

The Relationship between Fish Intake and the Prevalence of Asthma: The Tokorozawa Childhood Asthma and Pollinosis Study¹

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Objective. The Japanese have a higher intake of fish and a lower incidence of asthma than occupants of western countries. The present epidemiological study investigated the relationship between dietary fish intake and the prevalence of asthma among a childhood population.

Methods. Subjects represented all public elementary and junior high schools in Tokorozawa City in Japan (age range: 6–15 years old). The study population included 1,673 currently asthmatic students and 22,109 controls. Participants' parents completed the Japanese version of American Thoracic Society and Division of Lung Diseases, National Heart, Lung, and Blood Institute questionnaire for children, adopted by the Japan Environment Agency. We added supplementary questions (e.g., parental history of asthma and questions about frequency of foods eaten, including frequency of fish intake). Odds ratios for cases of current asthma according to frequency of fish intake were calculated, and a logistic regression analysis was used to adjust for possible confounding variables.

Results. After adjustments for age, gender, parental history of asthma, and vegetables and fruits intake, a significantly higher prevalence of asthma was noted among subjects who ate fish one to two times a week than among those who ate fish one to two times a month (adjusted odds ratio: 1.117; 95% confidence interval: 1.005–1.241; $P = 0.041$). The risk increased gradually with increasing frequency of fish intake, and the positive trend was statistically significant.

Conclusions. The results indicated that frequency of

fish intake was positively related to the prevalence of asthma. This result might have important implications for health. © 2002 American Health Foundation and Elsevier Science (USA)

Key Words: asthma; fish intake; ATS-DLD questionnaire; children.

INTRODUCTION

There is growing evidence that asthma is becoming more common in Japan, although its prevalence remains relatively low in Japan compared to that in western countries [1]. Because treatment of asthma is somewhat difficult, methods of prevention have been sought.

Many risk factors for asthma have been proposed, including age, gender (male), maternal smoking, and family history of asthma [2]. The role of diet in asthma has also been investigated. The Japanese have a higher intake of fish and a lower incidence of asthma than western countries. Several studies have led to great interest in the possible beneficial effects of fish intake on asthma [3–6]. However, other studies failed to show any significant association [7–11], and a few studies suggested that fish intake might, instead, lead to an increased risk for asthma [12,13]. All studies except two [5,6] were intervention studies: studies to see the effect of dietary supplementation with fish oil. Moreover, these studies were based on relatively small sample populations and did not adjust for possible confounding factors.

The present report examines the relationship between dietary fish intake and asthma by a population-based epidemiological study of children (age range: 6–15 years old) in Japan.

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METHODS

Study Population

We analyzed data from the Tokorozawa Childhood Asthma and Pollinosis Study, which was conducted by the Tokorozawa City Municipal Board of Education and the Tokorozawa Medical Association in Saitama, Japan. The Tokorozawa Asthma and Pollinosis Study investigated the prevalence of childhood asthma and other allergic diseases in Tokorozawa City and the factors related to these diseases.

Tokorozawa City is a suburban residential city adjacent to Tokyo. Data were collected between February 2 and February 17, 1998. The subjects were in grades 1 through 6, including students from all 33 public elementary schools, and in grades 1 through 3, including students at 15 junior high schools in Tokorozawa City. In all, a total of 25,767 subjects were used as the study population. Active parental consent for participation was obtained in the form of written permission. All activities were conducted in accordance with the human subject review policy at the National Defense Medical College.

Measures

The questionnaire used in this study was the Japanese version of the American Thoracic Society and Division of Lung Diseases, National Heart, Lung, and Blood Institute (ATS-DLD) questionnaire for children [14]. The questionnaire has been adopted by the Japan Environment Agency and includes a few additional items related to job history, dust exposure, ocular symptoms, family member smoking status, and exposure to other indoor air pollution [15]. We added supplementary questions such as questions relating to parental history of asthma and frequency of foods eaten, including frequency of fish intake. We used a modified food-frequency questionnaire, which was derived from the questionnaire by the study group on dioxins in breast milk, the Japanese Ministry of Health and Welfare [16].

