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ELSEVIER

Prevalence of Asthma and Wheeze in Relation to Passive Smoking in Japanese Children

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PURPOSE: Evidence remains inconclusive as to whether environmental tobacco smoke is a risk factor for allergic disorders in childhood. The present large-scale cross-sectional study examined the relationship between passive smoking at home and the prevalence of allergic disorders in Japanese schoolchildren.
METHODS: Study subjects were 23,044 children aged 6 to 15 years in Okinawa. Outcomes were based on diagnostic criteria from the International Study of Asthma and Allergies in Childhood. Adjustment was made for sex, age, region of residence, number of siblings, paternal and maternal history of asthma, atopic eczema, or allergic rhinitis, as well as paternal and maternal educational level.
RESULTS: The prevalence of wheeze, asthma, atopic eczema, and allergic rhinoconjunctivitis in the previous 12 months was 10.7%, 7.6%, 6.8%, and 7.7%, respectively. Current heavy passive smoking and 7.0 or more pack-years of smoking in the household were independently related to an increased prevalence of wheeze and asthma, especially in children 6 to 10 years of age and children with a positive parental allergic history. There was no dose-response relationship between pack-years of smoking in the household and atopic eczema or allergic rhinoconjunctivitis.
CONCLUSIONS: Our findings suggested that environmental tobacco smoke might be associated with an increased prevalence of wheeze and asthma in Japanese children.
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KEY WORDS: Asthma, Child, Cross-sectional Studies, Eczema, Japan, Rhinitis, Tobacco Smoke Pollution.

INTRODUCTION

The hygiene hypothesis has triggered etiological research to examine the effect of environmental factors on the development and behavior of the immune system in children (1). Regarding child health, environmental tobacco smoke (ETS) exposure is perhaps the most ubiquitous and hazardous among environmental factors. Recently, Feleszko et al. (2) suggested that passive smoking might shift the balance of T helper cells toward the allergic Th2 pathway. Exposure to ETS in childhood might modify immune responses and thereby contribute to the clarification of allergic disorders. Although many epidemiologic studies have investigated a possible association between exposure to ETS and childhood allergic diseases (3–19), epidemiologic evidence is not yet firmly established. A cross-sectional study in children aged 4 to 6 years in the United Kingdom (UK) showed that the prevalence of asthma increased with the number of smokers in the home (3). A positive association was observed between exposure to ETS and the prevalence of current wheeze in German female children (4). In a US cross-sectional study, current ETS exposure was associated with wheeze, but not physician-diagnosed asthma, among schoolchildren (5). Several studies showed no association between exposure to ETS and asthma (6–10), wheeze (8, 9), atopic eczema (10–12), hay fever (8, 10), or rhinitis (10, 11).

The majority of published studies on relationships between ETS exposure and allergic disorders were carried out in Western countries. To our knowledge, only 2 cross-sectional studies have addressed associations between ETS exposure and allergic disorders among Japanese children (11, 12). One study showed that smoking in the household was apparently not related to the prevalence of wheeze, atopic dermatitis, or allergic rhinoconjunctivitis (11), whereas another investigation found an inverse association of passive smoking with allergic rhinitis, but not asthma or atopic eczema (12).

In the present study, we analyzed data from the Ryukyus Child Health Study (RYUCHS) to evaluate the association between smoking in the household and childhood allergic disorders using the diagnostic criteria of the

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Selected Abbreviations and Acronyms

ETS = environmental tobacco smoke
RYUCHS = Ryukyus Child Health Study
ISAAC = International Study of Asthma and Allergy in Childhood
OR = odds ratio
CI = confidence interval

International Study of Asthma and Allergy in Childhood (ISAAC) (20).

METHODS

Study Population

Okinawa Prefecture is an island located in the southernmost area of Japan, with a subtropical climate and a total population of almost 1,360,000. Naha City, the largest city in Okinawa Prefecture and located in the south of the island, and Nago City, located in the center of the island, with a total population of almost 311,000 and 58,000, respectively, are 2 of the 41 municipalities in Okinawa Prefecture. During the period from September 2004 to January 2005, we conducted a cross-sectional school-based survey for investigating the associations between various selected factors and child health problems. All 35 public elementary schools and 17 junior high schools in Naha City and 17 public elementary schools and 8 junior high schools in Nago City participated in the RYUCHS. A set of 2 self-administered questionnaires was distributed by teachers to all 38,212 children at school. These were completed at home by parents of the elementary schoolchildren and the junior high school students themselves and/or their parents. Our research technicians checked the returned questionnaires according to the survey protocol. When missing answers and/or illogical data were detected, the teachers sent the questionnaires back to the parents. Finally, 28,885 sets of questionnaires were returned (participation rate = 75.6%). Our study was restricted to subjects who provided information on variables under study, leaving data on 23,044 children available for analysis (60.3% of all eligible children). Permission to perform this study was obtained from the ethics committee of the Faculty of Medicine, Fukuoka University.

Measurements

One of the questionnaires included questions regarding wheeze, asthma, atopic eczema, and allergic rhinoconjunctivitis in the previous 12 months based on the validated ISAAC phase-I questionnaire (20). We translated these questions into Japanese by using standard forward-backward translation. The definition of wheeze used in this study was determined by a positive response to the question, "Have you (Has your child) had wheezing or whistling in the chest in the last 12 months?". A positive response to both the aforementioned question and another question "Have you (Has your child) ever had asthma?" were considered to indicate asthma. A positive response to questioning about the presence of an itchy relapsing rash that had affected a child's skin creases in the past 12 months was considered to indicate atopic eczema. For the definition of allergic rhinoconjunctivitis, affirmative answers to the following two questions were required: "In the last 12 months, have you (Has your child) had a problem with sneezing or running or blocked nose when you (he/she) did not have a cold or flu?" and "In the last 12 months, has this nose problem been accompanied by itchy-watery eyes?". The questionnaire also included questions about sex, age, number of siblings, paternal and maternal history of asthma, atopic eczema, and allergic rhinitis, paternal and maternal educational level, and smoking in the household. A paternal or maternal history of asthma, atopic eczema, and allergic rhinitis was defined as positive if the respective parent had contracted any of these allergic disorders prior to the start of the survey.

The second questionnaire was a validated self-administered brief diet history questionnaire. Data regarding diet were not used in the current study.

Statistical Analysis

Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were estimated using multiple logistic regression analysis. The following potential confounders were identified *a priori* and were included in the multivariate model: sex, age, region of residence, number of siblings, paternal and maternal history of asthma, atopic eczema, or allergic rhinitis, and paternal and maternal educational level. Age was classified into 3 categories (6–8, 9–11, and 12–15 years), region of residence into 2 (Naha City and Nago City), number of siblings into 4 (0, 1, 2, and 3+), paternal and maternal educational level into 4 (junior high school, high school, junior college or vocational technical school, and university), smoking in the household into 4 (never, former, and current passive smoking exposure to <15 or 15+ cigarettes per day), pack-year of smoking in the household into 4 (none, 0.1–2.9, 3.0–6.9, and 7.0+ pack-years). To examine whether prevalence increased with pack-years of smoking in the household, trends of association were assessed using a logistic regression model assigning consecutive integers to the levels of the independent variable. Two-sided p values less than 0.05 were considered statistically significant. All statistical analyses were performed by using the SAS software package version 9.1 (SAS Institute, Inc., Cary, NC).

RESULTS

About 80% of the subjects lived in Naha City (Table 1). Approximately 60% had two or more siblings. The prevalence

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TABLE 1. Distribution of selected characteristics in 23,044 schoolchildren, RYUCHS, Japan

Variable	n (%)
Male sex	11,387 (49.4)
Age (y)	
6–8	6,843 (29.7)
9–11	8,249 (35.8)
12–15	7,952 (34.5)
Region of residence	
Naha city	18,923 (82.1)
Nago city	4,121 (17.9)
Siblings (n)	
0	2,160 (9.4)
1	7,688 (33.4)
2	8,688 (37.7)
3+	4,508 (19.6)
Paternal history of asthma, atopic eczema, or rhinitis	5,426 (23.6)
Maternal history of asthma atopic eczema, or rhinitis	6,499 (28.2)
Paternal educational level	
Junior high school	1,807 (7.8)
High school	10,226 (44.4)
Junior college or vocational technical school	3,365 (14.6)
University	7,646 (33.2)
Maternal educational level	
Junior high school	1,184 (5.1)
High school	10,269 (44.6)
Junior college or vocational technical school	9,546 (41.4)
University	2,045 (8.9)

RYUCHS = Ryukyus Child Health Study.

values for symptoms of wheeze, asthma, atopic eczema, and allergic rhinoconjunctivitis in the previous 12 months were 10.7%, 7.6%, 6.8%, and 7.7%, respectively. Of the 23,044 children, 10,113 (43.9%) were exposed to ETS at home at the time of the survey, whereas 10,770 subjects (46.7%) had not been exposed to ETS at home since birth until the time of the survey (Table 2). There was a stepwise increase in the prevalence of wheeze and asthma in relation to smoking status in the household; prevalence was highest among children exposed to ETS from at least 15 cigarettes a day.

