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High body mass index and allergies in schoolchildren: the French six cities study

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ABSTRACT

Background: The prevalence of allergic diseases such as asthma, allergic rhinitis and atopic dermatitis is increasing rapidly worldwide, especially among children and in western countries. This coincides with an increase in body mass index (BMI), which might be a major risk factor for atopic diseases.

Objectives: To study the relationship between high BMI and allergic diseases, as well as skin-prick test (SPT) positivity and exercise-induced asthma (EIA) in 6733 randomly selected schoolchildren aged 9–11 years in the French Six Cities Study.

Methods: A cross-sectional study was carried out in Bordeaux, Clermont-Ferrand, Créteil, Marseille, Reims and Strasbourg. Parental questionnaires based on the International Study on Asthma and Allergies in Childhood (ISAAC) were used to collect information on allergic diseases and potential risk factors. Skin-prick testing to common allergens was performed to identify the existence of an allergic hypersensitivity and an exercise test was also performed to assess EIA. Height and weight were collected by trained investigators. After computing the BMI (weight/height squared), the International Obesity Task Force (IOTF) cut-offs were used to define overweight and obesity. The children were also classified as wheezing or non-wheezing.

Results: After adjustment for confounding factors, lifetime asthma was associated with high BMI among non-wheezing children (adjusted OR, aOR=1.98, 95% CI (1.06 to 3.70)). In addition, lifetime and past-year allergic rhinitis was associated with high BMI in wheezing children (aOR=1.63, (1.09 to 2.45) and aOR=2.20, (1.13 to 4.27)). However, high BMI was not significantly associated with eczema, SPT positivity or EIA.

Conclusions: This study shows a positive association between high BMI and lifetime asthma in non-wheezing children. High BMI was also associated with lifetime and past-year allergic rhinitis. Further studies are needed to provide causal evidence.

KEY MESSAGES

- This study is the first to assess the prevalence of overweight and obesity in a large population-based sample of schoolchildren aged 9-11 years old living in Metropolitan France and the association of high BMI with allergic diseases.
- This study includes a large number of participants, a multicenter design and a detailed health outcome assessment including information on atopic sensitization assessed by SPT. The use of an internationally validated questionnaire constitutes strength to our study.
- The cross-sectional design is a major limitation since the same biases may arise as found in all observational studies, such as a recall bias and not being able to demonstrate causal relationships that could have affected the results. Furthermore, we have not taken into account all factors that may predict overweight and obesity in children. Therefore, these retrospective results need to be confirmed by future prospective studies and/or interventional trials.

INTRODUCTION

The prevalence of asthma and allergic diseases in western countries has rapidly increased over the past decade,[1 2] and this has coincided with an increase in overweight and obesity in adults and children.[3 4] Unfortunately, the reasons for this increase are not well understood.

In fact, asthma is a very variable disease expressed not only by wheezing symptoms but also by coughing and other respiratory symptoms known as exacerbations that vary over time in their occurrence, frequency and intensity.[5] Therefore, not all children with wheezing symptoms are considered asthmatics, nor are all children with symptoms of wheezing considered as non-asthmatics.

Obesity has been shown to have several effects on the immune system[6] that might play a major role in the development of allergic diseases. Several studies have demonstrated an association between increased body mass index (BMI) and the development of asthma in

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childhood.[7–9] Furthermore, a gender-specific relationship has been shown in female but not in male adults[10 11] that is not found in children.[7 8] The association between BMI and other chronic atopic diseases has received less attention, although positive skin-prick tests (SPT) were positively associated with high BMI in girls from Taiwan[12] and young adults from Finland.[13] However, another study showed no relationship between BMI and SPT positivity.[9] Moreover, exercise-induced asthma (EIA) has been shown to be more prevalent in obese children.[14]

These contradictory results led us to analyse the association between high BMI and allergic diseases as well as SPT positivity and EIA in a large French population-based sample of 9–11-year-old schoolchildren.

METHODS

Study population and design

A cross-sectional study was conducted in six French cities (Bordeaux, Clermont-Ferrand, Créteil, Marseille, Reims and Strasbourg) in 2000–2001; 6733 schoolchildren aged 9–11 years and in fourth and fifth grade agreed to participate in this survey.

