

Dietary fats and asthma in teenagers: analyses of the first Nutrition and Health Survey in Taiwan (NAHSIT)

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Summary

Background The occurrence of asthma may be associated with dietary factors.

Objective To examine the association between nutrient intake and physician-diagnosed asthma and allergic rhinitis.

Methods A stratified, multiple-staged sampling design was used to select study areas, in which household interviews were carried out to gather information on health status and 24-h food recall. Data from 1166 adolescents, 13–17 years of age, were analysed.

Results In univariate analysis, total calorie and energy-adjusted fat intake were associated with the prevalence of asthma, whereas vitamin A and vitamin C intake showed negative association with asthma. Multivariate logistic regression was used to adjust for sex and levels of urbanization; intake of saturated fats was associated with increased risk (OR = 2.02 for an increase of one SD, 95%CI 1.40–2.90), while monounsaturated fats were inversely related to asthma (OR = 0.65 for an increase of one SD, 95%CI 0.43–0.99). Vitamin C intake in the lowest quartile was associated with elevated risk for asthma with marginal significance (OR = 1.81, 95%CI 0.88–3.71, $P = 0.10$). None of the nutritional factors was associated with allergic rhinitis.

Conclusion Results from this cross-sectional survey suggest that saturated and monounsaturated fats may have different effects on airway inflammation.

Keywords: 24-hour recall, diet, asthma, fat, fatty acids, saturated, monounsaturated, vitamin C, epidemiology

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Introduction

The prevalence of childhood asthma in many parts of the world, including Taiwan, has increased dramatically in recent decades [1]. Investigations have found associations between higher risk of allergic symptoms and a more affluent lifestyle [2,3] and urbanization [4,5]. Dietary pattern is an important characteristic of lifestyle; both the types and amount of foods consumed may change with economic development and urbanization. Dietary components, especially fatty acids and antioxidants, may modulate the immunological and inflammatory responses [6,7].

Although there is support for an immunological role of antioxidants and fatty acids in animal studies, epidemiological evidence of a role for these nutrients in human allergic disease is limited. In a report of the Second National Health and Nutritional Examination Survey of the USA, high calorie intake and obesity were identified as risk factors for wheezing in children, but other measures of nutritional status, including dietary intake of protein, calcium and fish, were not found to be associated with wheezing or asthma [8].

We have reported part of the results from the Nutrition and Health Survey in Taiwan (NAHSIT), a government-sponsored survey which included 24-h dietary recall, food frequency questionnaire, and health status assessed by household interviews. The food frequency data showed that

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asthma was associated with intake frequencies of organ meat (especially liver), deep-fried foods and meat [9]. Here, we present results that were based on 24-h dietary recall of the same survey.

Food frequency and 24-h recall are different methods used in nutritional epidemiology. The food frequency method has advantages in feasibility and reflecting long-term diet intake. However, except when an extensive questionnaire is used, a food frequency questionnaire may account for only a portion of nutrient intake [10]. Differences in food preparation and portion size may further complicate inter-regional comparisons using food-frequency data. Thus, compared with food frequency, nutrient content offers a better platform for comparison among different geographical areas. For example, stirred frying is a major way of preparing Chinese foods, and the kind and amount of cooking oils used may greatly affect lipid intake. Since the previous report based on food frequency has suggested that dietary fat may be an important factor in asthma, better estimation of fat intake became critical. Using the 24-h recall data we were able to examine more closely the relationship between dietary fats and asthma. We identified that both the type and amount of fat consumed had a significant effect on asthma.

Materials and methods

Study design

The study design has been reported elsewhere [9,11]. Briefly, a stratified, multiple-staged, probability sampling design was used to select study areas. All the townships and city districts in Taiwan were stratified into seven strata according to dietary habit, degree of urbanization and geographical regions. Three townships or districts in each stratum were selected by probability proportional to size. In each sampled area a series of random points were used to select an area including 75 households within 200 square meters. All residents aged 4 years and above were eligible. Door-to-door visits were carried out to interview a designated number of people in each age-sex group. The response rate for the household interview was 86%. Offshore islands and mountain areas were excluded in this analysis because of their unusual diet patterns. Study areas in the remaining five strata were grouped by level of urbanization into high (two cities with population > 1.5 million), intermediate (population density > 3,000/km²) and low (others).