The questionnaire along with a consent form was distributed throughout the Tokorozawa City Municipal Board of Education, the parents were asked to complete it, and completed questionnaires and consent forms were collected 1 to 2 weeks later.

The definition of asthma used in this study is the one proposed by the Japan Environment Agency [15]. The reliability and validity of the ATS-DLD questionnaire in identifying children with asthma have been well established [17,18].

The criteria for determining whether a child ever had asthma were that a parental answer "yes" to all of the following questions: (a) Has your child ever had an attack of wheezing that has caused him/her to be short

of breath?, (b) Has your child had such an attack twice or more?, (c) Has a physician ever informed you that your child has asthma?, and (d) If so, did your child, at that time, suffer from shortness of breath with wheezing? Among the "ever asthmatic" subjects, the children whose parents responded "yes" to both of the following two questions were designated "currently asthmatic" subjects: (a) during the past 2 years, has a physician informed you that your child has asthma and, at that time, did your child have any episodes of the following symptoms: (a) cough or sputum; (b) wheezy or whistling sound while breathing; (c) shortness of breath with wheezing; and (d) such severe shortness of breath that he/she could not lie down; and (b) during the past 2 years, has your child received treatment for asthma? The subjects who were not ever asthmatic were used as controls.

In this report, we focused on a comparison between currently asthmatic subjects and controls in order to clarify the risk of fish intake for current cases of asthma. One thousand two hundred ninety subjects were excluded because of insufficient answers on the questionnaire. By the definition of asthma, 2,368 subjects were categorized as ever asthmatic and 22,109 as controls. Six hundred ninety-five subjects were excluded because they had previously experienced an asthma attack but were not currently asthmatic. In total, 11,993 boys and 11,789 girls were eligible for the following analysis.

Positive maternal smoking was defined as having a mother who smoked one or more cigarettes per day at the time of the survey. Subjects whose mother or father had ever been treated for asthma were defined as having a positive parental history of asthma.

The food-frequency questionnaire is widely used as a method in nutritional epidemiology in assessing the approximate food intake of individuals. In the food frequency questions, we asked, "How often does your child eat fish?" The parents chose from four frequency categories for each food item: almost none, 1–2/month, 1–2/week, and ≥ 3 –4/week. We did not ask the serving size of the foods in the questionnaire because most of the variation in intake of a food is explained by frequency of use rather than differences in serving sizes [19]. Spearman rank correlation coefficients observed in the validation study of the food-frequency questionnaire using four 7-day dietary records as the gold standard for 102 men and 113 women were 0.46 and 0.42 for fish, 0.33 and 0.35 for vegetables, and 0.61 and 0.50 for fruits, respectively (personal communication, Sasaki S, 2001). No information was gathered regarding the type of fish consumed, the way it is cooked, and whether subjects currently or had in the past consumed omega-3 fatty acid supplements. However, omega-3 fatty acid

TABLE 1Comparison between Currently Asthmatic Subjects and Controls, According to Selected Risk Factors^a

Variables	Asthma (N = 1,673)		Controls (N = 22,109)		Value	P value
	n (%)		n (%)			
Age (years), mean ± SD	10.41 ± 2.41		10.78 ± 2.54		6.15	<0.0001
Gender					92.2	0.001
Male	1,033	(61.8)	10,960	(49.6)		
Female	640	(38.2)	11,149	(50.4)		
Maternal smoker					0.527	0.47
(+)	255	(15.2)	3,226	(14.6)		
(−)	1,418	(84.8)	18,883	(85.4)		
Parental history of asthma					466.0	0.001
(+)	419	(25.0)	1,928	(8.7)		
(−)	1,254	(75.0)	20,181	(91.3)		

Note. SD, Standard deviation.

