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How the presence of rhinoconjunctivitis and the severity of asthma modify the relationship between obesity and asthma in children 6–7 years old

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Summary

Background The association between asthma and obesity in children, and the effect modification of allergy on this association have not been fully established.

Aims The objective of the study was to know the effect modification of the severity of asthma and of the coexistence of rhinoconjunctivitis (RC) in the relationship between obesity and asthma.

Methods A cross-sectional study of 17 145 schoolchildren 6–7 years old from eight Spanish cities who had completed information on height and weight of the ISAAC phase III questionnaire, which also included questions about asthma and RC symptoms and on various risk factors. Body mass index (BMI) was used to define obesity according to international standards. Two different logistic regressions, using current occasional asthma (COA) and current severe asthma (CSA) as dependent variables, were made stratifying for gender and for the coexistence of RC and controlling for age, older and younger siblings, exercise, mother's education, truck traffic, cat/dog during the first year of life and smoking father or mother.

Results Obesity was a risk factor of CSA without RC, both for boys (1.92, CI 95% 1.13–3.25) and for girls (2.99, CI 95% 1.68–5.32). Every BMI unit increment increased by 6.7% the risk of CSA without RC in boys and by 12.4% in girls. Obesity was not a risk factor for CSA with RC. The association between COA and obesity was weaker and the coexistence of RC did not modify it greatly.

Conclusions Obese schoolchildren are more at risk of suffering from non-allergic asthma than the non-obese subjects.

Keywords asthma, atopy, epidemiology, obesity, rhinoconjunctivitis

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Introduction

The association between obesity and asthma has been shown mainly in women. In children, this association is less consistent and seems to be modified both by age and by gender [1–3]. Furthermore, the relationship between atopy [as diagnosed by skin prick testing (SPT)] and obesity in children remains to be established, as discrepancies exist about whether or not there is any association between the two conditions [3–5].

The effect modification of atopy or of a concomitant allergic disease on the relationship between obesity and asthma has scarcely been studied. In Swedish young adults, an association between allergic rhinoconjunctivitis (RC) and obesity could not be found; however, obesity was a risk factor for asthma both in individuals with allergic RC and in those without it [6]. The study by Gilliland et al. [7] in schoolchildren has shown that the incidence rate of doctor-diagnosed asthma is significantly higher in overweight/obese children (more so in boys than in girls). The

coexistence of an allergic disease (reported by parents) modified the risk to the extent that among the allergic children (both boys and girls) it disappeared, while among the non-allergic ones it increased greatly. A similar trend has been recently reported in adults [8].

The aim of the present study is to establish the effect modification of RC – as a marker of atopy – and of the severity of asthma, on the relationship between this condition and obesity in a population of schoolchildren 6–7 years old.

Methods

By means of the ISAAC phase III core and environmental questionnaires (<http://isaac.auckland.ac.nz>), parents of children 6–7 years old were surveyed in the school setting in eight different Spanish centres: Cartagena, Barcelona, Bilbao, Valencia, Madrid, Asturias, San Sebastián and La Coruña. Except for Barcelona, Madrid and Asturias, the rest of the centres included all schools or a random sample of them within the city district, which had children of the targeted age range. Madrid included all the schools within the health area of 'Hospital 12 de Octubre' and Barcelona did the same with 'Hospital del Mar'. Asturias sampled schools randomly from the entire province. Questionnaires were translated into Spanish and then translated back into English according to the ISAAC protocol and were validated later [9]. The questionnaires were given to the children by their teachers, filled in by the parents at home and returned to the school within 1 week.

The core questionnaire included questions on asthma and RC symptoms. For the purpose of this study, current asthma was defined as answering positively to the question 'Has your child had wheezing or whistling in the chest during the last 12 months?'. 'Current severe asthma' (CSA) was defined as a combination of three questions assessing the severity of asthma. These questions were 'How many attacks of wheeze has your child had during the last 12 months? (none, 1–3, 4–12, more than 12)'; 'In the last 12 months, how often, on average, has your child's sleep been disturbed due to wheezing (never, less than one night per week, one or more nights per week) and 'In the last 12 months, has wheezing been severe enough to limit your child's speech to only one or two words at a time between breaths?'. It was considered 'CSA' when there were four or more asthma attacks, or when sleep was disturbed for one or more nights per week or when there had been an episode of speech limitation. Those children with 'current asthma' that was not 'clinically significant' were considered to have 'current occasional asthma' (COA). RC was defined as a positive answer to both the following questions: 'In the past 12 months, has your child had a problem with sneezing, or a runny, or blocked nose when he/she did not have a cold or the flu?', and 'In

the past 12 months, has this nose problem been accompanied by itchy-watery eyes?'