Compared with never smoking in the household, current heavy smoking in the household (15+ cigarettes per day) was independently associated with an increased prevalence of wheeze (OR = 1.17, 95% CI, 1.03–1.32) and asthma (OR = 1.22, 95% CI, 1.06–1.41), whereas former smoking in the household was not materially related to the prevalence of wheeze or asthma after adjustment for sex, age, region of residence, number of siblings, paternal and maternal history of asthma, atopic eczema, or allergic rhinitis, and paternal and maternal educational level (Table 3). Statistically significant dose-response relationships of cumulative passive smoking at home to the prevalence of wheeze and asthma were observed (p for trend = 0.008 and 0.01, respectively); the adjusted ORs of wheeze and asthma for 7.0 or more pack-years of smoking in the household were 1.17 (95% CI, 1.03–1.31) and 1.19 (95% CI, 1.04–1.37), respectively. Former smoking in the household was independently associated with an increased prevalence of atopic eczema, but not allergic rhinoconjunctivitis. No relationships were found between current smoking in the household and the prevalence of atopic eczema or allergic rhinoconjunctivitis. There was a tendency for a positive association of 7.0 or more pack-years of smoking in the household with atopic eczema and allergic rhinoconjunctivitis, although the trends were not statistically significant.

The positive associations of smoking status in the household with the prevalence of wheeze and asthma were attenuated with advancing age (Table 4). Significant positive relationships between current heavy smoking in the household and wheeze and asthma were observed only among children aged 6 to 10 years, although no measurable differences were found in the prevalence of wheeze or asthma between children aged 6 to 10 and 11 to 15 years (p = 0.24 and 0.08 for homogeneity of OR for current smoking in the household of at least 15 cigarettes a day, respectively). However, the interaction between age groups in relation to pack-years of smoking in the household and asthma, but not

TABLE 2. Prevalence of allergic disorders according to passive smoking status in 23,044 schoolchildren, RYUCHS, Japan

		Wheeze		Asthma		Atopic eczema		Allergic rhinoconjunctivitis	
	N	n	%	n	%	n	%	n	%
Smoking in household									
Never	10,770	1082	10.1	763	7.1	729	6.8	805	7.5
Former	2,161	239	11.1	157	7.3	171	7.9	189	8.8
Current <15*	6,098	681	11.2	477	7.8	390	6.4	480	7.9
Current ≥15*	4,015	463	11.5	343	8.5	269	6.7	302	7.5
Pack-years of smoking in household									
None	10,770	1082	10.1	763	7.1	729	6.8	805	7.5
0.1–2.9	3,919	440	11.2	300	7.7	270	6.9	302	7.7
3.0–6.9	4,047	462	11.4	328	8.1	264	6.5	295	7.3
≥7.0	4,308	481	11.2	349	8.1	296	6.9	374	8.7

RYUCHS = Ryukyus Child Health Study.
*Number of cigarettes smoked in the household per day.

TABLE 3. Adjusted odds ratios and 95% confidence intervals for allergy disorders according to smoking in the household of 23,044 schoolchildren, RYUCHS, Japan

	Wheeze OR (95% CI)*	Asthma OR (95% CI)*	Atopic eczema OR (95% CI)*	Allergic rhinoconjunctivitis OR (95% CI)*
Smoking in household				
Never	1.00	1.00	1.00	1.00
Former	1.09 (0.93–1.26)	0.99 (0.82–1.18)	1.21 (1.01–1.44)	1.12 (0.94–1.32)
Current <15†	1.09 (0.98–1.21)	1.07 (0.95–1.21)	0.99 (0.86–1.13)	1.07 (0.95–1.21)
Current ≥15†	1.17 (1.03–1.32)	1.22 (1.06–1.41)	1.09 (0.93–1.26)	1.02 (0.88–1.18)
Pack-years of smoking in household				
None	1.00	1.00	1.00	1.00
0.1–2.9	1.06 (0.94–1.20)	1.02 (0.88–1.17)	1.03 (0.89–1.19)	1.07 (0.92–1.23)
3.0–6.9	1.11 (0.99–1.25)	1.11 (0.96–1.27)	1.01 (0.87–1.18)	0.98 (0.85–1.13)
≥7.0	1.17 (1.03–1.31)	1.19 (1.04–1.37)	1.13 (0.98–1.31)	1.14 (0.99–1.30)
p for trend	0.008	0.01	0.15	0.15

OR = odds ratio; CI = confidence interval; RYUCHS = Ryukyus Child Health Study.
*Adjusted for sex, age, region of residence, number of siblings, paternal and maternal history of asthma, atopic eczema, or allergic rhinitis, and paternal and maternal educational level.
†Number of cigarettes smoked in the household each day.

wheeze, was statistically significant (p = 0.03 and 0.14 for homogeneity of OR for 7.0 or more pack-years of smoking in the household, respectively).

When study subjects were divided according to a positive or negative parental allergic history in at least one parent, positive associations of smoking status and pack-years of smoking in the household with prevalence of wheeze and asthma were more pronounced in children with a positive parental allergic history than in those with a negative parental allergic history (Table 5). No measurable differences were found in the prevalence of wheeze or asthma between children with a positive and negative parental allergic history (p = 0.31 and 0.39 for wheeze and 0.81 and 0.76 for asthma for homogeneity of OR for current smoking in the household of at least 15 cigarettes a day and 7.0 or more pack-years of smoking in the household, respectively).

DISCUSSION

The present findings are in agreement with previous studies showing a positive association between passive smoking and asthma and/or wheeze among children (3–5, 10, 13–16, 18) but at variance with other studies showing an inverse (19) or no association (6–12, 17). A significant positive relationship between passive smoking and wheeze in the last 12 months, but not wheeze ever, was observed among Maltese schoolchildren aged 5 to 8 years in a cross-sectional study (10). In a UK longitudinal study, exposure of the infant to ETS

TABLE 4. Adjusted odds ratios and 95% confidence intervals for wheeze and asthma according to smoking in the household of 23,044 schoolchildren 6 to 10 years of age or 11 to 15 years of age, RYUCHS, Japan

	Children aged 6–10 yr (n = 12,438)		Children aged 11–15 yr (n = 10,606)	
	Wheeze OR (95%CI)*	Asthma OR (95%CI)*	Wheeze OR (95%CI)*	Asthma OR (95%CI)*
Smoking in household				
Never	1.00	1.00	1.00	1.00
Former	0.93 (0.74–1.15)	0.87 (0.66–1.12)	1.27 (1.03–1.57)	1.14 (0.86–1.43)
Current <15†	1.11 (0.97–1.27)	1.12 (0.95–1.31)	1.05 (0.89–1.25)	1.00 (0.82–1.22)
Current ≥15†	1.18 (1.00–1.38)	1.27 (1.06–1.53)	1.15 (0.95–1.34)	1.15 (0.93–1.43)
Pack-years of smoking in household				
None	1.00	1.00	1.00	1.00
0.1–2.9	1.06 (0.91–1.23)	1.01 (0.85–1.21)	1.07 (0.87–1.32)	1.04 (0.81–1.33)
3.0–6.9	1.09 (0.93–1.28)	1.15 (0.96–1.37)	1.15 (0.95–1.39)	1.05 (0.83–1.31)
≥7.0	1.18 (1.00–1.40)	1.26 (1.03–1.53)	1.14 (0.96–1.36)	1.11 (0.91–1.36)
p for trend	0.05	0.09	0.08	0.30

OR = odds ratio; CI = confidence interval.; RYUCHS = Ryukyus Child Health Study.
*Adjusted for sex, region of residence, number of siblings, paternal and maternal history of asthma, atopic eczema, or allergic rhinitis, and paternal and maternal educational level.
†Number of cigarettes smoked in the household each day.