Twenty-four-hour dietary recall

The recall was carried out for those aged from 13 to 64 years. The recall process started with the most recent meal

or snack and included an individual recall of kinds and amounts of foods consumed within 24 h prior to the interview, and a cooking method recall by the household cook. Q-cards for oils and spices added to the dishes, drinks and snacks, and food piece models of 12 Chinese food items and abstract models of sizes and shapes were used to facilitate estimation of portion size. The daily nutrient intakes were calculated by multiplying the consumption of each food item by its nutrient contents and adding them together.

Asthma and allergic rhinitis

A health status questionnaire was included in the first NAHSIT. A questionnaire regarding 19 major diseases in youth was targeted for the age group 4–17 years, and estimated the cumulative prevalence of these diseases. This report analysed the age group 13–17 years as they had data from the 24-h recall and health questionnaire. Eighty-six per cent of those who reported asthmatic symptoms had been diagnosed as asthmatic by physicians. Subjects who reported symptoms but had not been diagnosed were excluded from the analysis. For the analysis of asthma, those with allergic rhinitis but not asthma were excluded from the control group; likewise, those with asthma but not allergic rhinitis were excluded for the analysis of rhinitis.

Statistical analysis

The intake data were not normally distributed; for each nutrient the distribution curve had a positive skewness. Non-parametric analysis of variance was used to compare the nutritional intakes among sex (Wilcoxon test), age and regional groups (Kruskal–Wallis test). To identify risk factors for asthma, the 24-h recall data were grouped into quartiles; the prevalence of asthma in each quartile was computed and tested for trend by the Mantel-Haenszel chi-square test. Risk estimates for variables reaching statistical significance in the univariate analysis were computed by multivariate logistic regression that also adjusted for sex and urbanization. Stepwise selection procedure was used to select significant ($P < 0.05$) factors in the final model of logistic regression. All statistical analyses were made using the Statistical Analysis System package (SAS 6.11 edition, SAS Institute, Cary, North Carolina, USA).

Results

The analyses here included data from 582 males and 584 females aged 13–17, the mean age ($\pm$ SD) was 14.7 ($\pm$ 1.4). Asthma and allergic rhinitis were more prevalent in males than in females (Table 1). There were significant differences in the total intake of calories and nutrients

Table 1. Comparison of prevalence of rhinitis and asthma, calories and macronutrient intake, between males and females

	Sex		Total	P
	Male	Female		
Subjects	582	584	1166	
Physician-diagnosed asthma (%)	3.95	2.05	3.0	0.058*
Physician-diagnosed allergic rhinitis (%)	12.4	6.85	9.6	0.001*
Calorie (kcal)	2198 ± 931	1575 ± 774		0.0001†
Protein intake (g)	82 ± 39	60 ± 32		0.0001†
Energy-adjusted protein intake (%)	15.4 ± 5.3	15.6 ± 5.6		0.92†
Fat intake (g)	74 ± 60	53 ± 42		0.0001†
Energy-adjusted fat intake (%)	28.3 ± 12.9	28.6 ± 11.6		0.11†

*P-value of chi-square tests. †P-value of Wilcoxon test.

between sexes. Adjusting for total calories negated the sex differences in nutrient intake. For example, fat and protein intakes were higher in males but energy-adjusted intakes, as percentages of calorie intake, were not different between sexes (Table 1). Intakes of some micronutrients showed gender differences; females had higher energy-adjusted intake of calcium, phosphorus, vitamin B₂ and vitamin E (not shown).

The prevalence of asthma and allergic rhinitis was not significantly different among age groups in either sex. There was no significant difference in the intake of calories and energy-adjusted intake of nutrients among ages. There was significantly more asthma and allergic rhinitis in areas with a higher degree of urbanization (Table 2). No significant difference in nutrient intake existed among different levels of urbanization.

