential confounders or effect mediators. Results are presented as odds ratios and the corresponding 95% confidence intervals (CIs). Deviance residuals were calculated to evaluate the model's goodness-of-fit. All reported probability values (p-values) were based on two-sided tests and compared to a significant level of 5%. SPSS 14 software was used for all the calculations (SPSS Inc., Chicago, IL, USA).

Results

Overall lifetime prevalence of asthma symptoms was 23.7% (27.6% among boys, 20.4% among girls, $p = 0.03$). Level of adherence to the Mediterranean diet (as measured using the KIDMED score, range 0–12) was 4.8 ± 1.9 in boys and 4.8 ± 2 in girls ($p = 0.87$). These figures suggest a very moderate adherence to the Mediterranean type of diet of the children participated in the study. Table 1 presents the prevalence of demographic, obesity status, and lifestyle characteristics by the level of adherence to the Mediterranean diet.

Table 1 Distribution of lifestyle and anthropometric characteristics by level of adherence to the Mediterranean type of diet among 10- to 12-yr-old children

	Adherence to the Mediterranean diet using the KIDMED score			p
	Bad (0–3)	Moderate (4–7)	Good (8–12)	
N	213	413	74	
KIDMED score (0–12)*	2.6 ± 0.6	5.3 ± 1.1	8.6 ± 1.2	
Boys (%)	46	45	53	0.48
Physical activity (%)	50	51	48	0.99
Hours of physical activity during the past week*	15.8 ± 8	15.9 ± 8	15.7 ± 9	0.84
Body mass index (kg/m ²)*	19.5 ± 4	19.7 ± 3	18.9 ± 2	0.74
Overweight/obese (%)	27	24	23	0.67

Results are presented as mean $\pm$ s.d. and relative frequencies. Mean values were compared using the anova, and associations between categorical variables were evaluated using the chi-square test.

Table 2 Distribution of asthma symptoms by level of adherence to the Mediterranean diet among 10- to 12-yr-old children

	Adherence to the Mediterranean diet using the KIDMED score			p
	Bad (0–3)	Moderate (4–7)	Good (8–12)	
N	213	413	74	
Ever had wheeze (%)	29	19	8	0.001
Exercise wheeze (%)	11	7	0	0.004
Night cough (%)	17	11	6	0.07
Ever had diagnosed asthma (%)	16	9	3	0.002
Any asthma symptoms (%)	34	22	5	<0.001

Results are presented as relative frequencies. Associations between categorical variables were evaluated using the chi-square test.

There were no significant associations between the level of adherence to Mediterranean diet and physical activity, BMI and obesity status of children.

In Table 2, the prevalence of asthma symptoms is presented according to the level of adherence to the Mediterranean diet. In particular, greater adherence to the Mediterranean diet (i.e., KIDMED score 8–12) was inversely associated with ever had wheeze ($p = 0.001$), exercise wheeze ($p = 0.004$), ever had diagnosed asthma ($p = 0.002$), and with any asthma symptoms ($p < 0.001$). In addition, there was a trend toward an inverse association between adherence

to the Mediterranean diet and night cough ($p = 0.07$). Unadjusted analysis showed that children who were very close to the Mediterranean diet had 89% lower likelihood of having asthma symptoms compared with those who were away from this dietary pattern (95% CI 69–97%), while children who were close to the Mediterranean diet had 48% lower likelihood of having diagnosed asthma compared to those who were away (95% CI 24–64%). However, food-specific analysis based on the information retrieved through the FFQ showed no significant associations between asthma symptoms and consumption of specific foods, like fruits ($p = 0.25$), vegetables ($p = 0.97$), legumes ($p = 0.76$), cereals ($p = 0.71$), dairy ($p = 0.61$), or margarine/butter ($p = 0.42$) consumption, while increased fish and meat intake was associated with less asthma symptoms ($p = 0.04$ and $p = 0.015$, respectively). Similar, insignificant results were revealed when the components of the KIDMED index that describe certain dietary behaviors were taken into account (Table 3). Despite these observations, as mentioned earlier the KIDMED score was significantly higher among children without asthma symptoms when compared with those with asthma; the latter finding underlines the influence of global diet and not individual foods *per se*.

