Early Childhood Overweight and Asthma and Allergic Sensitization at 8 Years of Age

WHAT'S KNOWN ON THIS SUBJECT: Overweight has been associated with an increased risk of asthma in children, although the published literature is contradictory. How change in overweight status during childhood affects asthma risk has not been well studied.

WHAT THIS STUDY ADDS: Among children whose weight has normalized, high BMI during the first 4 years of life does not increase the risk of asthma at school age. Current high BMI is associated with increased risk of asthma and sensitization to inhalant allergens.

abstract

FREE

OBJECTIVES: Our aim was to examine the associations between high BMI and changes in BMI status during the first 7 years of life and asthma and allergic sensitization at age 8 years.

METHODS: A birth cohort of newborn infants was followed for 8 years. Repeated parental questionnaires provided information on environmental exposures and health outcomes. Information on height and weight during childhood was retrieved from preschool and school health care records. The analyses included the 2075 children for whom information was available on weight and height, as well as on asthma, at age 8 years.

RESULTS: A high BMI (≥85th percentile) at age 1, 4, and/or 7 years was associated with an increased risk of asthma at age 8 years. However, no significant association was observed among children with high BMI at age 12 and/or 18 months (early age) or at age 4 years who developed a normal BMI by age 7 years. The risk was increased among children with high BMI at age 7 years, regardless of their earlier weight. Moreover, we observed an increased risk of sensitization to inhalant allergens among children with high BMI at age 7 years.

CONCLUSIONS: Our study indicates that high BMI during the first 4 years does not increase the risk of asthma at school age among children who have developed a normal weight by age 7 years. However, high BMI at age 7 years is associated with an increased risk of asthma and sensitization to inhalant allergens. *Pediatrics* 2012;129:70–76

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KEY WORDS

asthma, allergic sensitization, overweight, BMI, child, cohort study

ABBREVIATIONS

BAMSE—Swedish abbreviation for Children, Allergy, Milieu, Stockholm, Epidemiology
CI—confidence interval
OR—odds ratio

The authors' contributions were as follows: Dr Wickman (principal investigator of the BAMSE project) initiated the BAMSE project; Dr Bergström planned the current study; Drs Kull and Bergstöm supervised the data collection; Dr Öhman Magnusson collected the data from the school health care registers, prepared the data for analyses, and performed the analyses; Drs Bergström, Kull, Öhman Magnusson, and Wickman interpreted the data; Dr Öhman Magnusson drafted the manuscript; and Drs Bergstrom, Kull, Öhman Magnusson, Wickman, and Mai provided critical review of the manuscript.

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Both asthma and overweight are more prevalent among children today than a few decades ago.[1,2] The concurrent rise in prevalence of asthma and overweight has led to speculations about an association between them. Epidemiologic studies suggest that overweight (most often measured as high BMI) at various ages increases the risk of asthma in childhood.[3–17] Despite this, the nature of the association between overweight and asthma is not completely understood, and only 1 study has looked at change in BMI status during childhood and the risk of asthma.[17] Results from a Dutch birth cohort showed that children with high BMI at age 6 to 7 years had an increased risk of asthma symptoms at age 8 years, whereas children with high BMI earlier in life and with normal weight at age 6 to 7 years did not.[17] The association between high BMI and allergic sensitization has been less studied, and the results are inconsistent.[8,17–21] Thus, the association between change in BMI status and timing of overweight in relation to the occurrence of asthma and allergic sensitization merits additional study.

A previous report from our prospective birth cohort has shown that high BMI at age 4 years tended to be associated with wheezing only during the first 2 years of life and not at 4 years of age.[22] The aim of the current study was to examine the associations between BMI and changes in BMI status during the first 7 years of life and asthma and allergic sensitization at 8 years of age by using data from our Swedish birth cohort.

METHODS

Study Design and Population

The study population consisted of 4089 Swedish children who are participating in the prospective BAMSE (Swedish abbreviation for Children, Allergy, Milieu, Stockholm, Epidemiology) study. BAMSE is an ongoing birth cohort including children recruited between the years 1994 and 1996; additional description can be found elsewhere.[23] In brief, a baseline questionnaire about parental history of allergic disease and environmental exposures was answered by the parents when the children were on average 3 months old. When the children were aged 1, 2, 4, and 8 years, parents answered questionnaires about symptoms of allergic disease and key exposures. The response rates were 96%, 94%, 91%, and 84%, respectively.

During a clinical examination at age 8 years, blood was collected for 60% of the original cohort. The blood samples were analyzed for immunoglobulin E antibodies with Phadiatop and Food mix (Phadia, Uppsala, Sweden). All parts of the BAMSE study have been approved by the ethics committee of Karolinska Institutet, Stockholm, Sweden.

