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ORIGINAL ARTICLE

The Effect of Past Food Avoidance Due to Allergic Symptoms on the Growth of Children at School Age

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ABSTRACT

Background: The influence of food avoidance due to allergic symptoms in infancy on the growth of children at school age has not been well evaluated.

Methods: To determine the growth of schoolchildren who avoided eggs, milk, or wheat due to immediate allergic symptoms in infancy (food avoiders in infancy) (FAI), a questionnaire on the presence of allergic diseases, as well as present height and weight, was administered to the parents of 14,669 schoolchildren. 11,473 subjects had available data. The height and weight standard deviation scores (HtSDS and WtSDS) and body mass index percentile (BMI percentile) of each subject were calculated.

Results: FAI had significantly lower WtSDS than non-FAI (P = 0.01). Among those with avoidance at age 3 years, those who avoided two or more foods and those who avoided milk had significantly lower HtSDS than their counterparts (P = 0.02 and 0.04, respectively). FAI had a significantly lower prevalence of obesity (P = 0.01) and overweight (P = 0.002), while there was no difference in the prevalence of underweight (P = 0.58), resulting in a significantly higher prevalence of appropriate weight (P = 0.01) compared to non-FAI. Significantly lower prevalence of obesity and overweight was observed even among those who terminated the avoidance by age 3 years.

Conclusions: FAI were less likely to be obese or overweight, resulting in a higher prevalence of appropriate weight at school age. Further investigation should contribute to better management of food allergy and obesity.

KEY WORDS

body mass index, epidemiology, food avoidance, growth, schoolchildren

INTRODUCTION

The prevalence of allergic diseases has increased dramatically in children and young adults over the past few decades.[1] Food allergy constitutes a part of this increase[2,3] and is associated with a significant negative impact on quality of life.[4] Food allergy is much more common in children than in adults.[5]

At present, food avoidance is the only treatment for food allergy.[5] Parents and caregivers are concerned about growth retardation due to food avoidance in children with food allergy, and several studies have investigated this issue,[6-11] showing disturbed growth among children with elimination diet. In studies of children with atopic eczema who avoided cow's milk, their calcium intake tended to be below the estimated requirement.[12,13] However, each of these previous reports studied the present effect of ongoing food avoidance, not its future effects on height and weight at school age.

In addition to disturbed growth, excess calorie intake is another concern in children with restricted diets, as overweight or obesity may be a result of excluding foods, developing a strong attachment to calorie-dense, "safe" foods (e.g., special formula or juice), or from grazing behavior that may be allowed as a result of parental concern over diet restrictions.[14]

Thus, in order to evaluate the long-term effects of food avoidance due to allergic symptoms in infancy on height and weight at school age, we conducted a

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Table 1 Background characteristics of 11,473 subjects with sex, weight, or height data

Age, y, mean ± SD	10.8 ± 2.5
Birth order, mean ± SD	1.66 ± 0.78
Birth weight, g, mean ± SD	3,058 ± 425
Gestational age, wk, mean ± SD	39 ± 1.9
BA prevalence, *n* (%)	557 (4.9)
AD prevalence, *n* (%)	644 (5.6)
AR prevalence, *n* (%)	3,164 (27.6)
AC prevalence, *n* (%)	2,935 (25.6)
FA prevalence, *n* (%)	413 (3.6)

SD, standard deviation; BA, bronchial asthma; AD, atopic dermatitis; AR, allergic rhinitis; AC, allergic conjunctivitis; FA, food allergy.

large questionnaire-based survey to determine the growth of schoolchildren who started avoidance of eggs, milk, or wheat due to an immediate-type allergic symptoms experienced when they were under 1 year old.

METHODS

EPIDEMIOLOGIC STUDIES ON THE PREVALENCE OF ALLERGIC DISEASES IN SCHOOLCHILDREN

In June 2006, a questionnaire dealing with allergic diseases was distributed through teachers to the parents of all 14,669 children aged 7 to 15 years attending 30 randomly selected schools in Kyoto, Japan. Informed consent was obtained from the parents who responded to the questionnaires. We collected the questionnaires through the schools. This study was designated as the Allergic Schoolchildren in Kyoto (ASK) study, and was approved by the Ethics Committee of Kyoto University Graduate School of Medicine.