However, residual confounding may exist. Thus, we applied multiple logistic regression analysis (Table 4) that evaluated the KIDMED score with the prevalence of asthma symptoms, after taking into account several participants' characteristics. The multi-adjusted analysis showed that one-unit increase in the KIDMED score was associated with 14% lower likelihood of having asthma symptoms, adjusted for age, sex, BMI, physical activity status and energy intake (Table 4).

Table 3 Percentage of positive answers (i.e., higher adherence to the Mediterranean diet) to questions from the KIDMED index in relation to the presence or not of asthma symptoms among 10- to 12-yr-old children

KIDMED index components	Asthma symptoms	No asthma	p
N	166	534	
Takes a fruit or fruit juice every day	23.7	25.9	0.49
Has a second fruit every day	22.1	24.6	0.23
Has fresh or cooked vegetables regularly once a day	24.7	31.7	0.11
Has fresh or cooked vegetables more than once a day	23.8	26.0	0.86
Consumes fish regularly (at least 2–3/week)	57.0	59.0	0.66
Goes >1/week to a fast food restaurant	26.1	23.1	0.61
Likes pulses and eats them >1/week	60.4	56.7	0.76
Consumes pasta or rice almost every day (5 or more per week)	37.2	42.7	0.47
Has cereals or grains (bread, etc.) for breakfast	16.1	16.3	0.71
Consumes nuts regularly (at least 2–3/week)	40.0	34.5	0.33
Uses olive oil at home	92.9	97.9	0.37
Skips breakfast	8.0	9.2	0.95
Has a dairy product for breakfast (yoghurt, milk, etc.)	76.5	75.1	0.42
Has commercially baked goods or pastries for breakfast	2.5	0.6	0.44
Takes two yoghurts and/or some cheese (40 g) daily	5.9	8.5	0.18
Takes sweets and candy several times every day	13.1	11.1	0.33
KIDMED score (0–12)	4.1 ± 1.6	5.0 ± 1.9	<0.001

Results are presented as mean ± s.d. and relative frequencies. Mean values were compared using the *t*-test, and differences between proportions were evaluated using the *Z*-test.

Table 4 Results from multiple logistic regression analysis that evaluated the KIDMED score with the prevalence of asthma symptoms (*n* = 511)

	Odds ratio	95% Confidence interval
KIDMED score (per 1 unit)	0.86	0.75–0.98
Age (per 1 yr)	0.99	0.75–1.31
Sex (boys vs. girls)	1.58	1.03–2.42
Body mass index (per 1 kg/m ²)	1.02	0.97–1.08
Physical activity (yes vs. no)	1.14	0.75–1.74
Energy (per 1 category)	0.92	0.77–1.11

Discussion

Under the context of the PANACEA study, the hypothesis whether the adherence to the Mediterranean diet is associated with lower prevalence of asthma symptoms was evaluated. A strong, inverse relationship between level of adherence to the Mediterranean diet and prevalence of asthma was observed. Moreover, a greater adherence to the Mediterranean diet was inversely associated with ever had wheeze, exercise wheeze, ever had diagnosed asthma, and any asthma symptoms. One-unit increase in the KIDMED score was associated with 14% lower likelihood of having asthma symptoms, irrespective of potential confounders. Individual foods do not seem to influence the prevalence of asthma except fish and meat. However, it should be underlined here that most of the children had a moderate level of adherence to the pattern of the Mediterranean diet. Taking into consideration that asthma is prevalent among children in Greece, although less prevalent than in other northern European countries, the presented findings have important public health implications, because they suggest a strong, non-pharmacological means for preventing childhood asthma.

Findings from recent studies suggest that a high level of adherence to the Mediterranean diet in early life protects against the development of asthma and atopy in children (19). The presented results are consistent with previous studies that evaluated the association between the Mediterranean diet and asthma in children (2–4). Particularly, Chatzi and colleagues from Greece showed that a high level of adherence to the Mediterranean diet had a protective effect on allergic rhinitis, asthma-like symptoms, and atopy although it was not statistically significant for the last two outcomes (2). Garcia-Marcos and colleagues from Spain reported that the Mediterranean diet had a potential protective factor for current severe asthma in girls (3), while a recent one, also from Spain, showed a protective effect (primary prevention) of olive oil use during pregnancy on wheezing during the first year of the offspring's life (20). Another study in Mexican children showed that a greater adherence to a Mediterranean dietary pattern was associated with having less asthma, wheezing, allergic rhinitis, and current sneezing (4). There are two more relevant reports: in a study on pre-schoolers, Mediterranean diet was demonstrated as an independent protective factor for current wheezing, irrespective of obesity and physical activity (21), whereas in a recent cohort

study no association with Mediterranean dietary pattern during pregnancy and recurrent wheeze at 3 yr was observed (22).