Anthropometric Measurements

When the children were on average 12 years old, 2887 parents (71% of the original cohort) gave us their consent to collect information on their child's weight and height from school health care registers. In Sweden, 99% of the children aged <2 years participate in physical examinations at child health care centers, and 87% of the children between ages 2 and 6 years visit at least once.[24] When the child starts school, these records are transferred to the school health care. At school, the children's height and weight are measured by the school nurse in first grade. We extracted information on weight (kilograms) and height (centimeters) for 4 predefined ages (12 and 18 months [± 4 weeks], 4 years [± 6 months], and 7 years [measured during the first year of school]) for 2598 children. For all these ages, we obtained weight and height information for more than 84% of the children.

BMI was calculated as body weight in kilograms divided by height in meters squared (kg/m^2). Children were classified as having normal or high BMI at each age. Cutoff for high BMI was set to the 85th percentile of BMI based on children in the BAMSE study, taking gender and age into account. The 85th percentile was chosen because the cutoff points presented by Cole and colleagues do not apply to children <2 years of age.[25] In our analyses of change in BMI status, we combined the information from age 12 and 18 months, hereafter denoted "early age."

Change in BMI status between early age and 7 years was subdivided into 4 categories:

- persistent normal BMI (normal BMI at both early age and 7 years);
- early high BMI (high BMI at early age but normal BMI at age 7 years);
- late high BMI (normal BMI at early age but high BMI at age 7 years); and
- persistent high BMI (high BMI both at early age and at age 7 years).

Change in BMI status between 4 and 7 years was defined similarly.

Definition of Health Outcomes

On the basis of the questionnaire at age 8 years, asthma was defined as at least 4 episodes of wheeze in the previous 12 months or at least 1 episode of wheeze during the same period in combination with occasional or regular use of prescribed inhaled steroids.[26] Allergic sensitization was indicated if the child had at least 1 allergen-specific immunoglobulin E result of ≥0.35 kU/L against inhalant allergens (cat, dog, horse, birch, timothy, mugwort, *Dermatophagoides pteronyssinus*, and *Cladosporium* species) and/or food allergens (cow's milk, hen's egg, codfish, soybean, peanut, and wheat).

Statistical Analyses

Data analysis was conducted using Stata 11 (College Station, TX). The relation of environmental characteristics at baseline with child overweight at early age was tested with χ^2 test. Multivariate logistic regression models were used to analyze associations between key exposures (BMI status at age 1, 1.5, 4, and 7 years as well as change in BMI status) and asthma and allergic sensitization at 8 years of age. The results of logistic regression analyses are presented as adjusted odds ratios (OR) with 95% confidence intervals (95% CI). Several models were tested to identify potential confounders, and the final model was adjusted for maternal age (≤25 years vs older at birth of the child), maternal smoking (the mother smoked at least 1 cigarette per day at any point of time during the pregnancy and/or at baseline), parental history of allergic disease (doctor-diagnosed asthma and/or hay fever in combination with reported allergy to pollen or pets in 1 or both parents), gender, birth weight (in grams, divided into tertiles), and breastfeeding duration (exclusive breastfeeding <4 or ≥4 months). Additional adjustments were made for socioeconomic status, maternal BMI before pregnancy, child's physical activity at 4 and 8 years, and energy intake at 8 years. These factors did not change the observed ORs and were not included in the final model. The analyses of change in BMI status in relation to asthma were also stratified by parental history of allergic disease.

To test for disease-related modification of exposure, we adjusted the analyses for early symptoms of wheeze and/or eczema (defined as wheeze and/or eczema during the first 2 years of life). In addition, the χ^2 test was used to test for differences in the prevalence of high BMI at different ages in relation to symptoms of wheeze and/or eczema during the first 2 years of life. We also excluded children with reported wheeze between 3 months and 1 year of age and a reported doctor diagnosis of asthma during the first 2 years of life to address further the issue of disease-related modification of exposure.

Children were included if information was available from the baseline questionnaire, the questionnaires at ages 1 and/or 2 years, 4, and 8 years, as well as on weight and height at ages 1 and 7 years and on asthma at age 8 years (n = 2075 children, 51% of the original cohort). Of the children included, 1609 had information on allergic sensitization. In different analyses, we have used all included children with data on each specific variable; this explains why the number of children varies between analyses.

RESULTS

The 2075 children included in this study were highly representative when compared with the children in the baseline cohort regarding distribution of exposure factors such as gender, birth weight, maternal age at baseline, maternal overweight at baseline, parental history of allergic disease, socioeconomic status, smoking, breastfeeding duration, and asthma prevalence (data not shown).