The environmental questionnaire included other questions such as smoking habits of father or mother, having older or younger children, maternal studies, performing strenuous exercise, truck traffic and cat or dog ownership during the first year of the child's life. Parent-reported height and weight were used to calculate body mass index (BMI) in kg/m². The parent-reported BMI was recently validated against the measured BMI in a group of Spanish children of the same age as in the present study [10]. Obesity was defined according to the international cut-off points of BMI reported by Cole *et al.* [11] for each age and sex.

The relationship of BMI and obesity with current asthma, COA or CSA – with or without RC stratified by gender – was measured using the odds ratio (OR) unadjusted and adjusted (logistic regression) for age, older and younger siblings, exercise, mother's education, truck traffic, cat or dog during the first year of life and smoking father or mother, which were considered potential confounders (i.e. factors that might be associated with both asthma and obesity). Analyses of CSA excluded children with COA. BMI was used as a continuous variable in the logistic regression. Firstly, the way how the association of obesity with asthma was modified (something that occurs when the strength of an association depends on the level of another factor) by gender, RC or asthma severity was calculated; secondly, calculations were made for different strata: by gender, gender by asthma severity and asthma severity by RC. Although in the first analysis gender did not show an important impact on the relationship between asthma and obesity, the subsequent analyses was performed stratified by this factor, as some reports have shown that gender could – in fact – have some influence [1, 2]. Calculations were made by means of the Stata 7.0 software (College Station, TX, USA).

The regional ethics committee of Asturias approved this study for all ISAAC III centres in Spain.

Results

There was an overall participation rate of 78.7% (children who returned the questionnaire from the whole target population). For this analysis, those who had not been born in Spain ($n = 1249$), were outside the target age range ($n = 683$) or had no available data on the weight and/or height ($n = 2961$) were excluded. Consequently, the number of children included in the present study was 17 145.

The number of children suffering from COA, CSA with or without RC, together with the demographics of gender, obesity, BMI and strenuous exercise in each group is shown in Table 1. There was a modification effect of RC and of asthma severity on the association between obesity and asthma (Table 2). As shown in Table 3, there was a

Table 1. Characteristics and risk factors of the children without asthma, with current occasional asthma and current severe asthma, the latter two stratified by the coexistence of rhinoconjunctivitis (RC)

	Current occasional asthma <i>n</i> = 1379			Current severe asthma <i>n</i> = 390			No asthma <i>n</i> = 15 376
	RC ⁺	RC ⁻	Total	RC ⁺	RC ⁻	Total	Total
Gender							
Boys	236 (56.3)	537 (55.9)	773 (56.1)	114 (57.3)	108 (56.5)	222 (56.9)	7583 (49.4)
Girls	183 (43.7)	423 (44.1)	606 (43.9)	85 (42.7)	83 (43.5)	168 (43.1)	7768 (50.6)
Obesity							
Yes	50 (11.9)	113 (11.8)	163 (11.8)	26 (13.1)	40 (20.9)	66 (16.9)	1460 (9.5)
No	369 (88.1)	847 (88.2)	1216 (88.2)	173 (86.9)	151 (79.1)	324 (83.1)	13 888 (90.5)
BMI	17.12 ± 2.54	16.97 ± 2.69	17.02 ± 2.65	17.05 ± 2.77	17.80 ± 4.01	17.42 ± 3.45	16.80 ± 2.65
Strenuous exercise							
Never	95 (22.8)	199 (20.9)	294 (21.5)	37 (18.9)	30 (16.3)	67 (17.6)	2265 (15.0)
One or two per week	168 (40.4)	382 (40.3)	551 (40.3)	89 (45.4)	84 (45.7)	173 (45.5)	5907 (39.1)
Three+ per week	153 (36.8)	369 (38.8)	522 (38.2)	70 (35.7)	70 (38.0)	140 (36.8)	6936 (45.9)

n (%) or mean ± SD (percentages calculated on the number of children with non-missing values per each variable).