^a The χ^2 test (for nominal variables) or *t* test (for numerical variables) was employed.

supplementation is not common in Japan and, furthermore, it is very rare in the case of elementary or junior high school students.

Age, gender, and parental history of asthma were considered potential confounding factors. Body mass index and socioeconomic status were not obtained in this study although they may confound the relationship.

Statistical Analyses

The characteristics of cases of current asthma were examined by the χ^2 test or Student's *t* test.

In order to adjust for confounding factors, multiple logistic regression analysis was employed. The trend of association was assessed by a logistic regression model that assigned scores to the levels of the independent variables. We chose the 1–2/month frequency of fish consumption as the referent group because the majority of the study subjects belonged to this group.

Reported *P* values were all two-tailed. A *P* value <0.05 was regarded as significant. All data were stored and analyzed using SAS software version 6.12 on an IBM computer [20,21].

TABLE 2Comparison between Currently Asthmatic Subjects (N = 1,673) and Controls (N = 22,109), According to Frequency of Fish Intake^a

Frequency	Asthma		Controls	
	n (%)		n (%)	
Almost none	58	(3.5)	868	(3.9)
1–2/month	888	(53.1)	12,338	(55.8)
1–2/week	697	(41.6)	8,581	(38.8)
$\geq$ 3–4/week	30	(1.8)	322	(1.5)

RESULTS

Table 1 shows the comparison between subjects with asthma and controls according to age, gender, maternal smoking, and parental history of asthma. It was found that subjects with asthma were more likely to be younger and male and to have a parental history of asthma. No difference in maternal smoking status was observed between subjects with asthma and controls.

Table 2 shows the comparison between currently asthmatic subjects (*n* = 1,673) and controls (*n* = 22,109) according to frequency of fish intake.

Table 3 presents the adjusted odds ratios and 95% confidence intervals for cases of current asthma according to frequency of fish intake. After adjustment for age, gender, and parental history of asthma, a significantly higher prevalence of asthma was still noted among subjects who ate fish one to two times a week than among those who ate fish one to two times a

TABLE 3

Adjusted Odds Ratios (OR) and 95% Confidence Intervals (CI) for Cases of Current Asthma According to Frequency of Fish Intake

Frequency	Adjusted OR 1 ^a	95% CI	Adjusted OR 2 ^b	95% CI
Almost none	0.957	0.725–1.263	1.039	0.785–1.376
1–2/month	1.000	(Referent)	1.000	(Referent)
1–2/week	1.133	1.021–1.258	1.117	1.005–1.241
$\geq$ 3–4/week	1.334	0.907–1.963	1.319	0.896–1.943
<i>P</i> for trend ^c	0.0078		0.0349	

^a The logistic regression analysis was applied to adjust for age, gender, and parental history of asthma.

^b The logistic regression analysis was applied to adjust for age, gender, parental history of asthma, and vegetables and fruits intake.

^c Trend was based on a logistic regression model with scores of 0–3 assigned to the four levels.

month. We had the same result after adjusting for age, gender, parental history of asthma, and vegetables and fruits intake. The risk increased gradually with increasing frequency of fish intake, and the positive trend was statistically significant.