At age 12 months 15.6% of the children were classified as having high BMI (BMI ≥85th percentile) compared with 15.0% at age 18 months, 14.8% at age 4 years, and 14.1% at age 7 years. At early age (age 12 and/or 18 months), 22.0% (n = 430) of the children were classified as having high BMI. A high BMI at early age was more prevalent among children whose mothers' smoked during pregnancy and/or at baseline and among children in the highest tertile of birth weight (Table 1).

The prevalence of asthma was 6.0% (n = 124) at age 8 years. Figure 1 shows mean BMI at age 12 and 18 months and at age 4 and 7 years among children with versus without asthma at age 8 years (unadjusted data). Among children with asthma at 8 years of age, 78.2% had symptoms of wheeze and/or eczema during their first 2 years of life compared with 40.8% among children without asthma at 8 years (95% CI: 69.9–85.1 compared with 38.6–43.0). Children with early symptoms of wheeze and/or eczema had a tendency to be in the group with high BMI at all investigated ages, but these differences were not statistically significant.

High BMI at age 1, 4, and/or 7 years was associated with a significantly increased risk of asthma at age 8 years (Table 2). However, we observed no significant association with high BMI at age 18 months. Analysis of changes in BMI status between early age and 7 years showed that children with normal weight at early age who had a high BMI at 7 years had a significantly increased risk of asthma at age 8 years. Moreover, a tendency (P = .084) toward an increased risk was observed among children with high BMI at both ages. Likewise, when looking at change in BMI status between age 4 and 7 years, we noted that children with late or persistent high BMI had significantly increased risk of asthma at age 8 years. In contrast, no significant association between high BMI and asthma was observed among children with a high BMI at early age or age 4 years if their weight had normalized at age 7 years. To address the issue of disease-related modification of exposure, we also adjusted for wheeze and/or eczema during the first 2 years in the multivariate model. This had no major influence on the observed ORs (data not shown). In addition, we excluded children with early symptoms of wheeze and children with doctor's diagnosis of asthma before 2 years of age, leaving 1698 children in the analyses. High BMI at age 7 years was still associated with an

TABLE 1 Distribution of Exposure Characteristics in Relation to Overweight at Early Age (12 and/or 18 months)

	N	High BMI[a] at Early Age (*n* = 430)		
		n	%	95% CI
All children	1951	430	22.0	
Gender				
Female	951	210	22.1	19.5–24.9
Male	1000	220	22.0	19.5–24.7
Exclusive breastfeeding				
<4 mo	360	75	20.8	16.8–25.4
≥4 mo	1566	348	22.2	20.2–24.4
Maternal age at baseline				
≤25 y	136	22	16.2	10.4–23.5
>25 y	1814	408	22.5	20.6–24.5
Parental history of allergic disease				
No	1347	303	22.5	20.3–24.8
Yes	588	124	21.1	17.9–24.6
Maternal asthma				
No	1768	390	22.1	20.1–24.1
Yes	183	40	21.9	16.1–28.6
Maternal smoking[b]				
No	1717	361	21.0	19.1–23.0
Yes	234	69	29.5	23.7–35.8
Birth wt				
Quantile 1: ≤3335 g	632	93	14.7	12.0–17.7
Quantile 2: 3336–3765 g	644	134	20.8	17.7–24.2
Quantile 3: ≥3766 g	658	200	30.4	26.9–34.1
Maternal overweight[c]				
No	1330	272	20.5	18.3–22.7
Yes	357	91	25.5	21.0–30.3
Socioeconomic status				
White-collar worker	1633	355	21.7	19.8–23.8
Blue-collar worker	293	69	23.6	18.8–28.8
Early symptoms[d]				
No	1102	230	20.9	18.5–23.4
Yes	817	192	23.5	20.6–26.6

[a] Cutoff point of BMI was set to the 85th percentile based on children in the BAMSE study. High BMI was defined as a BMI ≥85th percentile.

[b] The mother smoked at least 1 cigarette per day at any point during pregnancy and/or at baseline.

[c] BMI ≥25 on the basis of the mother's prepregnancy weight.

[d] Symptoms of wheeze and/or eczema during the first 2 year of the child's life.

increased risk of asthma at 8 years (OR: 2.48; 95% CI: 1.40–4.38), whereas high BMI at earlier ages was not (OR: 1.17; 95% CI: 0.60–2.28 for age 1 year).

Stratifying for parental history of allergic disease showed that high BMI was significantly associated with asthma at 8 years only among children with no parental history of allergic disease, in a similar manner as for all children (OR: 2.64, 95% CI: 1.47–4.73 for 1 year; OR: 2.25, 95% CI: 1.20–4.24 for 4 years; and OR: 2.95, 95% CI: 1.61–5.39 for 7 years). Table 3 shows that persistent or late high BMI between early age and age 7 years and also between ages 4 and 7 years was associated with increased risk of asthma at 8 years of age in children without parental history of allergic disease. Moreover, high BMI at early age alone was associated with an increased risk of asthma at age 8 years.