Questionnaires

Standardised self-administered epidemiological questionnaires were developed on demographics, wheezing, asthma, allergic rhinitis (AR) and atopic dermatitis. The main questions were derived from the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire.[15] These included detailed questions on the occurrence and severity of atopic symptoms (asthma, AR, eczema) and their potential risk factors. Such questions had been previously validated and translated from English into French by a native French speaker, then back-translated into English by a native English-speaker. All questionnaires were completed by the parents.

Clinical tests and body mass index calculation

The children's consent was obtained before conducting the clinical examination in their classrooms. Then a physician conducted a physical examination including data on height, weight and respiratory symptoms. According to Williams' protocol, atopic dermatitis was assessed by the questionnaire and a physical examination.[16] Fieldworkers and investigators were trained to conduct these respiratory function tests and clinical examinations.

After computing the BMI (weight/height squared), the International Obesity Task Force (IOTF) cut-offs were used to define overweight and obesity. The IOTF has defined cut-off points for BMI for overweight and obesity by sex between 2 and 18 years by averaging across a heterogeneous population worldwide, whereas the appropriate cut-off point was defined here to pass through a BMI of 25–30 kg/m^2 at age 18. Gender-specific BMI reference values for 9–11-year-old children from the IOTF were used to identify high BMI in our study.[17] High BMI was defined in this study as overweight and obese children.

Skin-prick testing

SPT for atopy was performed on 5902 children using Stallerpoints (Stallergènes Laboratories, Antony, France). The skin tests were performed by the SPT technique according to the ISAAC protocol.[18] Children were tested for the following common food and aeroallergens: *Dermatophagoides pteronyssinus*, *Dermatophagoides farinaee*, cat fur, *Alternaria tenius*, mixed grass and tree pollens, peanut, codfish, *Blattella germanica* and egg. At least one positive reaction was defined as SPT positivity, therefore having an allergic sensitisation.

EIA challenge

EIA was assessed according to the standardised protocol of the run test.[19] Baseline peak expiratory flow (PEF) was measured in all children who agreed. Post-exercise PEF was recorded immediately after the challenge, 5, 10 and 15 min later. A child was considered to have EIA if the decrease in PEF after exercise exceeded 10%. Subsequently, if a decrease in PEF of 10% was determined or if the child presented any respiratory symptom, he was first examined by the physician and a β2-agonist with an inhalation chamber was administered in order to ensure the reversibility of the bronchospasm.

Health outcomes

The following health variables were considered in the analysis: *Past-year wheezing* (a history of "chest wheezing or whistling in the chest over the past 12 months" (Yes/No)); *Lifetime wheezing* (a history of chest wheezing in the chest at some point in life according to the standardised question "Has your child ever had wheezing and whistling?" (Yes/No)); *Past-year asthma* (chest wheezing or whistling over the past 12 months with a history of asthma at some point in life); *Lifetime asthma* (a history of asthma at some point in life according to the standardised question "Has your child ever had asthma?" (Yes/No)); *Past-year AR* (a history of AR over the past 12 months); *Lifetime AR* (a history of hay fever at least once in life; "Has your child ever had hay fever?" (Yes/No)); *Past-year eczema* (a history of eczema or atopic dermatitis over the past 12 months and a positive SPT); and *Lifetime eczema* (a history of eczema or atopic dermatitis at least once in life ("Has your child ever had eczema?" (Yes/No)). All these health outcomes were based on the child's parents' self-reported answers to the questions. Moreover, *EIA* and *SPT positivity* were also analysed as health variables.

Statistical analysis

All continuous variables are presented as the mean (m) and SD and the categorical variables are presented as frequencies. Pearson's χ^2 test was used for categorical variables and the marginal OR was calculated. Logistic regression analyses were then performed to assess the

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association between allergic diseases and high BMI. All variables that had a p value ≤0.2 in the univariate analysis were included as independent variables in the multivariate analysis and health outcomes as the dependent variables. The Hosmer-Lemeshow statistic was calculated to assess the model's goodness-of-fit. The associations between BMI and allergic diseases were estimated by calculating the adjusted OR (aOR) and corresponding 95% CIs. ORs were adjusted for the following potential confounders: gender, place of residence divided into north (Créteil, Reims and Strasbourg) and south (Bordeaux, Clermont-Ferrand and Marseille) of France, family history of allergic diseases (defined by whether the father or the mother of the child had ever suffered from asthma, AR or eczema), number of siblings (0, 1–2, ≥3), parental education, parental ethnic origins, breastfeeding, day care outside the home and exposure to passive smoking. Since asthma is a variable allergic disease with various symptoms including wheezing, coughing and other respiratory symptoms,[5] children with lifetime wheezing were separated from those with no wheezing symptoms, and multivariate analyses were performed for each group after adjusting for the same potential confounders. All reported probability values (p values) were based on two-sided tests and a p value <0.05 was considered statistically significant. All analyses were performed using the Statistical Package for Social Science (SPSS) V.17.0.