In univariate analysis, the energy-adjusted intake of each nutrient was grouped into quartiles (first quartile being the least) and the prevalences of physician-diagnosed asthma in

the four quartiles were tested for trend (Table 3). Several variables showed significant association with asthma. Total calorie intake showed significant association with asthma. Stratified by sex, the association was absent in males but still found in females. Among macronutrients, energy-adjusted intake of fat, but not protein or carbohydrate, was associated with asthma. Intake of fatty acids, but not cholesterol, had significant association with asthma. The ratio of monounsaturated to saturated fatty acids was inversely related to asthma with borderline significance. Among micronutrients, the intake of vitamin A and vitamin C showed negative association with asthma.

Variables significant in univariate analysis, as well as fatty acid variables, were examined in multiple logistic regression controlling for urbanization and sex. Stepwise logistic regression on asthma identified that energy-adjusted intake of saturated and monounsaturated fatty acids were associated with asthma in opposite directions (Table 4). In a separate model (with P-value cut-off set at

Table 2. Comparison of prevalence (%) of physician-diagnosed asthma and allergic rhinitis, and nutrient intake (mean ± SD), among areas with different levels of urbanization

	Level of urbanization			P*
	High	Intermediate	Low	
Subjects	202	235	729	
Asthma (%)	5.0	6.4	1.4	0.001*
Allergic rhinitis (%)	18.3	11.1	6.7	0.001*
Calorie (kcal)	1920 ± 881	1866 ± 882	1878 ± 912	0.65†
Protein intake (g)	75 ± 38	70 ± 38	69 ± 37	0.12†
Fat intake (g)	63 ± 47	63 ± 52	64 ± 55	0.64†

*P-value of chi-square. †P-value of analysis of variance (Kruskal–Wallis test).

Table 3. Prevalence of physician-diagnosed asthma according to quartiles of nutrient intake in teenagers ($n = 1055$)

Nutrient variable	Quartile				P^*
	1	2	3	4	
Total calorie	1.5	1.9	4.6	5.3	0.005
Male	3.9	3.9	5.4	4.7	0.64
Female	1.5	0.7	1.5	5.2	0.037
Protein	3.4	2.3	4.6	3.0	0.82
Animal protein	2.3	5.1	2.3	3.5	0.86
Carbohydrate	3.8	4.6	2.3	2.7	0.25
Fat	2.3	3.0	2.3	5.7	0.056
Cholesterol	2.3	3.0	5.3	2.7	0.49
Fatty acids, total	2.3	2.7	2.7	5.7	0.039
Saturated	3.0	2.3	3.0	4.9	0.19
Monounsaturated	3.0	3.4	3.0	3.8	0.71
Polyunsaturated	3.8	2.7	4.2	2.7	0.70
P : S ratio†	4.9	2.3	3.0	3.0	0.31
M : S ratio‡	4.6	3.8	2.3	2.7	0.14
Calcium	4.9	3.0	2.3	3.0	0.19
Phosphorus	4.6	2.7	3.0	3.0	0.39
Iron	4.6	4.2	1.1	3.4	0.19
Sodium	3.4	4.2	3.8	1.9	0.31
Vitamin A	4.6	4.2	3.0	1.5	0.037
Vitamin B1	4.2	2.3	3.8	3.0	0.70
Vitamin B2	3.8	3.4	3.4	2.7	0.48
Vitamin C	5.7	3.4	3.0	1.1	0.004
Vitamin E	3.4	3.0	3.4	3.4	0.95

* P -value of Mantel-Haenszel chi-square. †Ratio of polyunsaturated/saturated fatty acids. ‡Ratio of monounsaturated/saturated fatty acids.

Table 4. Logistic regression of nutrient factors associated with the risk of asthma in teenagers, with adjustment for sex and urbanization*

Risk factors	Odds ratio (95% CI)	P
High vs. low urbanization	5.05 (2.21–11.6)	0.0001
Intermediate vs. low urbanization	3.95 (1.57–9.93)	0.0035
Male vs. female	2.58 (1.22–5.47)	0.013
Saturated fatty acids†	2.02 (1.40–2.90)	0.0002
Monounsaturated fatty acids†	0.65 (0.43–0.99)	0.047

*Initial variables for logistic regression included: two dummy variables for urbanization, age, sex, total calories, total fatty acids, saturated fats, monounsaturated fats, polyunsaturated fats, vitamin A and vitamin C intakes. All nutrients were energy-adjusted. Vitamins A and C were entered as categorized variable (lowest quartile vs. other three quartiles). Stepwise procedure was used to select variables into the final model at significant level of 0.05. †Odds ratio estimation for an increase of one standard deviation.