TABLE 5. Adjusted odds ratios and 95% confidence intervals for wheeze and asthma according to smoking in the household of 23,044 schoolchildren with a positive or negative parental allergic history, RYUCHS, Japan

	Positive parental allergic history (n = 9,661)		Negative parental allergic history (n = 13,383)	
	Wheeze OR (95%CI)*	Asthma OR (95%CI)*	Wheeze OR (95%CI)*	Asthma OR (95%CI)*
Smoking in household				
Never	1.00	1.00	1.00	1.00
Former	1.04 (0.85–1.27)	0.92 (0.73–1.14)	1.16 (0.91–1.46)	1.10 (0.80–1.49)
Current <15†	1.12 (0.97–1.28)	1.05 (0.90–1.22)	1.06 (0.90–1.24)	1.12 (0.91–1.38)
Current ≥15†	1.23 (1.04–1.44)	1.22 (1.02–1.46)	1.09 (0.90–1.31)	1.19 (0.94–1.50)
Pack-years of smoking in household				
None	1.00	1.00	1.00	1.00
0.1–2.9	1.09 (0.93–1.28)	1.02 (0.85–1.21)	1.03 (0.85–1.24)	1.00 (0.77–1.27)
3.0–6.9	1.11 (0.94–1.29)	1.02 (0.85–1.22)	1.12 (0.93–1.35)	1.25 (0.99–1.56)
≥7.0	1.22 (1.04–1.43)	1.19 (1.00–1.42)	1.10 (0.91–1.31)	1.17 (0.93–1.47)
p for trend	0.02	0.09	0.21	0.07

OR = odds ratio; CI = confidence interval; RYUCHS = Ryukyus Child Health Study.
*Adjusted for sex, age, region of residence, number of siblings, and paternal and maternal educational level.
†Number of cigarettes smoked in the household each day.

at 6 months of age was significantly associated with wheeze between 18 and 30 months of age (15). On the other hand, data from a large population-based cohort study in Germany, which consisted of children aged 9 to 11 years at baseline and followed up for about 7 years, demonstrated that ETS exposure at home at baseline and at follow up was not associated with the incidence of wheeze and asthma (9). Cross-sectional studies have examined the association between ETS exposure and wheeze (11) and asthma (12) among Japanese children. Our previous study (11) demonstrated that there was no significant association between smoking in the household (10 or more cigarettes a day versus 0–9 cigarettes a day) and the prevalence of wheeze among schoolchildren aged 12 to 15 years. A cross-sectional study among 6-year-old children (12) also showed no association between living with a smoker and the prevalence of asthma. These findings are inconsistent with those of the present study. Because the information on ETS exposure gathered by these two cited investigations was crude, it might be difficult to detect a significant positive association between ETS exposure and the prevalence of asthma or wheeze.

Our findings are consistent with the assumption that respiratory symptoms associated with parental smoking seem to be evident at younger ages (21–24). A US study showed that the OR for current wheeze associated with passive smoking was 1.90 among children from birth to 2 years of age and only 1.07 among children aged 13 to 17 years (23). We have no clear explanation for the significant positive association found between household smoking and the prevalence of wheeze and asthma only in the young age group. The lack of a relation between passive smoking at home and wheeze and asthma prevalence among children aged 11 to 15 years may be explained by the fact that children spend less time in the presence of parents as they progress from childhood to adolescence, (i.e., exposure to ETS in the household decline with age) or because of maturation of the respiratory system in the older children, or both (21, 22). A positive association between former, but not current, passive smoking at home and the prevalence of wheeze in older children was observed in the current study. However, such a relationship in the younger age group was not found. Regarding asthma, there were no associations with former smoking in the household in either age group. Continuation of smoking by family members was not likely to be affected by the child's respiratory symptoms.

Many studies demonstrated that a family history of allergic disorders was associated with an increased prevalence of wheeze and asthma among children (13, 16–19, 25–27), which suggested that genetic factors might play an important role in the development of asthma (27). Some genetic markers could indicate susceptibility to environmental factors (27). However, in the current study, there were no significant differences in the prevalence of wheeze or asthma in relation to smoking status in the household between children with a positive and negative parental allergic history. In US children aged 8 to 18 years (18), it was reported that the strength of a positive association between in utero exposure to maternal smoking and asthma diagnosed in the first 5 years of life was approximately identical between children with and those without a family history of asthma. A study regarding new-onset adult asthma also showed no interaction effect between environmental factors in the home, such as ETS exposure, visible mold on walls, pet ownership, and parental atopy (28). The current findings were consistent with these findings. Further studies are needed to clarify the complex interaction between genetic factors and exposure to ETS in association with wheeze and asthma among children as well as adults.

In a cross-sectional study of schoolchildren 5 to 8 years of age, there was no relationship between passive smoking and the prevalence of eczema (10). Two cross-sectional studies also showed no relation between passive smoking and the prevalence of atopic dermatitis in Japanese children (11, 12). Our results showed that former, but not current, smoking in the household was associated with an increased prevalence of atopic eczema. It is possible that people in a household with an atopic eczema sufferer may have altered their smoking habits.

Our findings regarding passive smoking and allergic rhinoconjunctivitis are consistent with previous studies that showed no relation between ETS exposure and allergic rhinitis (6, 10, 11), but inconsistent with a study showing an inverse association (12). A significant positive relationship between current passive smoking at home and at work and the prevalence of allergic rhinitis among pregnant Japanese women was observed in our previous study (29).

There are several major strengths in the present investigation. Study subjects were homogeneous with respect to age and geographical background. The large number of subjects and variables allowed us to overcome problems such as small sample size, inadequate data on potential confounders, and reduced statistical power. Since 60.3% of all eligible children were included in this analysis, it seemed unlikely that the results of our study might be distorted by selection. In addition, we used an internationally standardized and validated measurement tool. There are some limitations that influence the interpretation of the current results, however. Our study design was cross-sectional; therefore this study does not necessarily indicate a causal relationship. Exposure to ETS was assessed using questionnaire responses and was not validated by objective measurements, such as salivary, serum or urine cotinine levels. Retrospective recall of exposure to ETS is likely to have produced some misclassification of exposure. Participants in this survey were informed of the main purpose of the study, which investigated the associations between various selected factors and child health problems, but no special attention was paid to ETS exposure. Blinding of the specific study question was likely to reduce information bias in reporting exposure. Children living in homes without smokers are also exposed to some ETS outside the house and are therefore not a true unexposed group. This misclassification could have contributed to an underestimation of the health effect of passive smoking. In the current study, we could not take active smoking among children into consideration because we collected information on active smoking only among junior high school students. However, the prevalence of active smoking among junior high school students was only 2%. Data on whether any of the participants came from the same family were not available for this study. Therefore, we were not able to take into account clustering within families, which might affect our findings. Study subjects in Okinawa may differ from Japanese children in the general population and we should be cautious in generalizing the current findings. In fact, the prevalence of allergic disorders in the current study was quite different from that in the mainland of Japan. According to another cross-sectional study among Japanese adolescents in Suita City, which is in an urban area of the mainland, the prevalence values for wheeze, atopic eczema, and allergic rhinoconjunctivitis in the past 12 months based on the ISAAC criteria were 6.7%, 14.5%, and 23.9%, respectively (11).

In conclusion, the results of our study have revealed that exposure to ETS in the household is associated with an increased prevalence of wheeze and asthma in Japanese schoolchildren, especially in the following two subgroups: children 6 to 10 years of age and children with a positive parental history of allergic history. Further investigations, in particular prospective studies, with more precise exposure measurements are needed to clarify the role of passive smoking exposure in allergic disorders in childhood.