RESULTS

This study included 6733 schoolchildren aged 9–11 years living in six different cities in France. Of these, 21% had a high BMI including 17% who were overweight and 4% who were obese children according to the IOTF cut-offs for overweight and obesity in 9–11-year-old children. No differences were found between high BMI and gender (p=0.440). Demographic and clinical characteristics of the children and their associations with BMI are shown in table 1.

In the univariate analysis, high BMI was not associated with any of the allergic diseases symptoms, SPT positivity or EIA (table 2). Multivariate analyses performed on all children aged 9–11 years showed no association between high BMI and the health outcomes studied. On the other hand, SPT positivity was positively associated with past-year wheezing (aOR=4.86, 95% CI 3.59 to 6.56), past-year asthma (aOR=8.31, 95% CI 5.77 to 11.96), past-year AR (aOR=2.81, 95% CI 2.14 to 3.70) and EIA (aOR=1.91, 95% CI 1.48 to 2.45). Moreover, parental history of allergic diseases was positively associated with

Table 2 Associations between BMI and prevalence of allergic symptoms, SPT positivity and EIA in univariate analysis (N=6733)

Variables	Normal weight (N=5316)	High BMI (N=1417)	p Value
Lifetime wheezing (%)	19.9	18.2	0.184
Past-year wheezing (%)	20.0	17.2	0.173
Lifetime asthma (%)	9.8	10.2	0.607
Past-year asthma (%)	4.9	4.5	0.568
Lifetime AR (%)	12.9	13.1	0.828
Past-year AR (%)	64.4	67.2	0.243
Lifetime eczema (%)	25.8	25.0	0.580
Past-year eczema (%)	3.9	3.0	0.124
SPT positivity (%)	27.2	28.6	0.337
EIA	9.1	9.5	0.714

AR, allergic rhinitis; BMI, body mass index; EIA, exercise-induced asthma; SPT, skin-prick test; %, proportion within BMI.

Table 1 Demographic and clinical characteristics of children and their associations with BMI (N=6733)

Variables	Normal weight (N=5316)	High BMI (N=1417)	p Value
Age (%), years			<0.001
9	26.7	33.1	
10	48.7	48.2	
11	24.6	18.7	
Gender (male, %)	49.3	50.5	0.440
Weight in kg (m±SD)	33.18±5.20	47.36±8.37	<0.001
Height in metres (m±SD)	1.40±0.07	1.45±0.07	<0.001
Passive smoking (%)	48.4	51.7	0.046
Family history of allergic diseases (%)	39.8	38.8	0.498
Breastfeeding (%)	48.2	48.4	0.894
Day care outside the home (%)	29.9	27.5	0.103
Place of residence (%)			0.009
North of France	48.1	51.9	
South of France	51.9	48.1	
Number of siblings (%)			0.910
No siblings	47.8	47.6	
1–2 siblings	46.2	46.6	
≥3 siblings	6.0	5.7	

BMI, body mass index; m±SD, mean±SD; %, proportion within BMI.

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Table 3 Multivariate analyses of the risk factors including high BMI associated significantly with allergic diseases, SPT positivity and EIA in non-wheezing and wheezing children