DEFINITION OF "FOOD AVOIDERS IN INFANCY" AND OTHER ALLERGIC DISEASES

Details of the definition of food allergy and food avoidance have been described previously.[15] In short, we asked the following questions: (1) Does your child ever have allergic symptoms, such as skin symptoms like hives or respiratory symptoms like cough/wheeze, within 1 to 2 hours after ingesting a particular food? (2) Has your child ever avoided particular foods due to these symptoms? (3) If so, what are the kinds of foods and the duration of avoidance? Those who answered "yes" to both questions 1 and 2 were regarded as having either a past history or present illness of immediate-type food allergy, and the kinds of foods avoided were tabulated. Among them, those who avoided any of the three major food allergens (eggs, milk or wheat) from less than 1 year of age were defined as "food avoiders in infancy" (FAI [total]). FAI (total) was further divided into several subgroups as follows. FAI (outgrown by age 3 years) was defined as those who could terminate the avoidance for all three foods by 3 years old. FAI (continuous at age 3 years) was defined as those who continued avoidance for any of the three foods at age 3 years. FAI (outgrown by age 3 to 6 years) was defined as those who could terminate the avoidance of all three foods between age 3 to 6 years. FAI (continuous at age 6 years) was defined as those who continued avoidance for any of the three foods at age 6 years.

The questionnaire on the prevalence of four other allergic diseases (bronchial asthma [BA], atopic dermatitis [AD], allergic rhinitis [AR], and allergic conjunctivitis [AC]) was based on and comparable to the one used by the International Collaborative Study of Asthma and Allergies in Childhood (ISAAC)[16] and was prepared and validated by the Study Group of Epidemiology of Allergic Diseases founded by the Japanese Ministry of Health and Welfare in 1993.[17] Definitions of these allergic diseases based on the questionnaire are described elsewhere.[18]

DEFINITION OF HtSDS AND WtSDS, AND CATEGORIES OF OBESE, OVERWEIGHT, AND UNDERWEIGHT

In Japanese schools, a physical examination is conducted at least once every 4 months on all children, during which time specially trained school nurses measure the height and weight of the children according to a standard technique. The results are reported to the parents in writing. In the questionnaire, parents were asked to report the height and weight of their children according to the latest physical examination. Based on the data, age- and sex-stratified height and weight standard deviation scores (HtSDS and WtSDS, respectively), as well as body mass index (BMI, calculated as a weight in kilograms divided by height in meters squared) percentiles were calculated. Subjects were divided into four groups according to the BMI percentile: obese ($\geq$95th), overweight (85th to 94th), appropriate weight (5th to 84th) and underweight (<5th).[14]

FAST FOOD CONSUMPTION AMONG SCHOOLCHILDREN

In order to explore the eating habits of the children, we asked the following questions: "How often does your child eat fast food, such as hamburgers or fried chicken?" The response options were: less than once a month, 1 to 2 times a month, once a week, once every 2 to 3 days, and every day.

STATISTICAL ANALYSIS

Following the descriptive statistics, we developed univariate and multivariate logistic regression models to evaluate the effects of food allergy in infancy on height and weight at school age. In multivariate

Table 2 Comparison of HtSDS and WtSDS between subgroups (mean ± SD)

(A) Comparison between food avoiders in infancy (total) and non-food avoiders in infancy

	FAI (total) (n = 491)	Non-food avoiders in infancy (n = 10,982)	P value (univariate)	P value (multivariate)
HtSDS	-0.02 ± 0.98	0.00 ± 1.00	0.73	0.73
WtSDS	-0.11 ± 0.88	0.01 ± 0.98	0.001	0.01

HtSDS, height standard deviation score; WtSDS, weight standard deviation score; FAI, food avoiders in infancy.

(B) Comparison between food avoiders in infancy (outgrown by age 3 years) and non-food avoiders in infancy

	FAI (outgrown by age 3 years) (n = 322)	Non-FAI (n = 10,982)	P value (univariate)	P value (multivariate)
HtSDS	0.08 ± 0.96	0.00 ± 1.00	0.19	0.45
WtSDS	-0.04 ± 0.87	0.01 ± 0.98	0.30	0.20

HtSDS, height standard deviation score; WtSDS, weight standard deviation score; FAI, food avoiders in infancy.

