ORIGINAL

Overweight is associated with allergy in school children of Taiwan and Vietnam but not Japan

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Abstract : We collected information concerning diagnosed allergy from 2027 school children in Japan, Taiwan and Vietnam. Children were classified according to the age and sex-specific body mass index (BMI) per-age as indicator of weight status. Logistic regression was performed to examine the relationship between percentiles of BMI-per-age and allergy. Compared with children at the lowest percentile group Taiwanese children at>85th percentile group showed a tendency toward higher risk of allergy (OR=1.79, 95% CI 0.98 to 3.27 ; *p*=0.060). When children with rhino-conjunctivitis were excluded from the analysis the association reached statistical significance (OR=2.89, 95% CI 1.08 to 7.75 ; *p* = 0.035). Vietnamese children at>85th percentile group showed a significantly higher risk of allergy (OR = 2.34, 95% CI 1.06 to 5.17 ; *p*=0.035). This association was not observed when children with atopic dermatitis or food allergy were excluded from the analysis, although a tendency toward increased risk of allergy at BMI-per-age>85th percentile remained. Our study sample of Japanese school children showed no association between being overweight and allergy. J. Med. Invest. 52 : 33-40, February, 2005

Keywords **:** *allergy, body mass index, school children, overweight.*

INTRODUCTION

The prevalence of allergic conditions has increased greatly in most countries (1-3). In Japan, the National Research on Allergy that took place in 1992 reported over 33% of males and 36% of females had self-reported allergy symptoms, which represents about 1/3 of the population (4). This is encompassed with increasing number of school-children experiencing difficulty at school because of allergy, and school absenteeism was found significantly higher among allergic school children (5). This increase took place in a relatively short time for any genetic change as a causative factor, and most studies have focused on the environmental factors to explain why the number of affected individuals has increased to the present levels. Several studies reported a positive correlation between overweight and asthma. Luder *et al.* found that overweight was associated with asthma in 2 to 18 year-old black and Hispanic children (6). Huang *et al.* reported a positive association between school-age girls in the highest quintile of body mass

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index (BMI) and the risk of asthma symptoms, atopy and rhinitis (7). Camargo *et al.* reported an increased risk of developing asthma at increased levels of BMI in a 4-year longitudinal study (8). Chen *et al.* evaluated the two-year incidence of asthma in adult Canadians and found that a baseline BMI$>$30kg/m^2 was a significant predictor of asthma in women (9).

In the present study we examined the relationship between overweight and IgE mediated allergic conditions including bronchial asthma, allergic rhinoconjunctivitis, atopic dermatitis and food allergy in school children in Japan, Taiwan and Vietnam.

METHODOLOGY

Study population : Study subject were school children from 9 to 13 years old (n=2027) from Japan, Taiwan and Vietnam. In Japan and Taiwan, participants were recruited from 2 schools in Tokushima Prefecture (n=584) and 4 schools in a central district of Taiwan (n=802). Children from Vietnam were randomly selected from those who referred to a Child Nutrition Center of Ho Chi Minh City for reasons other than allergy (n=641). Parents of all participants gave written informed consent before being included in the study. The study was approved by the Ethical Committee of Tokushima University for Human Studies and was in accordance with the ethical procedure of each study center.

Prevalence of allergy : A written, self-completed questionnaire modified from the ISAAC core questionnaire concerning symptoms of allergy (10) as well as physician-diagnosed allergy was addressed to all participants. Bronchial asthma symptom was defined as a positive answer to the question" Have you ever had wheezing or whistling in the chest at breathing ? ". Atopic dermatitis symptom was defined as a positive answer to the question" Have you ever had itchy rash in the skin ? ". Allergic rhino-conjunctivitis symptoms was defined as a positive answer to either one or both of the next question" Have you ever had snot and blocked nose without having a cold ? "and" Have you ever had red, swollen and watery eyes ? ". Food allergy symptoms was defined as a positive answer to the questions" Have you ever had rush in the skin and sickness within an hour of eating some food ? "and" Were these symptoms repeated each time the same food was eaten ? ". Prevalence of bronchial asthma, allergic rhinitis, allergic conjunctivitis, atopic dermatitis, and food allergy were defined as an answer of yes to the question" Was your allergy diagnosed by a physician ? ". The original study protocol did not include food allergy in Taiwan, where was added a posteriori. As a consequence, the number of children from Taiwan to whom food allergy was evaluated was reduced to 448 children. Children were defined as having allergy if allergy diagnosed by a physician was reported. Children with no physician-diagnosed allergy or allergic symptoms were included as control group. Data of passive smoking (Is there anyone who often smokes around you?), industrial dust emission in the neighborhood (Is there any factory that discard much smoke or smell in your neighborhood?), current pet ownership (Do you have pets at home?) and use of matting as flooring (Do you use rug or matting as flooring at home?) were collected as potential confounders.