	Non-wheezing children (N=5545) aOR* (95% CI)	Wheezing children (N=1188) aOR* (95% CI)
Risk factors for lifetime asthma†		
High BMI	1.98 (1.06 to 3.70)	
Gender (female vs male)	0.46 (0.25 to 0.86)	–
Passive smoking	2.86 (1.48 to 5.53)	
Risk factors for lifetime AR†		
Parental history of allergic diseases	–	2.40 (1.67 to 3.16)
High BMI		1.63 (1.09 to 2.45)
Risk factors for past-year AR†		
High BMI	–	2.20 (1.13 to 4.27)
Risk factors for lifetime eczema†		
Consumption of white fish	0.88 (0.79 to 0.98)	–
Gender (female vs male)	1.24 (1.04 to 1.49)	–
Parental history of allergic diseases	2.29 (1.92 to 2.74)	4.63 (1.20 to 2.21)
Risk factors for current eczema†		
Parental history of allergic diseases	2.06 (1.28 to 3.32)	–
Gender (female vs male)	–	1.97 (1.23 to 3.17)
Risk factors for SPT positivity†		
Place of residence (south vs north)	1.60 (1.32 to 1.94)	1.44 (1.05 to 1.96)
Consumption of fruits	–	0.86 (0.75 to 0.98)
Gender (female vs male)	0.68 (0.56 to 0.81)	–
Parental history of allergic diseases	1.21 (1.01 to 1.46)	–
Risk factors for EIA†		
Place of residence (south vs north)	1.40 (1.03 to 1.89)	1.62 (1.05 to 2.52)

*OR adjusted for the following confounders: gender, high BMI, parental history of allergic diseases, parental education, parental ethnic origin, place of residence, day care outside home, breastfeeding and passive smoking. Analyses include only factors that had a p value ≤0.2 in the univariate analyses.
†Only significant risk factors are shown in this logistic regression model.
–, No significant associations were found for the listed risk factors; aOR, adjusted OR; AR, allergic rhinitis; BMI, body mass index; EIA, exercise-induced asthma; SPT, skin-prick test.

past-year wheezing (aOR=2.28, 95% CI 1.67 to 3.11), past-year asthma (aOR=2.36, 95% CI 1.66 to 3.36), past-year AR (aOR=1.93, 95% CI 1.51 to 2.47) and past-year eczema (aOR=1.89, 95% CI 1.31 to 2.74).

Among non-wheezing children, only 1.7% presented with lifetime asthma. Since asthma is a variable allergic disease with various symptoms other than wheezing, children with lifetime wheezing were separated from those with no wheezing symptoms and multivariate analyses were performed for each group after adjusting for potential confounders. High BMI was positively associated with lifetime asthma in non-wheezing schoolchildren (aOR=1.98, 95% CI 1.06 to 3.70). Among wheezing children, high BMI was positively associated with lifetime AR (aOR=1.63, 95% CI 1.09 to 2.45) and past-year AR (aOR=2.20, 95% CI 1.13 to 4.27). High BMI was not significantly associated with eczema, SPT positivity or EIA in either of the groups (table 3).

Lifetime asthma and SPT positivity were more prevalent in non-wheezing boys than in girls from the same group. In contrast, eczema tended to be more prevalent in girls than in boys. In addition, passive smoking was a significant risk factor for lifetime asthma in children with no wheezing symptoms. Moreover, there was a significant relation between place of residence and SPT positivity and EIA among schoolchildren aged 9–11 years. Children living in the south of France were more subject to atopy and bronchial hyperresponsiveness defined by the presence of EIA than those living in the north of France.

Regarding dietary habits, univariate analyses showed significant associations between high BMI and cooked and raw vegetables, in addition to white fish (p=0.013; p=0.015 and p=0.024, respectively). Furthermore, multivariate analyses stratified for wheezing and non-wheezing children showed that consumption of fruits in wheezing children was negatively associated with atopy in general (aOR=0.86, 95% CI 0.75 to 0.98) and consumption of white fish was negatively associated with lifetime eczema in non-wheezing children (aOR=0.88, 95% CI 0.79 to 0.98).

DISCUSSION

This study is the first to assess the prevalence of overweight and obesity in a large population-based sample of schoolchildren aged 9–11 years and living in Metropolitan France, and the association of high BMI with allergic diseases (asthma, AR and eczema), SPT positivity and EIA. High BMI in children was positively associated with lifetime asthma in children with no

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wheezing symptoms ever. Furthermore, positive associations were also found in wheezing children between high BMI and lifetime and past-year AR.

The association between high BMI and lifetime asthma in non-wheezing children is consistent with previous studies.[20–24] In addition, obesity and overweight as assessed by waist circumference, waist-to-height ratio and BMI were found to be associated with a diagnosis of asthma in children aged 5–11 years.[25] Therefore, children with lifetime asthma, but without current wheezing, might have a high BMI because of insufficient physical activity, although this hypothesis cannot be ascertained since we did not collect data on physical activity.