DISCUSSION

The effect of fish on asthma is a controversial issue. A study of the effects of fish oil on asthma has shown that fish oil can reduce the activity of lipid mediators and blunt a late allergic response (the inflammatory component of the asthmatic reaction) [3]. Another investigation indicated that supplementing the diet with fatty acids was associated after 9 months with a 23% increase in forced expiratory volume in 1 s [4]. Among Australian children, increased consumption of fish was associated with a reduced odds ratio for asthma [5,6]. However, several studies using fish oil supplements showed no clinical improvement in patients with asthma, despite some changes seen in *in vitro* results [7–11]. Moreover, one study showed that a diet of fish oil increased the bronchoconstrictor response to an antigen challenge in passively sensitized guinea pigs [12]. Another pilot study also reported the result that diets containing fish oil may worsen airflow obstruction and have a deteriorating effect on patients with aspirin-intolerant asthma [13]. Our study supports the results of the latter studies [12,13]; a positive association between fish intake and asthma was found. Most studies investigating the relationship between fish intake and asthma are intervention studies using dietary supplementation with fish oil or omega-3 fatty acids. It is well known that fish oil is the only concentrated source of eicosapentaenoic acid (20:5 omega-3 fatty acid) and docosahexapentaenoic acid (22:6 omega-3 fatty acid) [22]. Only two studies evaluated consumption of fish per se and supported the inverse association between dietary fish intake and asthma [5,6]. To our knowledge, the present study is the first noninterventional epidemiological study to show the positive relationship between dietary fish intake and the prevalence of asthma.

The mechanism of the positive relationship between fish intake and the prevalence of asthma is unknown. Lee et al. suggested that inhibition of the cyclooxygenase pathway and decreased production of bronchodilator prostaglandins, associated with diversion of arachidonic acid metabolites into the lipoxygenase cascade, which causes asthmatic attacks, might be causes of the increased bronchial response [12]. They concluded that a diet that includes fish oil or omega-3 fatty acids (eicosapentaenoic and docosahexapentaenoic acid) could increase the immunologically mediated pulmonary response through this inhibition of the cyclooxygenase pathway, which is a mechanism similar to that by which aspirin is thought to provoke attacks of asthma in some

patients [12]. The other possibility is that salt might be related to the connection between fish intake and asthma. Japanese often eat fish cooked with salt or a salty seasoning, e.g., shoyu. Several research groups have investigated the relationship between salt intake and asthma [23–25]. Evidence from two intervention studies suggests the positive association between salt consumption and mortality from asthma only in men, not women [23,24]. Indeed, when we analyzed the relationship between frequency of fish intake and prevalence of asthma by gender separately, the significant trend was detected only in males (*P* for trend: 0.049 in males, 0.36 in females). These findings agree with the hypothesis that salt consumption with fish was associated with the prevalence of asthma. However, we had no data of accurate salt intake in this study to confirm this. We also suspect that subjects with asthma may be more likely to eat more “healthy” food such as fish rather than meat, which would also explain this association.

The large number of subjects increases the power of the analysis in this study. Further, several aspects of homogeneity were advantageous for the purposes of our analysis. First, the subjects represented all public elementary and junior high schools in Tokorozawa City and can be considered representative of most 6- to 15-year-old children in this area. Given that there are no private elementary or junior high schools in Tokorozawa City, the selection bias according to socioeconomic differences and the demand for higher quality of education are minimal. Second, all of the study subjects were Japanese; thus, racial differences in the prevalence of asthma were irrelevant. Important confounding factors were accounted for in this study, which was not the case in previous reports. Vegetables and fruits intake was considered confounder because it is known to be associated with chronic lung disease [26,27]. Adjustment for these confounding factors is expected to clarify the independent association between cases of asthma and fish intake. However, we also must admit that several potential confounders including body mass index, socioeconomic status, the type of fish, and the way it is cooked were not obtained in this study. Indeed, several studies showed that body mass index might be a risk factor for asthma [28] and that there was an association between socioeconomic status and asthma in Britain [29]. Furthermore, a research reported that socioeconomic status contributed to variations in fish consumption [30]. The authors will consider these confounders when we perform future research.

Our findings must be viewed in conjunction with several limitations of the study design. First, the present study was cross-sectional; therefore, causative effects cannot be inferred from its results. We need to conduct another prospective study in which the subjects are examined at specific intervals with respect to asthma.

Second, the validity of our results were not confirmed by the use of more objective measures of asthma (e.g., respiratory function test). However, the validity and reliability of the questions to identify childhood asthma have been previously established [17,18].

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