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Relationship between Intake of Vegetables, Fruit, and Grains and the Prevalence of Tooth Loss in Japanese Women

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Summary Epidemiological evidence regarding dental status and its relationship to diet and nutritional status has been limited. The present cross-sectional study examined the relationship between intake of vegetables, fruit, grains, antioxidants, and fiber and the prevalence of tooth loss. Study subjects were 1,002 pregnant Japanese women. Tooth loss was defined as the previous extraction of 1 or more teeth. Adjustment was made for age, gestation, parity, cigarette smoking, passive smoking at home and at work, family income, education, changes in diet in the previous 1 mo, season when data were collected, and body mass index. Of the 1,002 subjects, 256 women had lost 1 or more teeth. Compared with intake of vegetables other than green and yellow vegetables in the lowest quartile, consumption of the other vegetables in the highest quartile was independently associated with a decreased prevalence of tooth loss, showing a clear inverse dose-response relationship. There was a marginally significant inverse dose-response relationship between the intake of insoluble fiber and tooth loss. No association was observed between intake of green and yellow vegetables, soluble fiber, or antioxidant nutrients and tooth loss. These findings suggested that consumption of vegetables other than green and yellow vegetables and insoluble fiber may be related to a decreased prevalence of tooth loss among young Japanese women.
Key Words cross-sectional studies, dietary fiber, pregnant women, tooth loss, vegetables

Epidemiological evidence regarding dental status and its relationship to diet and nutritional status has been limited. Previous studies evaluating diet and tooth loss have mainly focused on the middle-aged and the elderly (*1–7*). These studies generally suggested that tooth loss affected food preference and food consumption patterns because of reduced masticating efficiency, leading to nutritional deficiency among those who have fewer natural teeth or are edentulous. Several cross-sectional studies showed that the edentate elderly consumed fewer fruits and vegetables (*1, 2*), less fiber (*1, 3–5*), vitamin C (*3, 4*), carotene (*1, 5*), vitamin E (*3, 5*), calcium (*3, 4*), magnesium (*4*) and protein (*3, 4*) and more cholesterol and saturated fat (*1*) than the dentate. A cross-sectional survey among older Chinese vegetarians found that in the group with poor dental functional status due to tooth loss, intake of fiber was lower than in those with adequate dental functional status, although there was no difference between the 2 groups in consumption of total calories, carbohydrates, protein, fat, vitamin C, or calcium (*6*). The Health Professionals Follow-up Study demonstrated that subjects who had lost 5 or more teeth changed their dietary intake differently than did those who had no tooth loss during the 8-y period. The men who had lost 5 or more teeth had a significantly smaller reduction in consumption of dietary cholesterol and vitamin B_{12}, a greater reduction in consumption of polyunsaturated fat and a smaller increase in consumption of dietary fiber and whole fruit than did those who did not lose any teeth (*7*).

On the other hand, it is considered that young adults have retained their natural teeth with sufficient adequate occlusive function for mastication, even if they have experienced tooth loss. Therefore, tooth loss is unlikely to affect selection of foods among young adults. The major cause of tooth loss is extraction due to caries or periodontitis, which is an infection-mediated destruction of tooth-supporting tissues. Both caries and periodontitis are preventable. In order to maintain natural dentition across the adult life span, expanding knowledge of the role of nutrition on oral health among young adults would provide insights into health prac-

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tices that can be effective in preventing tooth loss. The purpose of the present study was to investigate the association of intake of vegetables, fruit, grains, fiber and antioxidants and the prevalence of tooth loss among pregnant Japanese women by using baseline data from the Osaka Maternal and Child Health Study (OMCHS).

MATERIALS AND METHODS

Study population. The OMCHS is an ongoing prospective cohort study of risk factors for maternal and child health such as allergic disorders and postpartum depression. The background and general procedure of the OMCHS have been described previously (*8, 9*). In brief, the OMCHS requested that pregnant women complete a baseline survey, which was followed by several post-natal surveys. Eligible women were those who became pregnant in Neyagawa City, which is one of 44 municipalities in Osaka Prefecture, a metropolis in Japan with a total population of approximately 8.8 million. Of 3,639 eligible subjects, 627 pregnant women (17.2%) in Neyagawa City took part in this study during the period from November 2001 to March 2003. Eight pregnant women who did not live in Neyagawa City but who had become aware of the present study at an obstetric clinic before August 2002 decided by themselves to participate. There were also 77 participants who received explanations of the OMCHS from public health nurses in 6 other municipalities from August 2002 to March 2003. From October 2002 to March 2003, 290 participants were recruited from a university hospital and 3 obstetric hospitals in 3 other municipalities; those women were recommended for participation in the OMCHS by an obstetrician. Finally, a total of 1,002 pregnant women gave their fully informed consent in writing and completed the baseline survey. The OMCHS was approved by the ethics committees of the Osaka City University School of Medicine and the Osaka Prefectural Institute of Public Health.

Questionnaire. In the baseline survey, the participants filled out a set of two self-administered questionnaires. The participants mailed the questionnaires to the data management center. The questionnaires were checked by research technicians, and missing or illogical answers were completed by telephone interview.

A validated self-administered diet history questionnaire (DHQ) was used to assess dietary habits over the previous 1 mo. The structure and validity of the questionnaire were described in detail elsewhere (*10, 11*). In this instrument, intake of 147 food items was calculated using an ad-hoc computer algorithm developed to analyze the questionnaire. We adjusted for energy intake by using the residual method (*12*). Our DHQ also included questions about height and weight. Body mass index was defined as the self-reported body weight in kg divided by the square of the self-reported height in m.

Another self-administered questionnaire elicited information on age, gestation, parity, smoking habits, passive smoking exposure at home and at work, family income, education, changes in diet in the previous 1 mo, experience of extraction of permanent teeth excluding third molars, and the number of remaining teeth. Tooth loss was defined as the extraction of 1 or more teeth.

Statistical analysis. Intake of selected foods and nutrients was categorized at quartile points on the basis of the distribution of all study subjects. Age was classified into 3 categories (<29, 29–31, and 32+y); gestation into 3 (<15, 15–20, and 21+wk); parity into 2 (0 and 1+); cigarette smoking into 3 (never, former, and current); passive smoking at home into 3 (never, former, and current); passive smoking at work into 3 (never, former, and current); family income into 3 (<4,000,000, 4,000,000–5,99,999, and 6,000,000+ JPY/y); education into 3 (<13, 13–14, and 15+y); changes in diet in the previous 1 mo into 3 (none or seldom, slight, and substantial); and season when data were collected into 4 (spring, summer, fall, and winter). Body mass index was used as a continuous variable. The association between intake of selected foods and nutrients and the prevalence of tooth loss was analyzed by using a logistic regression model. Multiple logistic regression analysis was conducted to control for the potential confounding effects of the selected factors. The trend of association was assessed by assigning ordinal scores to the levels of the independent variable. Two-sided p values less than 0.05 were regarded as statistically significant. All analyses were done with SAS statistical software (SAS Institute, Inc., Cary, NC, version 8.2).

RESULTS

Of the 1,002 study subjects, 21.4% had lost 1 to 4 teeth and 4.2% had lost 5 or more teeth (Table 1). The mean age of the subjects was 29.8, with approximately 30% being between 29 and 31 y (Table 2). About 70% of the subjects participated in the study by the 20th week of gestation, and about half had a parity of one or more. Current active smoking was observed in 18% of pregnant women. The prevalence values for current passive smoking exposure at home and at work were 49% and 12%, respectively. Slight or substantial changes in diet in the previous 1 mo were experienced by 702 pregnant women because of nausea gravidarum (585 women), maternal and fetal health (107 women), and other reasons (10 women). Mean daily total energy and energy-adjusted intake of green and

Table 1. Distribution of tooth loss in 1,002 pregnant women, OMCHS, Japan.

Number of teeth lost	Number of subjects (%)
0	746 (74.5)
1	85 (8.5)
2	57 (5.7)
3	29 (2.9)
4	43 (4.3)
5+	42 (4.2)

OMCHS: Osaka Maternal and Child Health Study.

Table 2. Distribution of selected characteristics in 1,002 pregnant women, OMCHS, Japan.