BMI, body mass index.

Table 2. Unadjusted and adjusted odds ratios (OR) for asthma in relation to obesity with their 95% confidence interval (CI)

	OR	95% CI	OR	95% CI
Whole population	1.41	(1.21–1.64)	1.38	(1.18–1.62)
Current occasional asthma	1.27	(1.07–1.51)	1.25	(1.04–1.50)
Current severe asthma	1.94	(1.48–2.54)	1.87	(1.40–2.49)
Rhinoconjunctivitis ⁺	1.12	(0.81–1.54)	1.21	(0.86–1.72)
Rhinoconjunctivitis ⁻	1.47	(1.23–1.76)	1.42	(1.28–1.71)
Male gender	1.37	(1.13–1.67)	1.39	(1.13–1.80)
Female gender	1.45	(1.16–1.82)	1.34	(1.05–1.71)

Effect modification by asthma severity, rhinoconjunctivitis and gender. OR is adjusted for age, older and younger siblings, exercise, mother's education, truck traffic, cat or dog during the first year of life and smoking father or mother.

significant association between being obese and suffering from CSA without RC. Conversely, no association was found between CSA and obesity when CSA coexisted with RC. This situation was equivalent for both boys and girls, although the association between CSA without RC and obesity was stronger for girls. The strength of the association was very similar before and after adjusting for the different factors.

When using BMI as a dependent continuous variable, the significant associations were the same as the ones obtained with obesity as the dependent variable. One unit of increased BMI among boys without RC was associated with approximately 7% of excess risk of suffering from CSA, the corresponding figure for girls being 12% (Table 4).

Discussion

The results of the present study confirm the previous finding that allergy modifies the relationship between

Table 3. Unadjusted and adjusted odds ratios (OR) for asthma in relation to obesity with their 95% confidence interval (CI), stratified by sex, asthma severity and the coexistence of rhinoconjunctivitis (RC)

	OR	95% CI	OR*	95% CI
Boys				
Current asthma	1.37	1.13–1.67	1.39	1.13–1.80
Current occasional asthma	1.30	1.04–1.63	1.34	1.06–1.69
RC ⁺	1.22	0.77–1.96	1.32	0.80–2.19
RC ⁻	1.26	0.96–1.65	1.32	0.99–1.74
Current severe asthma	1.60	1.10–2.31	1.48	1.00–2.20
RC ⁺	0.94	0.50–1.74	1.09	0.57–2.07
RC ⁻	2.17	1.34–3.51	1.92	1.13–3.25
Girls				
Current asthma	1.45	1.16–1.82	1.34	1.05–1.71
Current occasional asthma	1.22	0.94–1.59	1.09	0.81–1.45
RC ⁺	0.89	0.50–1.61	0.89	0.45–1.76
RC ⁻	1.29	0.95–1.76	1.15	0.82–1.61
Current severe asthma	2.32	1.56–3.43	2.34	1.53–3.56
RC ⁺	1.54	0.80–2.95	1.78	0.88–3.62
RC ⁻	2.95	1.76–4.96	2.99	1.68–5.32

*OR is adjusted for age, older and younger siblings, exercise, mother's education, truck traffic, cat or dog during the first year of life and smoking father or mother.

obesity and asthma in the direction of obese subjects being more at risk of suffering from non-allergic asthma than the non-obese subjects; on the other hand, obese subjects have the same risk of allergic asthma as the non-obese subjects. This applies both for adults and for children [7, 8]. The present results show that this modification effect is mainly noted in the more severe type of asthma.