Anthropometry : Body weight was measured to the nearest 0.1 kg with an electronic scale, with the child dressed in light clothing. Height was measured to the nearest 0.5 cm with a wall-mounted stadiometer. Body weight and height were measured in all children by trained health personnel following standard procedures. Body mass index (BMI), defined as the weight (kg) of the individual divided by the square of the height (m), was determined in all children and assigned to one of three categories according to age-and sex-specific BMI-per-age ($<15^{th}$, 15^{th} to 85^{th} and $>85^{th}$ percentile groups). The BMI-per-age cut-off points used were based on WHO standard reference (11).

Statistical Analysis : Analysis of variances (ANOVA) was used to evaluate differences in continuous variables between children with physician-diagnosed allergy, children with allergic symptoms but no physician diagnosed allergy, and children without allergy or allergic symptoms. Body weight was transformed to decimal logarithm and normalized for statistical analysis. Chi-square test was used to evaluate differences in categorical variables between groups. Logistic regression analysis was performed to examine the relationship between BMI-per-age and allergy. Other variables included in the model were age, sex, parental history of allergy, passive smoking, industrial dust emission in the neighborhood, current pet ownership, and use of matting as flooring as potential confounders. All outcomes with $p<0.05$ were considered statistically significant. Data processing and statistical analysis were conducted using the SPSS version 10.0 software package (SPSS Inc, Chicago).

RESULTS

The study originally included 2403 children aged

7 to 13 years old from Japan, Taiwan and Vietnam. The current analysis was limited to the 2027 children (84.4%) in the age-rank of 9 to 13 for whom BMI-per-age grouping was available based on WHO references (11). General characteristics of the study population are shown in Table 1. Reported passive smoking was significantly higher among Vietnamese children (69.9%, n=448) than Japanese (60.3%, n=352) and Taiwanese (64.0%, n=513) children (p=0.003). Reported current pet ownership was slightly higher among Vietnamese children (39.0%, n=250) than Japanese (34.8%, n=203) and Taiwanese (34.5%, n=277) children. Yearly used of matting as

Table 1. General characteristics of the study population[1,2]