Factor	Number (%) or mean (SD)
Age (% y)	
<29	380 (37.9)
29–31	299 (29.8)
32+	323 (32.4)
Gestation (% wk)	
<15	357 (35.6)
15–20	329 (32.8)
21+	316 (31.5)
Parity of one or more (%)	513 (51.2)
Cigarette smoking	
Never	697 (69.6)
Former	121 (12.1)
Current	184 (18.4)
Passive smoking at home	
Never	284 (28.3)
Former	224 (22.4)
Current	494 (49.3)
Passive smoking at work	
Never	344 (34.3)
Former	538 (53.7)
Current	120 (12.0)
Family income (% JPY/y)	
<4,000,000	301 (30.0)
4,000,000–5,999,999	403 (40.2)
6,000,000+	298 (29.7)
Education (% y)	
<13	323 (32.2)
13–14	413 (41.2)
15+	266 (26.6)
Change in diet in the previous 1 mo (%)	
None or seldom	300 (29.9)
Slight	435 (43.4)
Substantial	267 (26.7)
Season when data were collected (%)	
Spring	318 (31.7)
Summer	162 (16.2)
Fall	223 (22.3)
Winter	299 (29.8)
Body mass index (kg/m^2)	21.4 (2.8)
Daily nutrient intake[a]	
Total energy (kJ)	6,815.3 (1,793.8)
Green and yellow vegetables (g)	69.5 (46.0)
Other vegetables (g)	109.2 (68.9)
Fruit (g)	173.2 (182.4)
Grains (g)	340.5 (95.9)
Soluble fiber (g)	2.0 (0.7)
Insoluble fiber (g)	8.5 (2.3)
Vitamin C (mg)	120.7 (58.7)
Vitamin E (mg)	7.5 (1.8)
β-Carotene (mg)	1,840.4 (1,222.2)

OMCHS: Osaka Maternal and Child Health Study; SD: standard deviation; JPY: Japanese Yen.

[a] Nutrient and food intake were adjusted for total energy intake using the residual method.

yellow vegetables, other vegetables, fruit, and grains were 6,815 kJ, 69.5 g, 109.2 g, 173.2 g, and 340.5 g, respectively.

Odds ratios (ORs) and their 95% confidence intervals (CIs) for relationships between consumption of vegetables, fruit, and grains and the prevalence of tooth loss are presented in Table 3. Compared with intake of vegetables other than yellow and green vegetables such as cabbages, radishes, and onions in the first quartile, consumption of such other vegetables in the third and fourth quartiles, but not the second quartile, were statistically significantly associated with a decreased prevalence of tooth loss, showing a clear inverse dose-response relationship. Adjustment for age, gestation, parity, cigarette smoking, passive smoking at home and at work, family income, education, changes in diet in the previous 1 mo, season when data were collected, and body mass index did not materially change the results although the adjusted OR for the third quartile fell just short of the significance level. There was no measurable relationship between consumption of green and yellow vegetables, fruit, or grains and the prevalence of tooth loss.

There was a tendency for an inverse dose-response relationship of insoluble fiber consumption with the prevalence of tooth loss by the multivariate model although the adjusted OR for comparison of the highest with the lowest quartile was not statistically significant (p for trend=0.05) (Table 4). No evident association was observed between intake of soluble fiber, vitamins C and E, or β-carotene and the prevalence of tooth loss.

After further adjustment for insoluble fiber intake, a statistically significant inverse association between consumption of vegetables other than green and yellow vegetables and the prevalence of tooth loss had disappeared: the adjusted ORs for comparison of the second, third, and fourth quartiles with the lowest quartile were 0.69 (95% CI: 0.45–1.05), 0.68 (95% CI: 0.44–1.07), and 0.72 (95% CI: 0.44–1.17), respectively.

DISCUSSION

To our knowledge, no epidemiological information is available regarding the relationship between dietary intake and tooth loss among young adults. Our findings are partially consistent with several epidemiological studies among middle-aged or elderly people showing that the edentate consumed fewer fruits and vegetables, less fiber, carotene, and vitamin C than their dentate counterparts (*1–7*). These previously cited studies indicated that the edentate had compromised masticating ability and efficiency that led to dietary restrictions. Our study subjects were likely to retain their natural teeth so that they could sufficiently masticate, since only 4.2% had lost 5 or more teeth. We did not have information on the reasons for tooth extraction in our subjects. According to a report on reasons for extraction of teeth in Japanese aged 9–35 y (*13*), the proportions of extractions resulting from caries, periodontal disease, eruption problems, orthodontic indications, trauma, and other causes were 51.5, 6.2, 21.9, 5.1, 0.1, and 15.2%, respectively. More than 90% of extractions for eruption problems were third molars (*13*). In the current population, more than one half of tooth loss is likely to be ascribed to dental or oral pathology, such as caries and

Table 3. Odds ratios and 95% CIs for tooth loss by quartiles of intake of vegetables, fruit, and grains, OMCHS, Japan.

Variable[a]	Prevalence	Crude odds ratio	(95% CI)	Adjusted odds ratio	(95% CI)[b]
Green and yellow vegetables					
Q1 (28.6)	73/250 (29.2%)	1.00		1.00	
Q2 (50.2)	61/251 (24.3%)	0.78	0.52–1.16	0.79	0.52–1.19
Q3 (71.2)	62/250 (24.8%)	0.80	0.54–1.19	0.82	0.54–1.24
Q4 (115.6)	60/251 (23.9%)	0.76	0.51–1.13	0.78	0.51–1.19
p for linear trend		0.21		0.29	
Other vegetables					
Q1 (51.7)	78/250 (31.2%)	1.00		1.00	
Q2 (80.6)	62/251 (24.7%)	0.72	0.49–1.07	0.71	0.47–1.07
Q3 (111.8)	58/250 (23.2%)	0.67	0.45–0.99	0.67	0.44–1.01
Q4 (171.6)	58/251 (23.1%)	0.66	0.44–0.98	0.64	0.42–0.98
p for linear trend		0.04		0.04	
Fruit					
Q1 (44.3)	68/250 (27.2%)	1.00		1.00	
Q2 (114.2)	59/251 (23.5%)	0.82	0.55–1.23	0.80	0.53–1.22
Q3 (174.3)	64/250 (25.6%)	0.92	0.62–1.37	0.90	0.59–1.37
Q4 (289.7)	65/251 (25.9%)	0.94	0.63–1.39	0.94	0.61–1.44
p for linear trend		0.88		0.91	
Grains					
Q1 (236.8)	71/250 (28.4%)	1.00		1.00	
Q2 (311.3)	59/251 (23.5%)	0.78	0.52–1.16	0.72	0.47–1.10
Q3 (360.1)	62/250 (24.8%)	0.83	0.56–1.24	0.79	0.52–1.19
Q4 (441.0)	64/251 (25.5%)	0.86	0.58–1.28	0.77	0.51–1.17
p for linear trend		0.55		0.29	

CI: confidence interval; OMCHS: Osaka Maternal and Child Health Study.

[a] Quartile medians in g/d adjusted for energy intake with the residual methods given in parentheses.

[b] Odds ratios were separately calculated for each dietary variable adjusted for age (<29, 29–31, and 32+), gestation (<15, 15–20, and 21+ wk), parity (0 and 1+), cigarette smoking (never, former, and current), passive smoking at home (never, former and current), passive smoking at work (never, former, and current), family income (<4,000,000, 4,000,000–5,999,999, and 6,000,000+ JPY/y), education (<13, 13–14, and 15+ y), changes in diet in the previous 1 mo (none or seldom, slight, and substantial), season when data were collected (spring, summer, fall, and winter), and a continuous variable for body mass index.

periodontal diseases, and the small number of orthodontic indications might be negligible. Both caries and periodontal diseases are plaque-mediated conditions. Nutrition may impact on the formation and maturation of dental plaque (*14*). However, it is unclear whether the contribution by nutrition to the development of caries is the same as that of periodontitis.