(C) Comparison between food avoiders in infancy (outgrown by age 3 to 6 years) and non-food avoiders in infancy

	FAI (outgrown by age 3 to 6 years) (n = 112)	Non-FAI (n = 10,982)	P value (univariate)	P value (multivariate)
HtSDS	-0.19 ± 1.07	0.00 ± 1.00	0.05	0.07
WtSDS	-0.20 ± 0.95	0.01 ± 0.98	0.03	0.01

HtSDS, height standard deviation score; WtSDS, weight standard deviation score; FAI, food avoiders in infancy.

(D) Comparison between food avoiders in infancy (continuous at age 6 years) and non-food avoiders in infancy

	FAI (continuous at age 6 years) (n = 57)	Non-FAI (n = 10,982)	P value (univariate)	P value (multivariate)
HtSDS	-0.19 ± 0.89	0.00 ± 1.00	0.15	0.35
WtSDS	-0.33 ± 0.74	0.01 ± 0.98	0.01	0.01

Ht SDS, height standard deviation score; Wt SDS, weight standard deviation score; FAI, food avoiders in infancy.

analysis, data were adjusted for age, sex, birth order, birth weight, gestational age, family history of allergy, present food allergy, and other allergic diseases, unless indicated otherwise. P values less than 0.05 were considered statistically significant. All statistical analyses were carried out using SPSS software (Version 17.0; SPSS, Chicago, IL, USA).

RESULTS

PROFILES OF THE PARTICIPANTS

Among a total of 14,669 questionnaires, 13,215 were collected (response rate, 90.1%). Among the collected questionnaires, sex, present height, and present weight were available for 11,473 children (78.2% of total population). Background characteristics of those children were shown in Table 1. We used the data from those children for the subsequent analysis. Among them, there were 491 FAI, which were subdivided into 322 FAI (outgrown by age 3 years), 112 FAI (outgrown by age 3 to 6 years), 57 FAI (continuous at age 6 years). Consequently, there were 169 FAI (continuous at age 3 years), which was the sum of 112 FAI (outgrown by age 3 to 6 years) and 57 FAI (continuous at age 6 years).

COMPARISON OF HtSDS AND WtSDS BETWEEN SUBGROUPS

FAI (total) showed significantly lower WtSDS (P = 0.01) than non-FAI (Table 2A). While FAI (outgrown by age 3 years) showed no significant difference in WtSDS (Table 2B) compared to non-FAI, both FAI (outgrown by age 3 to 6 years) (Table 2C) and FAI (continuous at age 6 years) (Table 2D) showed significantly lower WtSDS (P = 0.01, respectively) than non-FAI. Throughout the subgroup analysis, no significant difference in HtSDS was observed between any FAI subgroups and non-food avoiders (Table 2A to C).

There was no significant difference in HtSDS or WtSDS among FAI (total) according to the number and kinds of foods avoided (data not shown). However, for FAI (continuous at age 3 years), those who avoided two or more foods in infancy (Table 3A) and those who avoided milk in infancy (Table 3B) had significantly lower HtSDS than those who avoided one food and those who did not avoid cow's milk, respectively.

COMPARISON OF BMI PERCENTILE DISTRIBUTIONS BETWEEN SUBGROUPS

The distribution of BMI percentiles according to the presence or absence of food avoidance in infancy is

Table 3 HtSDS and WtSDS according to (**A**) the number and (**B**) the kinds of avoided foods among food avoiders in infancy (continuous at age 3 years)

(A) Comparison according to the number of avoided foods

Number of avoided foods	HtSDS (mean ± SD)	*P* value (univariate)	*P* value (multivariate)
1 (*n* = 73)	0.00 ± 1.09	0.04†	0.02†
2 (*n* = 50)	-0.35 ± 0.95		
3 (*n* = 46)	-0.31 ± 0.91		

Number of avoided foods	WtSDS (mean ± SD)	*P* value (univariate)	*P* value (multivariate)
1 (*n* = 73)	-0.13 ± 0.95	0.14†	0.17†
2 (*n* = 50)	-0.36 ± 0.86		
3 (*n* = 46)	-0.30 ± 0.78		

†Data of those who avoided one food were compared with others.