	With allergy	With symptoms	Without allergy	p-value[3]
Japan, n (%)	244(41.8)	200(34.2)	140(24.0)	
Male, n (%)	127(52.0)	92(46.0)	79(56.4)	0.059
Age, y	11.5±1.2	11.4±1.3	11.8±1.3	0.005
Height, cm	146.5±9.7	148.3±9.9	150.0±9.7	0.089
Weight, kg[4]	40.6±10.1	43.1±11.7	43.7±10.4	0.435
BMI, kg/m^2	18.8±3.5	19.4±4.0	19.2±3.3	0.639
Family history of allergy, n (%)	75(30.7)	18(9.0)	17(12.1)	0.349
Passive smoking, n (%)	145(59.9)	126(63.3)	81(58.7)	0.392
Pets at home, n (%)	82(33.6)	65(32.5)	56(40.0)	0.156
Industrial dust in the neighborhood, n (%)	25(10.3)	16(8.0)	8(5.8)	0.439
Use of matting, n (%)	85(35.6)	71(35.9)	37(28.0)	0.138
Taiwan, n (%)	212(26.4)	269(33.5)	321(40.0)	
Male, n (%)	101(47.6)	136(50.6)	144(44.9)	0.168
Age, y	11.2±0.7	11.1±0.7	10.8±0.8	<0.001
Height, cm	140.8±7.6	146.5±0.8	143.9±38.8	0.001
Weight, kg[4]	40.7±8.4	41.4±10.0	38.8±10.1	<0.001
BMI, kg/m^2	18.8±3.1	19.2±3.6	18.6±3.7	0.014
Family history of allergy, n (%)	31(14.6)	45(16.9)	32(10)	0.011
Passive smoking, n (%)	132(62.9)	177(66.0)	204(63.8)	0.562
Pets at home, n (%)	67(31.8)	110(40.9)	100(31.3)	0.015
Industrial dust in the neighborhood, n (%)	25(11.9)	29(10.9)	18(5.7)	0.020
Use of matting, n (%)	81(38.4)	107(40.5)	124(38.8)	0.662
Vietnam, n (%)	162(25.3)	319(49.8)	160(25.0)	
Male, n (%)	88(54.3)	162(50.8)	70(43.8)	0.147
Age, y	9.6±0.7	9.5±0.7	9.6±0.7	0.485
Height, cm	134.6±6.8	132.7±7.3	133.5±6.9	0.266
Weight, kg[4]	30.4±7.6	28.2±7.0	28.6±6.7	0.432
BMI, kg/m^2	16.7±3.1	15.8±2.7	15.9±2.5	0.424
Family history of allergy, n (%)	135(83.3)	192(60.2)	77(48.1)	0.012
Passive smoking, n (%)	113(69.8)	223(69.9)	112(70.0)	0.983
Pets at home, n (%)	58(35.8)	131(41.1)	61(38.1)	0.536
Industrial dust in the neighborhood, n (%)	61(37.7)	99(31.0)	32(20.0)	0.011
Use of matting, n (%)	150(92.6)	270(84.6)	143(89.4)	0.157

[1] Children with diagnosed allergy compared to children with no allergy or allergy symptoms (those children with allergy symptoms were excluded from the control group.

[2] Participants with no answer in questions regarding environmental characteristics and family history of allergy were treated as missing values in the analysis.

[3] ANOVA with post-hoc Bonferroni (values are mean±SD), Chi-square for categorical variables

[4] Weight was log-transformed for statistical analysis

flooring was significantly higher among Vietnamese children (87.8%, n=563) than Japanese (33.0%, n=193) and Taiwanese (38.9%, n=312) children ($p<0.001$). Similarly, industrial dust emission in the neighborhood was significantly higher among Vietnamese children (30.0%, n=192) than Japanese (8.4%, n=49) and Taiwanese (9.0%, n=72%) children ($p<0.001$). Prevalence of allergy was higher in Japan (n=244, 41.8%) than in Taiwan (n=212, 26.4%) and Vietnam (n=162, 25.3%). Allergic rhino-conjunctivitis was the most prevalent allergy among Japanese (n=172, 29.5%) and Taiwanese (n=142, 17.7%) children. In Vietnam, atopic dermatitis was the most prevalent allergic disease (n=94, 14.7%). There was no gender difference in the prevalence of allergy. In univariate analysis, allergy was positively associated with age among Japanese children, with age, current pet ownership, industrial dust emission in the neighborhood and parental history of allergy among Taiwanese children, and industrial dust emission in the neighborhood and parental history of allergy among Vietnamese children. Surprisingly, we observed no association between allergy and parental history of allergy in the Japanese group.

Japanese and Taiwanese children showed increasing prevalence of allergy at higher percentile groups (in the Japanese group, 27.5%, 34.7% and 37.3% in the $<15^{th}$, 15^{th} to 85^{th} and $>85^{th}$ percentile groups, respectively ; in the Taiwanese group, 29.8%, 32.1% and 39, 3% in the $<15^{th}$, 15^{th} to 85^{th} and $>85^{th}$ percentile groups, respectively). Prevalence of allergy among Vietnamese children was similar in all percentile groups (52.2%, 50.5% and 57.9% in the $<15^{th}$, 15^{th} to 85^{th} and $>85^{th}$ percentile groups, respectively).