We have no immediate explanation as to underlying mechanisms for the observed inverse association between intake of vegetables other than green and yellow vegetables and the prevalence of tooth loss. Some of the beneficial effects of a high intake of these vegetables may be due to consumption of insoluble fiber or unrecognized agents in relation to insoluble fiber intake. Required vigorous chewing due to dietary fiber consumption may provide a mechanical stimulus to salivary flow (*15*). Saliva acts as a protective agent against dental caries and periodontal diseases through several functions including antimicrobial effects, clearance, buffering power, and saturation with respect to tooth minerals (*16, 17*). Additionally, fiber itself may remove dental plaque from the tooth surfaces through the mechanical action of chewing. Alternatively, dietary fiber intake may serve as a mediator for the relationship between diet and inflammation. Increased fiber intake was associated with a significantly lower likelihood of elevated C-reactive protein (*18*). Saito et al. showed a positive relationship between alveolar bone loss, which leads to tooth loss, and C-reactive protein among Japanese men aged 50 to 54 y (*19*). Another possible explanation is that uncontrolled dietary or nondietary factors may produce a spurious inverse association between intake of vegetables other than green and yellow vegetables and the prevalence of tooth loss. Persons who have a high intake of vegetables other than green and yellow vegetables are likely to practice behaviours protective of oral health such as regular tooth brushing and dental visits.

In the present study, we used self-reported tooth loss as a proxy for dental diseases. We did not have information on the validity of self-reported tooth loss in our subjects. However, several validation studies of self-reported dental health showed that there was no significant difference between the self-reported residual number of teeth and the actual number of teeth determined by clinical examination in spite of age or sex (*20, 21*).

Table 4. Odds ratios for tooth loss by quartiles of intake of fiber and antioxidants, OMCHS, Japan.

Variable[a]	Prevalence	Crude odds ratio	(95% CI)	Adjusted odds ratio	(95% CI)[b]
Soluble fiber					
Q1 (1.4)	67/250 (26.8%)	1.00		1.00	
Q2 (1.7)	66/251 (26.3%)	0.97	0.66–1.45	0.95	0.63–1.44
Q3 (2.1)	60/250 (24.0%)	0.86	0.58–1.29	0.86	0.56–1.31
Q4 (2.7)	63/251 (25.1%)	0.92	0.61–1.37	0.89	0.58–1.36
p for linear trend		0.55		0.50	
Insoluble fiber					
Q1 (6.3)	65/250 (26.0%)	1.00		1.00	
Q2 (7.6)	78/251 (31.1%)	1.28	0.87–1.90	1.27	0.85–1.91
Q3 (8.8)	62/250 (24.8%)	0.94	0.63–1.41	0.91	0.59–1.39
Q4 (10.8)	51/251 (20.3%)	0.73	0.48–1.10	0.70	0.44–1.09
p for linear trend		0.06		0.05	
Vitamin C					
Q1 (69.9)	64/250 (25.6%)	1.00		1.00	
Q2 (97.2)	65/251 (25.9%)	1.02	0.68–1.52	1.09	0.71–1.65
Q3 (123.5)	66/250 (26.4%)	1.04	0.70–1.56	1.13	0.74–1.72
Q4 (179.6)	61/251 (24.3%)	0.93	0.62–1.40	0.98	0.63–1.51
p for linear trend		0.78		0.96	
Vitamin E					
Q1 (5.7)	64/250 (25.6%)	1.00		1.00	
Q2 (6.8)	66/251 (26.3%)	1.04	0.70–1.55	1.01	0.67–1.54
Q3 (7.8)	52/250 (20.8%)	0.76	0.50–1.16	0.72	0.46–1.11
Q4 (9.5)	74/251 (29.5%)	1.22	0.82–1.80	1.09	0.72–1.65
p for linear trend		0.62		0.95	
β-Carotene					
Q1 (758.8)	72/250 (28.8%)	1.00		1.00	
Q2 (1,346.0)	63/251 (25.1%)	0.83	0.56–1.23	0.88	0.58–1.32
Q3 (1,916.8)	59/250 (23.6%)	0.76	0.51–1.14	0.83	0.55–1.27
Q4 (3,010.3)	62/251 (24.7%)	0.81	0.55–1.21	0.85	0.56–1.30
p for linear trend		0.26		0.42	

CI: confidence interval; OMCHS: Osaka Maternal and Child Health Study.

[a] Quartile medians in g (except for vitamins C and E and β-carotene; mg)/d adjusted for energy intake with the residual methods given in parentheses.

[b] Odds ratios were separately calculated for each dietary variable adjusted for age (<29, 29–31, and 32+), gestation (<15, 15–20, and 21+ wk), parity (0 and 1+), cigarette smoking (never, former, and current), passive smoking at home (never, former and current), passive smoking at work (never, former, and current), family income (<4,000,000, 4,000,000–5,999,999, and 6,000,000+ JPY/y), education (<13, 13–14, and 15+ y), changes in diet in the previous 1 mo (none or seldom, slight, and substantial), season when data were collected (spring, summer, fall, and winter), and a continuous variable for body mass index.

Axelsson and Helgadóttir reported that the kappa statistic for agreement between the self-reported number of remaining teeth and the number found at a clinical examination in the 18-y group, 35-to-44-y group, and the group aged 65 y or older were 0.56, 0.60, and 0.63, respectively (*21*). Persons are more knowledgeable about tooth loss than about signs and symptoms of disturbances of oral health, such as toothache, sore or swollen gums, and sensitivity of teeth to cold or heat (*22*). Pitiphat et al. showed that the self-reported number of remaining teeth, fillings, root canal therapies, and prostheses were strongly correlated with clinical records whereas self-reports appear to be less useful for the assessment of dental caries and periodontal disease (*23*). These data could support the use of self-reported tooth loss in epidemiological research as a key indicator of dental health status.

This present study had several methodological advantages: the homogeneity of study subjects with respect to all being young adults and adjustment for extensive information on potential confounding factors. The dietary information was derived from a DHQ. Since we did not actually observe the dietary habits of the subjects, the possibility of misclassification might be a concern. According to validation studies, the correlation coefficient between vitamin C estimated from the DHQ and that observed by a 3-d dietary record was 0.45 in women (*10*); the correlation coefficients between intake and the corresponding serum concentrations were 0.40 and 0.60 in men and women, respectively, for β-carotene and −0.23 and −0.22 in men and women, respectively, for vitamin E (*11*). Participants with tooth loss might not be aware of the possible ill effects of diet. Thus, any misclassification would be nondifferential between cases and noncases and would most likely weaken any true relationship. The DHQ was designed to assess recent dietary intake, i.e. for 1 mo prior to completing the questionnaire. Adjustment for season when data were collected is likely to ease this limitation, however. There are other disadvantages that should be considered. The study subjects were pregnant women who may differ from young adults in the general population in terms of lifestyle characteristics, such as dietary habits. Thus we controlled for changes in diet in the 1 mo prior to the survey. Of a total of 3,639 eligible pregnant women in Neyagawa City, only 627 (17.2%) took part in this study. We were uncertain whether there was a difference between participants and non-participants in Neyagawa City, because data on personal characteristics such as age, socioeconomic status, and experience of extraction of permanent teeth among the non-participants were not available. With regard to the remaining 375 participants, we were not able to calculate the participation rate because the exact number of eligible subjects was not available. Nor could we not compare participants with non-participants in the 4 collaborating hospitals and 6 municipalities. Our subjects were not representative of Japanese women in the general population and the present findings may not be generalized. In fact, educational levels in the present study population were higher than in the general population. According to the 2,000 population census of Japan, the proportions of women aged 30 to 34 y in Osaka Prefecture with years of education of <13, 13–14, 15+, and unknown were 49.2, 32.3, 13.6, and 4.9%, respectively (*24*). The corresponding figures for the present study were 32.2, 41.2, 26.6, and 0.0%, respectively. However, the prevalence of tooth extraction in this study population (25.5%) is close to that in a sample that consisted of Japanese women aged 25–30 y for a survey of dental diseases in 1999 (27.3%) (*25*). Our analysis could not include detailed information on oral status such as oral hygiene, dental caries, periodontal diseases, or oral health behavior variables such as tooth brushing frequency and access to professional dental services. Tooth loss explained only severe dental caries and periodontal diseases, i.e. the early stage of dental diseases was not taken into account in this study. The consequence would have given rise to an underestimation of our findings.

This is the first epidemiological study to assess the association between dietary intake and the prevalence of tooth loss among young adults. The data used were cross-sectional, so it was not possible to determine whether any observed relation between diet and tooth loss was causal. Further studies with more detailed and objective indicators of dental health status should be performed to evaluate the role of foods and nutrients in oral health.