(B) Comparison according to the kind of foods

Food	HtSDS (mean ± SD)		*P* value (univariate)	*P* value (multi-variate)
	Avoided	Not avoided		
Eggs	-0.18 ± 1.02 (*n* = 164)	0.44 ± 0.74 (*n* = 5)	0.58	0.58
Milk	-0.33 ± 0.93 (*n* = 91)	-0.02 ± 1.07 (*n* = 78)	0.04	0.04
Wheat	-0.34 ± 87 (*n* = 55)	-0.11 ± 1.06 (*n* = 114)	0.16	0.92

Food	WtSDS (mean ± SD)		*P* value (univariate)	*P* value (multivariate)
	Avoided	Not avoided		
Eggs	-0.23 ± 0.89 (*n* = 164)	-0.63 ± 0.38 (*n* = 5)	0.32	0.23
Milk	-0.33 ± 0.83 (*n* = 91)	-0.14 ± 0.94 (*n* = 78)	0.16	0.20
Wheat	-0.33 ± 0.74 (*n* = 55)	-0.20 ± 0.94 (*n* = 114)	0.37	0.53

shown in Table 4. FAI (total) had a significantly lower prevalence of obesity or overweight than non-FAI in both univariate ($P = 0.03$ and 0.01, respectively) and multivariate ($P = 0.01$ and 0.002, respectively) analyses. There was no significant difference in the prevalence of underweight between FAI (total) and non-FAI. Accordingly, FAI (total) showed a significantly greater prevalence of appropriate weight than non-FAI in multivariate analysis ($P = 0.01$).

Similar results were obtained in subgroup analysis. FAI (outgrown by age 3 years) had significantly lower prevalence of obesity and overweight ($P = 0.02$ and 0.04, respectively). Also, FAI (outgrown by age 3 to 6 years) and FAI (continuous at age 6 years) showed significantly lower prevalence of overweight ($P = 0.02$ and 0.03, respectively), than non-FAI, respectively (data not shown). There was no significant difference in the prevalence of underweight between any subgroup and non-FAI (data not shown), resulting in greater prevalence of appropriate weight than non-FAI, although there was no statistic significance in subgroup analysis.

FAST FOOD CONSUMPTION AMONG SCHOOLCHILDREN

In order to see whether there were differences in eating habits among children with or without FAI, the frequency of fast food consumption was compared among subgroups. Compared to non-FAI, both FAI (total) and FAI (continuous at age 3 years) had a significantly lower intake of fast food (response of "less than once a month") (Table 5).

DISCUSSION

This is, to our knowledge, the first report examining the influence of food avoidance due to allergic symptoms in infancy on children's growth at school age. One strength of our study is that it is a large-scale survey including 11,473 general schoolchildren (78.2% of total subjects). There have been several reports investigating the association of obesity and atopy and allergic symptoms in children, with mixed results.[19-25] We also previously showed a higher prevalence of asthma among female schoolchildren with obesity.[18] These studies showed the association of obesity and present atopic status but did not investigate the effect of former allergic status on present obesity.

We showed that FAI (total) had significantly lower WtSDS at school age. Moreover, FAI (outgrown by age 3 to 6 years) and FAI (continuous at age 6 years) also showed significantly lower WtSDS, while FAI (outgrown by age 3 years) did not show any difference in WtSDS, compared to non-FAI. Importantly, among FAI (continuous at age 3 years), those with avoidance of two or more foods or avoidance of milk had lower HtSDS than those with avoidance of one food or non-avoidance of milk, respectively. These results agree with previous studies showing that children who consumed smaller amounts of dietary calcium due to milk allergy did not grow as tall as those without milk allergy,[7-10] although low intake of calcium has not been confirmed in our group. These results indicate the need for regular nutritional assessment by a qualified dietitian of children who have to continue food avoidance after infancy, as well as the termination of food avoidance as early as possible, in order to prevent growth problems at school age. Especially, based on the present finding, children who are milk allergic may need monitoring and parents need education at the time of diagnosis to prevent the possibility of not reaching their linear growth potential.

On the other hand, while FAI (total) had a significantly lower prevalence of obesity and overweight than non-FAI, there was no significant difference in the prevalence of underweight between the two groups. This resulted in a greater prevalence of ap-

Table 4 BMI percentile distribution of schoolchildren-comparison between food avoiders in infancy (total) and non-food avoiders in infancy

BMI percentile	Prevalence	*P* value (univariate)	*P* value (multi-variate)	Adjusted OR (95% CI)
Obese (≥95th)				
Non-FAI	591/10,982 (5.4%)			
FAI (total)	15/491 (3.1%)	0.03	0.01	0.49 (0.28-0.86)
Overweight (85th-94th)				
Non-FAI	1685/10,982 (15.3%)			
FAI (total)	55/491 (11.2%)	0.01	0.002	0.60 (0.43-0.82)
Appropriate (5th-84th)				
Non-FAI	8731/10,982 (79.5%)			
FAI (total)	406/491 (82.7%)	0.09	0.01	1.41 (1.08-1.85)
Underweight (<5th)				
Non-FAI	566/10,982 (5.2%)			
FAI (total)	30/491 (6.1%)	0.35	0.58	1.13 (0.73-1.74)

FAI, food avoiders in infancy; OR, odds ratio; CI, confidence interval; BMI, body mass index.