0.10), low vitamin C intake was also associated with higher risk (OR = 1.81, 95%CI 0.88–3.71, for the lowest quartile vs. others). Age, calorie, total fat, polyunsaturated fatty acids and vitamin A intake were excluded from the final model ($P > 0.1$). Males in this study had a higher proportion of monounsaturated fats in total fat intake (36.6% in males vs. 35.4% in females, t -test $P = 0.003$). To exclude confounding, sex-specific logistic regression was performed. In males, the intake of polyunsaturated fats (OR = 1.45 for an increase of one standard deviation, 95%CI 0.96–2.17, $P = 0.075$) and low vitamin C (OR = 2.62, 95%CI 1.10–6.27, $P = 0.03$) was associated with asthma. In females the results were similar to the original model, with saturated fats associated with higher risk (OR = 3.38, 95%CI 1.93–5.93, $P = 0.0001$) and monounsaturated fats associated with lower risk (OR = 0.46, 95% CI 0.21–1.02, $P = 0.056$).

The same analyses were applied to examine the relationship between nutrient intake and physician-diagnosed allergic rhinitis. In univariate analysis, none of the factors associated with asthma showed significant association with allergic rhinitis. Higher intake of monounsaturated fats was associated with reduced prevalence of rhinitis, with marginal statistical significance ($P = 0.091$). High calcium intake was associated with rhinitis ($P = 0.062$). In multivariate analysis with adjustment for urbanization and sex, none of the nutrient factors was associated with allergic rhinitis.

Discussion

In the study population aged 13–17, the data from 24-h recall suggested that asthma was associated with saturated fats and polyunsaturated fats, and inversely associated with monounsaturated fats and vitamin C. On the other hand, none of these nutrients was an independent predictor of allergic rhinitis. The subjects in this report ranged from 13 to 17 years of age. Age did not seem a confounding factor, as there was similar prevalence of asthma as well as nutrient intake among age groups. Nutrient intakes were different between sexes, but using energy-adjusted variables negated the difference for most nutrients. Sex-specific logistic regression also confirmed that the association between fats and asthma was not confounded by sex.

To minimize misclassification of cases, we have excluded those who were symptomatic but lacked physician diagnosis. However, the results were similar when the analysis was done for those with self-reported asthmatic symptoms. The risk estimate associated with urbanization, as assessed by logistic regression, was not significantly affected by nutrient factors, implying that nutritional factors did not explain the higher asthma prevalence in cities.

We have previously reported, based on food frequency questionnaire completed by the same study population, that intake frequencies of some foods were related to asthma, including animal internal organs (particularly liver), deep-fried foods and meat [9]. To better assess the intake of fats, 24-h data were analysed. The primary source of dietary fat in Taiwan included, in order of contribution, pork and pork products, vegetable oil, soybean and soya products, animal fats, eggs and egg products, pastries and cookies, and milk and dairy products. These foods contributed to over 75% of dietary lipids [12]. Thus, the results from food-frequency and 24-h recall seemed to agree that fat intake was an important risk factor for asthma. In addition, the 24-h recall data identified monounsaturated fats as inversely related to asthma.

One major drawback of the 24-h recall method is the existence of large within-person errors (from day-to-day variation in foods) in addition to between-person errors. Sampling on a single day will artificially increase the standard deviation because of extreme values that are away from the true long-term average intake for any subjects. However, the variation tends to be random and the general effect is to reduce the strength of associations [13]. Therefore, the errors should not have introduced false association. On the other hand, as the variation in micronutrients is in general much greater than macronutrients, the role of micronutrients can be underestimated by this type of study.

A particular nutrient may be linked to asthma by several means: it may correlate with other risk factors for atopy or asthma (e.g. socioeconomic status), it may affect systemic immunological function (e.g. IgE production), or it may perturb the bronchoalveolar microenvironment (e.g. increasing local production of leukotrienes or altering the composition of pulmonary surfactant). The lack of association between fats and allergic rhinitis seemed to favour the third explanation but clearly more data are required.