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Appendix

Space limitations preclude the inclusion as authors of the following members of the Osaka Maternal and Child Health Study Group:

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REVIEW ARTICLE

Environmental Factors and Allergic Disorders

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ABSTRACT

Despite numerous studies on possible associations between environmental exposure and allergic disorders, any conclusions made remain a matter of controversy. We conducted a review of evidence in relation to environmental and nutritional determinants and wheeze, asthma, atopic dermatitis, and allergic rhinitis. Identified were 263 articles for analysis after consideration of 1093 papers that were published since 2000 and selected by electronic search of the PubMed database using keywords relevant to epidemiological studies. Most were cross-sectional and case-control studies. Several prospective cohort studies revealed inconsistent associations between various environmental factors and the risk of any allergic disorder. Therefore, the evidence was inadequate to infer the presence or absence of a causal relationship between various environmental exposures and allergic diseases. However, evidence is suggestive of positive associations of allergies with heredity. Because almost all the studies were performed in Western countries, the application of these findings to people in other countries, including Japan, may not be appropriate. Further epidemiological information gained from population-based prospective cohort studies, in particular among Japanese together with other Asians, is needed to assess causal relationships between various environmental factors and allergic diseases.

KEY WORDS

allergic rhinitis, asthma, atopic dermatitis, environmental factors, review, wheeze

INTRODUCTION

Recently, the prevalence of allergic diseases has increased significantly. In 1989 Strachan observed that birth order and family size were inversely associated with the risk of allergic rhinitis and postulated the hygiene hypothesis, which suggests that infections within households in early childhood have a role in preventing allergic diseases.[1] This hygiene hypothesis has been given an immunological framework in which the balance between Th1 (associated with bacterial and viral infections) and Th2 (associated with allergic diseases) immune responses is pivotal.[2] Although the Th1/Th2 paradigm has not been confirmed in humans, the hygiene hypothesis has triggered numerous epidemiological studies on the relation between environmental factors and allergic disorders. However, so far no data conclusively explain the rising prevalence of allergic diseases. A number of epidemiological studies have focused on the relationship between dietary intake and allergic disorders. Especially, it remains unclear whether n-3 polyunsaturated fatty acid intake is preventive against allergic disorders and whether n-6 polyunsaturated fatty acid intake increases the risk of allergic disorders.[3]

Genetic factors may influence immunologic development. However the current rapid rise in allergic diseases cannot be fully explained only by genetic factors. The complex interplay between immune responses of the host, the level and variety of the environmental exposure, and the interactions between the genetic background and the range of exposures are likely to affect the development of allergic diseases. To assess the involvement of the gene-environment interaction in the onset of allergic disorders, we felt that it would be useful to list candidate environmental factors associated with allergic disorders. We have reviewed the scientific literature to identify, appraise and synthesize evidence regarding the possible association of various environmental and nutritional factors with wheeze, asthma, atopic eczema, and allergic rhinitis.

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METHODS

A literature search of the PubMed database was performed to identify epidemiologic studies in the English language from January 2000 to August 2006 using the following keyword terms: (asthma OR wheeze OR "atopic dermatitis" OR "atopic eczema" OR "allergic rhinitis") AND (risk OR prevalence OR preventive OR protective) AND (association OR relationship) AND human AND (cross-sectional OR case-control OR prospective OR cohort OR intervention) NOT polymorphism. A total of 1093 studies (original articles, correspondence, and reviews) were identified. We scanned the titles and abstracts of these studies manually to identify those that met the following *a priori* criteria: (1) original article; (2) comparative epidemiologic study design; (3) wheeze, asthma, atopic dermatitis, or allergic rhinitis (hay fever) listed as an outcome. A final set of 263 articles meeting these criteria was identified.[4-266]

From the 263 papers, we retrieved examined factors such as environmental and occupational exposure, demographic variables (e.g. sex, age, socioeconomic status), body build, past medications, medical history, and dietary factors and the results associated with each outcome: wheeze, asthma, atopic dermatitis, and allergic rhinitis. We synthesized the information regarding the examined factors and the results into 3 tables in which the direction of the associations and the cited reference numbers are listed. The results were considered statistically significant when either of the following conditions was met: (1)p value was less than 0.05, or (2)p for trend between exposure variables and the risk or prevalence of allergic diseases was statistically significant (<0.05).

Whenever possible we retrieved the results of analysis of all participants. However, for articles that presented results for only stratified analysis or that included two or more studies, we examined each of the studies presented in the paper separately. Some studies presented results for several different definitions of an outcome. In these cases we obtained the results for all definitions available.

RESULTS

OVERVIEW OF INCLUDED STUDIES

The number of studies investigating wheeze, asthma, atopic dermatitis, and allergic rhinitis as an outcome was 113, 192, 64, and 78, respectively. Almost all studies were performed in Western countries, while only 7 studies were reported from Japan.[16,41,95,121,189,245,262]

SOCIOECONOMIC FACTORS

We identified 74 reports in which the associations between socioeconomic factors such as socio-economic status, income, and education and allergic diseases were identified (Table 1). Half of these results provided a lack of association. Several studies found a lower frequency of allergic illnesses in populations with low socioeconomic status, whereas others showed positive associations with socioeconomic status. It was not possible to draw conclusions from these observations. Socioeconomic status may merely reflect predisposition to infections, less stringent control of microbial contamination of water and food, and/or poorer housing conditions.

SMOKING EXPOSURE

A number of studies examined the association between smoking exposure and allergic disorders. Many, but not all, studies found that active smoking was positively associated with the risk and prevalence of wheeze and asthma. Sex difference in the association with active smoking was observed in 2 cross-sectional studies.[22,23] In a study of New York State adults, active smoking was inversely associated with asthma in men (adjusted odds ratio [OR] = 0.49, 95% confidence interval [CI]: 0.27–0.89).[22] Another US cross-sectional study showed a positive association between active smoking and asthma in women (adjusted OR = 1.43, 95% CI: 1.20–1.64).[23] One cross-sectional study indicated that active smoking was inversely associated with the prevalence of allergic rhinitis: adjusted OR was 0.5 (95% CI: 0.4–0.7) for smoking of at least 20 cigarettes a day, compared with never smoking.[123] No association between active smoking and allergic disorders was observed in 13 studies.

Four cohort studies,[31,36,75,124] 3 case-control studies, [45,61,126] and 9 cross-sectional studies,[9,25,120,121,129,130-133] showed a positive association between passive smoking and the risk and prevalence of wheeze, asthma, and allergic rhinitis. Most of the studies found no association between passive smoking exposure and allergic disorders.

Recently, investigations of the association between maternal smoking during pregnancy and allergic disorders have been increasing. Several studies found that *in utero* exposure to maternal smoking increased the risk and prevalence of wheeze and asthma among children born to those mothers.[26,31,45,127,135,136] In contrast, no published report suggested an inverse association between maternal smoking in pregnancy and allergic diseases in offspring. More than half of the studies that examined the association between maternal smoking during pregnancy and allergic disorders found no statistically significant relationship between them.

In research that assessed smoking exposure by using a questionnaire and/or interview, exposure misclassification was likely to occur. Only one cohort study found no association between the serum cotinine level and asthma in adults.[59]