To evaluate the association between BMI-per-age and allergy we performed logistic regression analysis, unadjusted and adjusted by sex, age, industrial dust emission in the neighborhood, current pet ownership, yearly use of matting as flooring and parental history of allergy (Table 2). We observed no association be-

Table 2. Unadjusted and adjusted odds ratios (OR) and 95% confidence intervals (CI) of allergies in relation to BMI-per-age in Japanese, Taiwanese and Vietnemese children[1]

	<15 th percentile	15^{th}-85^{th} percentile		$>85^{th}$ percentile	
		OR(95% CI)	p-value	OR(95% CI)	p-value
Japan					
Unadjusted	1.00	0.73(0.40, 1.35)	0.316	0.83(0.40, 1.73)	0.620
Adjusted	1.00	0.86(0.43, 1.71)	0.659	0.82(0.37, 1.84)	0.629
Bronchial asthma excluded	1.00	0.88(0.42, 1.84)	0.740	0.87(0.37, 2.06)	0.751
A. dermatitis excluded	1.00	0.86(0.42, 1.74)	0.669	0.82(0.36, 1.88)	0.645
Rhino-conjunctivitis excluded	1.00	0.49(0.21, 1.16)	0.103	0.72(0.27, 1.93)	0.514
Food allergy excluded	1.00	0.93(0.45, 1.90)	0.836	0.96(0.42, 2.20)	0.930
Taiwan					
Unadjusted	1.00	1.17(0.72, 1.89)	0.529	1.37(0.79, 2.40)	0.264
Adjusted	1.00	1.32(0.79, 2.21)	0.289	1.79(0.98, 3.27)	0.060
Bronchial asthma excluded	1.00	1.15(0.66, 1.98)	0.623	1.39(0.72, 2.67)	0.324
A. dermatitis excluded	1.00	1.04(0.60, 1.83)	0.884	1.52(0.78, 2.93)	0.216
Rhino-conjunctivitis excluded	1.00	1.89(0.78, 4.58)	0.189	2.89(1.08, 7.75)	0.035
Food allergy excluded	1.00	1.19(0.55, 2.61)	0.657	1.93(0.80, 4.67)	0.144
Vietnam					
Unadjusted	1.00	1.19(0.74, 1.91)	0.479	2.60(1.29, 5.26)	0.008
Adjusted	1.00	1.25(0.74, 2.12)	0.398	2.34(1.06, 5.17)	0.035
Bronchial asthma excluded	1.00	1.45(0.82, 2.58)	0.203	2.43(1.03, 5.72)	0.043
A. dermatitis excluded	1.00	1.05(0.52, 2.10)	0.899	2.67(1.00, 7.18)	0.051
Rhino-conjunctivitis excluded	1.00	1.05(0.59, 1.89)	0.861	2.36(1.01, 5.52)	0.048
Food allergy excluded	1.00	1.24(0.72, 2.12)	0.433	2.17(0.96, 4.92)	0.062

[1] Odds ratios were estimated for all allergies compared with the lowest percentile group, unadjusted and adjusted for potential confounders. The adjusted model included sex, age, parental history of allergy, passive smoking, current pet ownership, industrial dust in the neighborhood and use of matting as flooring as potential confounders. Adjusted odds ratios were further estimated excluding one type of allergy at a time to evaluated its effect compared to the risk of all allergies.

tween BMI-per-age and allergy among Japanese children, even after adjusting for possible confounders. Among Taiwanese children, those in the highest percentile of BMI-per-age showed a tendency toward an increased risk of allergy after adjustment for potential confounders (OR=1.79, 95% CI 0.98 to 3.27; p=0.060). Among Vietnamese children, unadjusted odds of reporting physician diagnosed allergy was significantly higher at the highest percentile of BMI-per-age (OR= 2.60, 95% CI 1.29 to 5.26 ; p=0.008). This association remained even after adjustment for potential confounders (OR=2.34, 95% CI 1.06 to 5.17 ; p=0.035).