Dietary fats have complex effects on immune and inflammatory responses. Polyunsaturated fatty acids (PUFAs) have been shown to modify cell-mediated immunity as well as IgE production and allergic responses [14–16]. Besides their general ability to suppress lymphocyte functions, ω -6 and ω -3 PUFAs have different effects on inflammation. Omega-6 PUFAs, especially linoleic acid found in plant oils, can be metabolized to arachidonic acid and further into prostaglandins and leukotrienes. Omega-3 PUFAs, such as eicosapentaenoic acid and docosahexaenoic acid in fish oil, reduce the production of these inflammatory mediators [17,18]. In this study population, vegetable and soybean oils (both rich in ω -6 PUFA) contributed to over 19% of dietary fat, while sea fish contributed only 1.8% [12]. Thus, the association between

PUFA and asthma is most likely ascribable to ω -6 PUFAs. By analysis of food frequency, sea fish intake was not a significant diet factor in this study population [9].

Monounsaturated fatty acids (MUFAs) have also been shown to modulate immunological responses. In a study to examine the immunomodulatory effect of various dietary fatty acids, the *ex vivo* proliferation of rat spleen lymphocytes and spleen natural killer activity decreased as the level of oleic acid increased [19]. In rats fed with diet rich in oleic acid for 4 or 8 weeks, there was a small but significant reduction in lipopolysaccharide-induced tumour necrosis factor- α production by peritoneal macrophages [20]. A controlled trial in healthy subjects suggested some anti-inflammatory effect of MUFA. After consuming a MUFA diet consisting of olive oil for 2 months, peripheral blood mononuclear cells from these subjects had significant decreases in the expression of adhesion molecules [21]. Most significantly, a prospective study (the Nurses' Health Study) of diet and adult-onset asthma found that energy-adjusted intake of monounsaturated fat was inversely associated with asthma [22]. These studies provided theoretical basis for the observation in this study that consumption of MUFA was inversely associated with asthma.

Much less attention has been paid to the role of saturated fats in inflammation. In the same study which suggested the inhibitory effect of oleic acid, the spleen natural killer cell activity increased as palmitic acid content of the diet increased [19]. The effect of dietary saturated fatty acid on lymphocyte proliferation depended on the chain length as well as position of the fatty acids. Spleen lymphocyte proliferation was enhanced by palmitic acid-rich diets, particularly if palmitic acid was in the sn-2 position of dietary triacylglycerol [23]. It was suggested that dietary saturated fat might affect serum cholesterol level and cell membrane content of arachidonic acid, both of which may affect lymphocyte functions. However, to what extent and how saturated fatty acids affect other aspects of airway inflammation remains unknown. Indeed, dietary lipid may have a stimulatory or inhibitory effect on macrophages, depending upon which inflammatory mediator was chosen for comparison [24]. In addition to investigating the effects of lipids on isolated cells, testing dietary effects in animal models of asthma may provide data of more physiological and pathological relevance.

We have also found that vitamin C and possibly vitamin A intake was inversely associated with asthma. Vitamin C is an important antioxidant in the extracellular lining fluid of human airways and lungs. It is also possible that vitamin C was a marker for vegetables and fruits that are rich in other bioactive compounds. The role of dietary vitamin C in asthma development is not clear. Earlier studies showed that ascorbate levels in blood and leucocytes were lower in asthmatics, and supplementing vitamin C could reduce

methacholine-induced bronchoconstriction [7,25]. However, no protective effect against asthma was found for vitamin C supplementation in a prospective study [22]. The antioxidant status of the respiratory system is dependent on dietary intake, transport to bronchoalveolar fluid, and oxidant stress caused by environmental exposure and inflammation. One study demonstrated that calorie intake may modulate the antioxidant levels in the bronchoalveolar compartment [26]. Dietary records alone, or even plasma concentrations of antioxidants, may not be sufficient to reflect antioxidant levels in the lungs [27].

This is a cross-sectional survey and data interpretation should be made with caution. However, the highly significant association between fat intake and asthma observed in this study warrants more careful examination of the role of nutrients, particularly the amount and composition of dietary fats, in the development of asthma.

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