PET OWNERSHIP

A large number of studies examined the association

Table 1 Environmental factors and allergic diseases

Factors	Design	Outcome			
		Wheeze	Asthma	Atopic dermatitis	Allergic rhinitis (Hay fever)
Basic characteristics					
Age	Cohort		*N*: 4	*N*: 5	
	Case-control		↑: 6, 7 ↓: 8		
	Cross-sectional	↑: 9, 10, 11 ↓: 12 *N*: 9 (ever), 13, 14, 15, 16, 17, 18	↑: 9 (DD), 11, 12, 17, 19, 20 ↓: 21, 22 (men), 23 *N*: 9 (ever), 10, 13, 14, 18, 22 (women), 24, 25, 26	↑: 27 *N*: 16, 24, 26, 28	↑: 16, 26, 29 ↓: 21 *N*: 9, 24
Sex (male)	Cohort	↑: 30, 31 *N*: 31, 32, 33	↑: 30, 34, 35, 36, 37, 38 ↓: 4 *N*: 32, 39, 40, 41, 42	*N*: 5, 43	
	Case-control	*N*: 44	↑: 45, 46 ↓: 7 *N*: 6, 8, 47 (grass pollen asthma), 48		
	Cross-sectional	↑: 13, 14, 17 ↓: 9, 10 (ever), 11, 15, 49 *N*: 9, 10 (current), 50	↑: 12, 14, 51 (childhood onset), 52 ↓: 9 (DD), 11, 19, 49 (current), 51 (adult onset) *N*: 9 (ever), 9, 10, 13, 24, 27, 41, 49 (ever), 51 (adolescent onset)	↓: 16, 27, 28 *N*: 24, 26	↓: 9 (ever), 49 *N*: 9, 9 (current, DD), 16, 24, 26
Socioeconomic factors					
High socioeconomic status	Cohort	*N*: 53	↑: 54 (with allergic rhinitis) ↓: 54 (without allergic rhinitis) *N*: 53	*N*: 43	↑: 54
	Case-control		↓: 45 *N*: 6		
	Cross-sectional	↑: 55	*N*: 55	*N*: 27	
High social class	Cohort			↑: 5	
	Case-control		↓: 47		
	Cross-sectional		↓: 19 *N*: 21		↑: 21
Poverty	Cohort	*N*: 33	*N*: 36		
High income	Cohort	*N*: 56	↓: 35 *N*: 33, 57		
	Case-control			*N*: 58	
	Cross-sectional	*N*: 15	*N*: 23, 24, 26	*N*: 24, 26	↑: 24, 26 *N*: 29
High education	Cohort		↓: 59 *N*: 57		
	Case-control		↓: 48		
	Cross-sectional	↓: 18 *N*: 15, 60	↓: 19, 20, 22 (men) *N*: 18, 19, 22 (women), 23, 60		↑: 60 *N*: 9
Parental high education	Cohort	*N*: 33	*N*: 33		
	Case-control		*N*: 61	↑: 58 *N*: 61	
	Cross-sectional	↑: 9, 17, 58	↑: 9 (ever), 62 ↓: 17 *N*: 9 (DD), 17	↑: 28	

Factors	Design	Outcome			
		Wheeze	Asthma	Atopic dermatitis	Allergic rhinitis (Hay fever)
Maternal higher education	Cohort	N: 30	↓: 34 N: 30, 36	N: 5, 63	
Paternal higher education	Cohort			N: 5	
Inability to see a doctor due to cost	Cross-sectional		↑: 23		
Beneficiary status (active duty vs retired or family member)	Case-control		↑: 7		
Health care coverage	Cross-sectional		↑: 23		
Medical insurance	Cross-sectional		↑: 22 (men)		
Marital status	Cohort		N: 38		
Residence					
Rural	Case-control		↓: 47 (grass pollen asthma)		
	Cross-sectional	↓: 17 N: 15	↑: 25 (girls) ↓: 17, 64 N: 20, 25 (boys), 65	↓: 64	N: 64
Farm	Cohort			N: 66	
	Cross-sectional	↑: 13 N: 67	↓: 68 N: 65, 69	N: 68	↓: 68, 69
Urban	Case-control		↑: 48		
	Cross-sectional	↑: 70	↑: 71 N: 70	N: 27	↑: 71
Urbanization	Cohort			N: 5	
Dump area	Cohort		↑: 72		
Siblings					
Number of siblings	Cohort	↑: 31	↓: 57 N: 38, 73, 74	N: 66	↓: 73, 75, 76
	Case-control	N: 77	N: 77 (wheeze + asthma)	N: 58	
	Cross-sectional	N: 50	↓: 52, 78 (asthma with allergic rhinitis) N: 24, 26	N: 24, 26	N: 24, 26, 29
Older siblings	Cohort	N: 30, 79, 80 (asthma or wheezing), 81	N: 30, 82	N: 43, 63, 79, 80, 82, 83	N: 82
	Case-control	N: 77	↓: 84 N: 77 (wheeze + asthma)		
	Cross-sectional	N: 16	↓: 51 (adult onset), 78 (asthma with allergic rhinitis) N: 51 (childhood and adolescence on set)	N: 16	↓: 16
Younger siblings	Case-control	N: 77	↓: 77 (wheeze + asthma)		
	Cross-sectional		N: 78 (asthma with allergic rhinitis)		
Brothers	Cross-sectional		↓: 78 (asthma with allergic rhinitis)		
Sisters	Cross-sectional		↓: 78 (asthma with allergic rhinitis)		
Older brothers	Cross-sectional		↓: 78 (asthma with allergic rhinitis)		
Older sisters	Cross-sectional		↓: 78 (asthma with allergic rhinitis)		
Younger brothers	Cross-sectional		N: 78 (asthma with allergic rhinitis)		
Younger sisters	Cross-sectional		N: 78 (asthma with allergic rhinitis)		
Family size	Cross-sectional	N: 15			
Crowding	Cohort	N: 31	↓: 57	↓: 83 N: 5	N: 76

Factors	Design	Outcome: Wheeze	Outcome: Asthma	Outcome: Atopic dermatitis	Outcome: Allergic rhinitis (Hay fever)
	Case-control		↓: 85	*N*: 58	
	Cross-sectional	*N*: 86	↓: 20 *N*: 86		
Anthropometric measurement					
High birth weight	Cohort	↓: 30 *N*: 80 (asthma or wheezing), 81, 87	↑: 35, 88 *N*: 38, 87	*N*: 80	↑: 89
Low birth weight	Cohort	↑: 56 (repeated wheeze), 90 *N*: 32, 56 (any wheeze), 80 (asthma or wheezing), 87	↑: 32 (ever), 34, 36 *N*: 30, 32 (DD), 35, 38, 57, 73, 74, 87, 89	*N*: 80, 89, 91	*N*: 73, 91
	Cross-sectional	*N*: 92	*N*: 93	*N*: 93	*N*: 93
Birth length	Cohort	*N*: 87	*N*: 57, 87		
Ponderal index (g/cm³)at birth	Cohort		↑: 88 *N*: 73, 94		*N*: 73
Head circumference at birth	Cohort	*N*: 87	*N*: 87, 89	*N*: 89, 91	*N*: 89, 91
Head circumference/birth weight ratio	Cohort	*N*: 87	*N*: 87, 89	*N*: 89	↓: 89
Head circumference/weight at 1 month ratio	Cohort		*N*: 89	*N*: 896	*N*: 89
Height	Cross-sectional				*N*: 99
Overweight, obesity	Cohort	*N*: 96	↑: 4, 40, 59, 97, 98, 99, 100, 94, 101 *N*: 57, 89	*N*: 43, 89	*N*: 89, 98
	Case-control		↑: 7, 8, 102 *N*: 84, 103		
	Cross-sectional	↑: 10, 14 (with sleep-disordered breathing), 15, 17, 18, 104 (current), 105, 106, 107 *N*: 14 (without sleep-disordered breathing), 104 (ever), 109	↑: 14, 17, 19, 20, 22, 23 (women), 104, 105 (women), 106, 107, 108 (women) *N*: 10, 18, 23 (men), 52, 105 (men), 108 (men), 109, 110	*N*: 110	↑: 106, 110 *N*: 95, 105
Body fat	Cross-sectional		*N*: 110	*N*: 110	↑: 110
Underweight	Cohort		↑: 98 *N*: 59, 101		↑: 98
	Case-control		*N*: 8, 102		
	Cross-sectional	↑: 17 ↓: 109 *N*: 104, 105	↑: 20, 22 (men) *N*: 17, 22 (women), 23, 104, 105		
Waist circumference	Cross-sectional	*N*: 109	↑: 108 (women) *N*: 108 (men), 109		
Maternal factors					
Maternal age	Cohort	↓: 31 *N*: 31, 33	↑: 34 *N*: 33, 36, 38, 73		*N*: 73
	Case-control		*N*: 84	*N*: 58	
	Cross-sectional	*N*: 16	*N*: 93	*N*: 16, 93	*N*: 16, 93
Maternal age at menarche	Cohort		*N*: 111	*N*: 111	*N*: 111
Maternal BMI before pregnancy	Cohort		*N*: 38		
Maternal weight gain during pregnancy	Cohort		*N*: 38, 57		
Maternal complications during pregnancy	Cohort	*N*: 80 (asthma or wheezing)		*N*: 80	
Maternal hospital admission during pregnancy	Cohort	*N*: 80 (asthma or wheezing)		*N*: 80	