In order to evaluate the effect of BMI-per-age in specific allergic diseases, we repeated the analysis excluding children with a specific allergic disease at a time to observe the variation in the association between BMI-per-age and allergy. We performed this analysis to be able to evaluate the effect of BMI-per age on specific allergies without reducing the number of allergy cases in the statistical analysis. We observed no association between BMI-per-age and allergies among Japanese children (Table 2). Among Taiwanese children, the association between BMI-per-age and allergies was strengthen when children with rhino-conjunctivitis were excluded from the analysis, reaching statistical significance (OR=2.89, 95% CI 1.08 to 7.75 ; p =0.035) suggesting that BMI-per-age was not associated with rhino-conjunctivitis among Taiwanese children. No association was observed when other allergy cases were excluded from the analysis. When we performed this procedure in the Vietnamese group, the association between BMI-per-age and allergies persisted when we excluded children with bronchial asthma (OR=2.43, 95% CI 1.03 to 5.72 ; p=0.043) or rhino-conjunctivitis (OR=2.36, 95% CI 1.01 to 5.52 ; p=0.048). We observed a not significant tendency towards an increased risk of allergies in the highest percentile of BMI-per-age when children with atopic dermatitis (p=0.051) or food allergy (p=0.062) were excluded from the analysis. These results suggest that BMI-per-age was positively associated with a risk of all allergies and this association was strongest for atopic dermatitis and food allergy among Vietnamese children.

DISCUSSION

In the present study we observed two different patterns in the relation between BMI and allergies. BMI-per-age was not associated with allergy in Japanese school children. However, our results from Taiwanese and Vietnamese children suggest that being overweight increased the risk of allergy to about 1.8 to 2.3 times the risk observed at the lowest percentile group. We repeated the logistic regression analysis excluding one type of allergy case at a time to evaluate which allergies were more likely to be associated with BMI-per-age. In Taiwanese children, the exclusion of cases with bronchial asthma, atopic dermatitis or food allergy approached the odds ratio to unity, while the exclusion of cases with rhino-conjunctivitis strengthened the association between BMI-per-age and allergies. These results suggest that in our Taiwanese study sample the risk of having bronchial asthma, atopic dermatitis or food allergy, but not rhino-conjunctivitis, increases 2.9 times in children at the $>85^{th}$ percentile group compared to those in the lowest percentile group, while the risk of having allergic rhino-conjunctivitis seems unrelated to increases in BMI-per-age. On the other hand, in Vietnamese children the exclusion of cases with bronchial asthma or allergic rhino-conjunctivitis did not modify the association between BMI-per-age and all allergies, while the exclusion of atopic dermatitis or food allergy reduced the strength of the association (p=0.051 and p=0.062, respectively) although the tendency towards increased risk of allergy in the highest percentile group remained. These results may indicate that the association between BMI-per-age and bronchial asthma or allergic rhino-conjunctivitis is low compared to that observed with atopic dermatitis or food allergy among Vietnamese children. The lack of association observed when cases of atopic dermatitis were excluded from the analysis might also be attributed to a reduced number of allergy cases, as atopic dermatitis was the main type of allergy among Vietnamese children and the tendency toward an increased risk of allergies at the highest percentile group remained (OR=2.67, p= 0.051).

Previous studies on overweight and allergy in children reported conflicting results. Somerville and colleagues found that overweight in 5 to 11 year old children, as determined by skinfold thickness and/or weight for height, was positively associated to wheezing and other respiratory symptoms but negatively associated to others (12). Schwartz and colleagues reported a significant association of skinfold thickness as well as BMI to asthma symptoms but not to diagnosed asthma (13). Gold and colleagues reported a positive association between asthma and BMI in school children (14). Luder and colleagues found a significant association between BMI and asthma in a 2 to 18 year-old children sample (6). A survey carried out in 13 to 15 year-old students of Taiwan found a positive association between BMI and atopy and allergic symptoms in girls but not in boyss (7).

Chinn and Rona reported that the odds ratio for trends in asthma varied in less than 0.01 adjusted or unadjusted by BMI and concluded that overweight could not explain the increases in the prevalence of asthma (15). A more recent longitudinal study reported an increased asthma incidence in overweight and obese 7 to 18 year-old children and adolescents (16). Such controversial results suggest that, if there is an association between BMI and allergy, several mechanisms might be involved.