However, these results should be taken with some caution as allergy was measured in a quite indirect way, asking the parents about allergic RC symptoms in their

Table 4. Unadjusted and adjusted odds ratios (OR) for asthma in relation to 1 unit increment in BMI with their 95% confidence interval (CI), stratified by sex, asthma severity and the concomitant presence of rhinoconjunctivitis (RC)

	OR	95% CI	OR*	95% CI
Boys				
Current asthma	1.03	1.01–1.06	1.03	1.01–1.06
Current occasional asthma	1.03	1.00–1.06	1.03	1.00–1.06
RC ⁺	1.01	0.95–1.06	1.01	0.95–1.07
RC [−]	1.03	1.00–1.06	1.03	1.00–1.07
Current severe asthma	1.04	0.99–1.09	1.04	0.99–1.09
RC ⁺	0.96	0.89–1.04	0.99	0.92–1.07
RC [−]	1.08	1.02–1.14	1.07	1.00–1.13
Girls				
Current asthma	1.05	1.02–1.07	1.04	1.02–1.07
Current occasional asthma	1.02	0.99–1.05	1.02	0.99–1.05
RC ⁺	1.04	0.97–1.11	1.04	0.96–1.12
RC [−]	1.02	0.98–1.05	1.01	0.98–1.05
Current severe asthma	1.10	1.06–1.14	1.10	1.06–1.15
RC ⁺	1.06	0.98–1.15	1.06	0.97–1.16
RC [−]	1.12	1.07–1.17	1.12	1.07–1.18

*OR is adjusted for age, older and younger siblings, exercise, mother education's, truck traffic, cat or dog during the first year of life and smoking father or mother.

BMI, body mass index.

children. Nevertheless, in four of the centres included in the present study, there are unpublished data on SPT and RC symptoms in 2720 children somewhat older (9–11 years; ISAAC II). These data show that RC is good for ruling out allergy, but is not as good for diagnosing it (specificity 88%, sensitivity 35%), a result that is in agreement with that by Braun-Fahrlander *et al.* [12]. The results of the present study show that among RC-negative children (most of whom are not allergic), there is a clear association between CSA and obesity, while in the RC-positive group there is not. Having non-atopic children in the RC-positive group (which is the expected situation due to the low sensitivity of RC symptoms) will push the results away from the null hypothesis, thus making the lack of association between CSA and obesity in this group more consistent. The two prior studies, which – to the best of our knowledge – have addressed this issue, defined allergy in a different way. In both, the question asked was whether the subject had ever been diagnosed as having an allergic disease by a doctor [7] or by a health care professional [8].

An additional limitation of the present study comes from the fact that height and weight were reported by parents, and this could be a source of some error. However, we have previously demonstrated that parent-reported measurements are reliable for epidemiological purposes in our environment [10].

Obesity has been previously related to asthma in children, although it is not clear as to how the gender

affects this relationship [1, 2, 7]. Stratifying by asthma severity and finding that the association is stronger in the more severe type of asthma may suggest that obesity might be an add-on risk factor, which makes asthma worse. However, it is striking that this add-on effect seems to act only in non-allergic children. Obesity has been related to 'leptin-induced inflammation', mediated by IFN- γ , which is independent of allergic inflammation [13]. However, this non-allergic inflammation does not seem to fully explain the gender effect of the present results (7% increase in the risk for every BMI unit in boys vs. 12% in girls). It does not seem likely that sex hormones could explain the difference at the age of 6–7 years, as has been suggested in adults [14]. It is possible that exercise might explain this difference, at least in part. Boys usually exercise more than girls [the OR of boys as compared with that of girls of performing strenuous exercise three or more times a week was 1.87 (CI 95% 1.72–2.05)]. Exercise has been hypothesized to be a protective factor for bronchial narrowing by avoiding the underextension of annular bronchial muscles, due to more frequent and profound inspirations [15]. Furthermore, it is possible that a given amount of exercise could protect boys and girls differently, as at this age boys have a higher airway resistance than girls for a given lung volume [16], and consequently they might need more exercise to avoid underextension of bronchial muscles. The disparity between the amount of exercise and the possible gender-differential effect of exercise might explain the different effect of obesity on boys and girls, especially in non-atopic severe asthma.

Nevertheless, studies on the relationships between asthma, obesity, atopy and exercise in the paediatric population have not used objective measurements yet. It would be very useful to perform investigations that include these type of measurements in different populations to definitely establish those relationships, which could be very useful from the public health point of view.

In summary, the present study shows that the association between obesity and asthma in schoolchildren is modified by the severity of asthma and by the coexistence of RC. This modification is more manifested in girls when asthma is severe. The presence of RC in obese girls or boys makes the risk of having severe asthma similar to that of non-obese children.

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