The association of seafood with asthma symptoms is in agreement with a report from the Netherlands in children in phase II of the ISAAC study, which showed a protective effect of seafood consumption (23). Many other studies have also suggested the protective effect of fish consumption on asthma in children (12, 24). Fish is rich in *n*-3 PUFAs, which are thought to have anti-inflammatory effects through their effects on eicosanoids synthesis. It was also found that the consumption of meat is significantly associated with asthma prevalence. This was an unexpected finding for us. Increased meat intake not only is a characteristic of the Mediterranean diet, but also it has been associated with increased risk of several chronic diseases, such as cardiovascular diseases and type 2 diabetes mellitus. However, two studies indicated that cream and butter, which are sources of saturated fatty acids, were associated with reduced risk of asthma in young children (25, 26), and one recent study suggested that there is no evidence that meat intake is associated with asthma in adults (27). Therefore, our finding renders further investigation. However, no other study has found an association between meat consumption and asthma symptoms in children; a fact that makes the generalization of the aforementioned finding difficult. This study showed no strong association between fruit and vegetable intake and asthma symptoms. The latter is in agreement with other published epidemiological studies that have found no association between fruit intake and asthma (26).

Despite the lack of association between single foods and asthma prevalence, the results from this study suggest a protective effect of a high level of adherence to the Mediterranean dietary pattern on asthma symptoms. At this point, it should be underlined that although there are several nutritional studies assessing single nutrients, instead of assessing dietary patterns, the single food approach may fail to account for the interactions and inter-correlation among nutrients. It is a fact that people do not eat isolated nutrients, but meals consisting of a variety of foods with complex combinations of nutrients (5). Moreover, food-specific analyses in relation to the characteristics of people or incidence of a disease share many methodological limitations (i.e., high collinearity of the food variables, unknown synergistic effects, etc.). Thus, several investigators in the nutritional epidemiology field have suggested using a dietary pattern approach on disease prevention.

The Mediterranean diet is, perhaps, one of the healthiest dietary models currently existing, having been corroborated by numerous epidemiological and experimental nutrition studies that show Mediterranean countries benefiting from lower rates of chronic disease morbidity and higher life expectancy (28). The high content of vegetables, fresh fruits, cereals, and olive oil guarantee a high intake of β -carotene (in fruits and vegetables), vitamins C (or ascorbate mainly derived from fruits, vegetables and potatoes) and E (or tocopherols, mostly from olive oil), and various important protective substances like selenium, flavonoids, and polyphenols with marked antioxidant activity (8). These key elements have been suggested to be responsible for the beneficial effect of diet on human health. Especially, fruits and vegetables may provide fiber and

antioxidants, which may reduce oxidative stress-related inflammatory disease. Vitamin C, β -carotene, magnesium, and selenium are associated with reduction in asthma prevalence and may prevent or limit an inflammatory response in the airways by reducing reactive oxygen species and inhibiting lipid peroxidation (29). Flavonoids may also be potential anti-allergic substances, and a recent study suggested that antioxidant defences such as glutathione peroxidase and superoxide dismutase were lowered in asthmatic children (30). In this work, greater adherence to the Mediterranean diet, as assessed by a special diet score, was associated with a considerable reduction in the likelihood of having asthma symptoms. The above-mentioned mechanisms may play a role in the observed relationship; however, future intervention trials or prospective studies may clarify these speculations.

Limitations

The PANACEA study, as a cross-sectional study, shares the limitations of this type of observational studies, like recall

bias and not been able to document causal relationships. The retrieval of information about the diet was stated by children's parents who could be subject to recall bias, and a reason for the very strong results observed.

Conclusion

The presented data reveal the protective role of Mediterranean diet on asthma symptoms in school-aged children. We also found unexpectedly an inverse association between asthma symptoms and meat intake that renders further investigation. The previous findings may state a hypothesis for the prevention of asthma in childhood, by adopting a dietary pattern rich in fruits, vegetables, non-refined cereals, fish, and other seafood. Public health policy makers should encourage the development of similar studies in order the observed associations to be considered as causal.

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