Table 5 Frequency of schoolchildren eating fast food less than once a month

	Frequency	OR (95% CI)	*P* value
Non-FAI (*n* = 10,982)	3,264 (29.7%)	reference	
FAI (total) (*n* = 491)	171 (34.8%)	1.26 (1.05-1.53)	0.02†
FAI (continuous at age 3 years) (*n* = 169)	69 (40.8%)	1.63 (1.20-2.22)	0.002†

†Compared to non-food avoiders in infancy.

OR, odds ratio; CI, confidence interval.

propriate weight in FAI (total) compared to non-FAI. These results suggest that food avoidance in infancy contributes, unexpectedly, to a reduced risk of obesity or overweight at school age. Lower prevalence of obesity or overweight was also seen among FAI (outgrown by age 3 years) and FAI (outgrown by age 3 to 6 years), indicating that, in addition to present food avoidance, former food avoidance also affected the results later at school age.

One possible mechanism by which food avoidance in infancy reduce the risk of obesity or overweight at school age might be the change in dietary lifestyles associated with food avoidance. It can be speculated that total caloric consumption and fat intake in food avoiders are lower due to the continuation of an elimination diet since infancy. Furthermore, families of children with food allergy may have a tendency to establish "healthier" eating habits, such as less meat and more vegetables, due to concern for the development of the atopic march. Foods rich in antioxidants (fruits and vegetables) and n-3 polyunsaturated fatty acids (oily fish), such as in the Mediterranean diet, may contribute to the prevention of allergy.[26] The fact that lower prevalence of obesity and overweight could be seen even among those who terminated the avoidance by age 3 years suggest that they have continued such healthier dietary habits until school age. In support of this possibility, we found that FAI consumed significantly less fast food (less than once a month) compared to non-food avoiders in infancy, suggesting the healthier dietary habits among FAI. However, this data is obviously not enough and needs more detailed survey on the dietary lives of food-allergic children. In the meanwhile, recent National Health and Nutrition Examination Survey (NHANES) data in the United States have shown that obesity might be a contributor to the increased prevalence of allergy, especially food allergy, in children.[25] In the Discussion section of the paper,[25] the possibility of reverse causation was mentioned; e.g., children with milk allergy drink more juice or sweetened beverages, which have been shown to increase obesity in children. This possibility apparently contradicts our findings and needs further evaluation.

Another possibility is that hyperpermeability of the intestinal barrier due to allergic mucosal inflammation[27] might lead to lower weight gain. In experiments with a murine food allergy model, wild-type mice exposed to a food allergen had weight loss accompanied by disturbed gut integrity and mucosal inflammation, while IL-4-/- mice did not.[28] Th2/IL-4-dependent mechanisms have been shown to be involved in this intestinal pathology. Although food-allergic children should avoid causative foods, trace amounts of allergens can still be present in food. This inadvertent exposure to food allergens might cause similar mucosal inflammation, despite the fact it would be very mild, which could lead to smaller weight gain and less obesity.

Limitation of the study is that, due to its large scale, it was not possible to strictly confirm whether those who avoided the foods were really food allergic or simply avoiding the foods due to unspecific symptoms. However, parents were asked about the exis-

tence of food-induced allergic reactions, and those avoiding foods without any food-specific immediate-type reactions were excluded from the analysis, making the data more reliable than simply including all those who avoided foods in the analysis.

In conclusion, present data showed that, although schoolchildren who used to be FAI had the risk of lower WtSDS and HtSDS, they were less likely to be obese or overweight and more likely to be in the appropriate weight range. Further investigation to elucidate the underlying mechanisms for the negative relationship between food avoidance in infancy and obesity at school age should contribute to understanding and better management of allergy and obesity, both of which have been on the rise and are serious problems among children.

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