Even though most studies on overweight and allergy focus on asthma and rhino-conjunctivitis, the results of our study suggest that overweight is associated with an increased risk of bronchial asthma, atopic dermatitis and food allergy in school children of Taiwan but not with allergic rhino-conjunctivitis, while in school children of Vietnam, the risk of all allergies seemed to be increased at higher BMI levels.

Due to the cross-sectional design of our study we cannot determine whether overweight preceded the diagnosis of allergy. It was suggested that the relationship between asthma and obesity might be due to a reduced physical activity in asthmatic children after the diagnosis (17). However, this issue was clearly addressed by Gilliland *et al*. In a 5-year longitudinal study, Gilliland and colleagues found an increased risk of newly diagnosed asthma in overweight school children (16). These works clearly addressed the issue of directionality, that is, obesity is a risk factor for developing asthma in the future. Moreover, in our study being overweight was associated with allergies other than bronchial asthma where a reduction in physical activity after diagnosis is not expected, and consequently our results are not consistent with the hypothesis of overweight after diagnosis due to lifestyle changes after diagnosis.

It was also suggested that the association between overweight and asthma might be caused by a reduction in the respiratory tract due to local deposition of fatty tissue, as well as an over-diagnosed asthma in obese subjects (18). However, this hypothesis can only be applied for bronchial asthma and the obstruction of the respiratory tract is more likely to occur at extreme obesity, while there was no extreme obesity in our study sample.

A suggested plausible mechanism by which obesity might influence in the development of allergy is the role of hormones that are influenced by obesity, such as estrogen (7). This hypothesis is in accordance with the more consistent association between BMI and allergy in female subjects after puberty (7, 9). Unluckily, pubertal status was not evaluated in our study. However, this hypothesis alone cannot explain the association observed between overweight and allergy before puberty (19). Another hormone related to fatty tissues, leptin, was recently associated to a number of immune-related responses (20), with a protective effect against allergy. Consequently, obese subjects with a deficit in leptin levels might tend to develop allergy. Varner purposed that an overproduction of ciclooxigenase (COX) 2 found in human adipose tissue and leptin-deficient obese mice might be related to the increased risk of allergy in obese subjects. COX-2 dependent prostanglandin E-2 (PGE-2) is associated to an increased Th2 type cytokine production and enhance allergic responses in predisposed overweight subjects (21-25).

We were unable to find an association between BMI-per-age and physician diagnosed allergy in our Japanese sample. A possible explanation for our result is that the association between BMI-per-age and allergy might rely on the percentage of body fat, and a lack of association between BMI and the percentage of body fat among Japanese children might be involved. It was previously reported that BMI had a poor correlation with the percentage of body fat in Japanese population (27-28). There are increasing numbers of Japanese adolescents with weight concern even at normal or low body weight (29). We hypothesize that inadequate dietary pattern in order to lose weight, accompanied with poor physical activity might lead to low BMI levels without reducing the percentage of body fat, lessen the effectiveness of BMI as a predictor of body fat composition in this population. We are currently addressing this issue to test our hypothesis.

The major limitation of our study is the lack of an objective measure to test the reported diagnosed allergy. We based our questionnaire in physician-diagnosed allergy and included generally accepted symptoms of allergy to avoid possible under-diagnosis. Although we believe that this procedure has strengthened our results, we might have excluded positive cases that have not been diagnosed by a physician, and several non-diagnosed allergies (especially those that do not require medical treatment) might have been excluded as well. On the other hand, it would have been desirable to evaluate the individual effect of BMI-per-age in each type of allergy in a higher sample. However, we performed the exclusion method in order to evaluate its effect compared with the effect of BMI-per-age in all allergies to be able to weight the role of each type of allergy by comparing its effect with that observed for all allergies.

In summary, our results suggest that a BMI-per-age $>$ 85th percentile was associated to an increased risk of

allergy in school children from Taiwan and Vietnam. No association was observed between BMI-per-age and allergies among Japanese school children.

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