The positive associations between high BMI and AR in wheezing children, thus atopic children, are inconsistent with previous studies that found no association between overweight and obesity and AR.[26 27] This discrepancy might be due to the differences in the prevalence of rhinitis in the populations studied and to the fluctuation in the size of our sample. Moreover, we considered wheezing children with AR as allergic and not as asthmatic,[28] unlike other authors.[29 30]

The absence of a significant association between high BMI and SPT positivity is in accordance with results from the National Health and Nutrition Examination Study III.[9] In addition, the absence of a significant association between high BMI and EIA is consistent with data from seven epidemiological studies performed in Australia on Caucasian children and a cohort study conducted on asthmatic adults in Korea.[31 32]

Several of our findings about the risk factors associated with allergic diseases have already been demonstrated in other studies: the association of gender with the development of asthma in children is in agreement with other studies showing that male sex is a risk factor for respiratory symptoms in childhood,[33 34] especially wheezing, which was found to be more prevalent in overweight children, especially boys.[31 35] Furthermore, the inverse association between fruit consumption and allergies is consistent with previous studies concluding in the protective effect of fruits and antioxidants against allergies in children.[36 37] There were also differences between children from the north and south of France. Therefore, children living in the south of France were more affected by atopy and EIA than those living in the north. This is consistent with a study conducted in children in China living in different geographical areas.[38] These disparities might be due to differences in lifestyle and environment between residential areas.[39 40] Moreover, passive smoking was positively associated with lifetime asthma in non-wheezing children, which is in accordance with several studies that have also shown the risks of passive smoking on respiratory health in children.[41]

The strengths of the current study include the large number of participants, its multicentre design and the detailed health outcome assessment including information on atopic sensitisation assessed by SPT which was performed in a large number of children aged 9–11 years. Furthermore, the use of an internationally validated questionnaire, filled out by the parents of the children who are very likely the people who are most aware of their children's health and lifestyle, and indicators to evaluate respiratory manifestations constitute strengths.[15 42 43]

Limitations of the study

The cross-sectional design is a major limitation since the same biases may arise as found in all observational studies, such as a recall bias and not being able to demonstrate causal relationships that could have affected the results. In addition, the time factor should be taken into account: this survey was conducted 14 years ago at a time when the epidemiological situation regarding allergic diseases and obesity status varied greatly. Therefore, these retrospective results need to be confirmed by future prospective studies and/or interventional trials. Furthermore, physical activity status was not assessed owing to the lack of information about it and the difficulty of assessing it in epidemiology. However, the multivariate analysis decreased the probability of confounding and an effort was made to correct for the following potential confounders: sex, passive smoking, parental education, parental ethnic origins, breastfeeding, day care outside the home and family history of allergic diseases.[44–47] An underestimation of asthma and wheezing prevalence might also affect our results. Asthma and wheezing were reported subjectively by parents, without a doctor's diagnosis, as well as the identification of tobacco use and smoking. Furthermore, the prevalence of atopic dermatitis may have been overestimated in this study compared to other parts of Europe,[48 49] owing to the subjective nature of reporting by parents.[50] However, the internationally validated indicators we used to evaluate respiratory symptoms decrease the risk of having a differential bias.[15 42 43]

CONCLUSION

In conclusion, the relationship between high BMI and allergic diseases in childhood could be explained by the existence or the absence of respiratory symptoms such as wheezing. Hence, overweight and obesity could be associated with allergic diseases in children. This study provides further evidence that a high BMI in children might be a major risk factor for allergies and especially asthma and AR. As the development of allergic diseases is probably multifactorial, future prospective and experimental studies are needed to confirm these results and provide sufficient power to demonstrate a causal relationship.

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Contributors All the authors contributed substantially to this study. DS performed statistical analysis and wrote the paper. DS, CR and PS have the main responsibility for the final content. All authors have read and approved the final manuscript.

Competing interests None.

Ethics approval Authorisation by the "National Commission of Informatics and Civil Liberties (CNIL)" was sought and obtained before conducting the survey. The parents of the children were informed by mail of the purposes and modalities of the survey, and their informed consent was obtained.

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