The association between high BMI and sensitization to inhalant allergens at age 8 years is explored in Table 4. Children with normal BMI at early age who had high BMI at age 7 years had a significantly increased risk of sensitization to inhalant allergens. Moreover, a tendency toward an increased risk was observed for children with persistent or late high BMI between 4 and 7 years. In contrast, no associations were observed for sensitization to food allergens (data not shown).

DISCUSSION

In our prospective cohort of 2075 Swedish children, high BMI values at age 1, 4, and 7 years were all associated with an increased risk of asthma at age 8 years. However, no significant association was observed among children with high BMI at 12 and/or 18 months (early age) or at 4 years who had developed a normal BMI by age 7 years. In contrast, children with high BMI at age 7 years had an elevated risk of asthma at age 8 years, regardless of their BMI earlier in life. Moreover, we observed an increased risk of sensitization to inhalant allergens among children with high BMI at age 7 years.

Strengths of the current study include the prospective population-based design, the longitudinal analyses, and the fact that the weight and height were measured by trained nurses. Differential misclassification of exposure is unlikely because the measurements took place during routine controls at child health care centers and schools. Information on asthma symptoms was collected repeatedly during the follow-up. In addition to information on asthma symptoms, we also had information on sensitization to inhalant and food allergens.

Disease-related modification of exposure (also referred to as reverse causality) may be an important concern. We tried to eliminate this by adjusting for early symptoms of wheeze and eczema in the multivariate analyses. These adjustments had no major influence on the observed ORs. In addition, children with wheeze during the first year of life and with a doctor's diagnosis of asthma before 2 years of age were excluded from the analyses. After this exclusion, high BMI at age 7 years was still significantly associated with asthma at 8 years of age. These analyses indicate

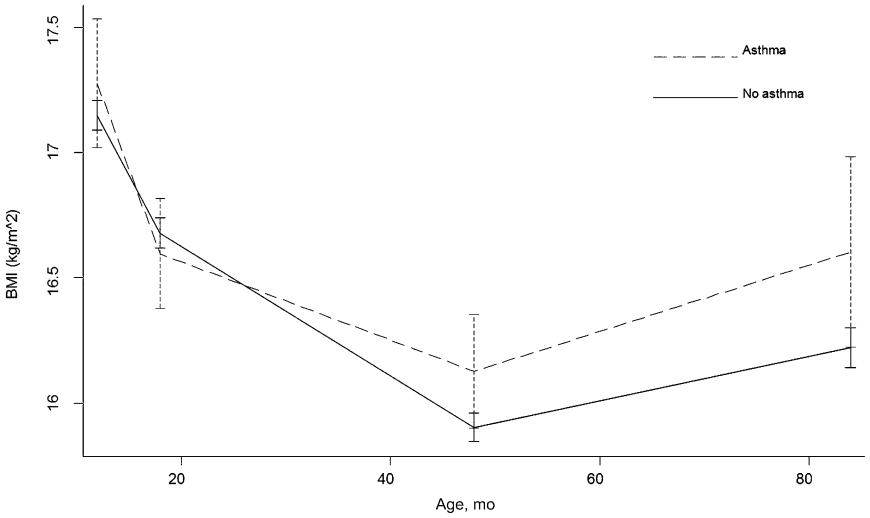

FIGURE 1
BMI from 1 to 7 years for children without asthma at 8 years (solid line) and for children with asthma at 8 years (dashed line) in the BAMSE study.

TABLE 2 Adjusted Associations Between High BMI at 1, 1.5, 4, and 7 Years and Change in BMI Status During Childhood and Asthma at 8 Years of Age

	n	Asthma at 8 Years of Age		
		n	Adjusted OR[a]	95% CI
BMI status at 1 y				
Normal	1751	98	1.00	
High	324	26	1.62[b]	1.01–2.60
BMI status at 1.5 y				
Normal	1633	98	1.00	
High	288	16	0.96	0.55–1.69
BMI status at 4 y				
Normal	1688	89	1.00	
High	294	25	1.72[b]	1.06–2.80
BMI status at 7 y				
Normal	1782	94	1.00	
High	293	30	2.13[b]	1.36–3.35
Change in BMI status between 1–1.5 and 7 y				
Persistent normal	1358	69	1.00	
Early high	308	17	1.21	0.69–2.11
Late high	171	19	2.51[b]	1.45–4.35
Persistent high	122	11	1.89	0.92–3.87
Change in BMI status between 4 and 7 y				
Persistent normal	1560	77	1.00	
Early high	140	8	1.25	0.58–2.67
Late high	128	12	2.09[b]	1.09–3.98
Persistent high	154	17	2.49[b]	1.38–4.49

[a] Adjusted for parental history of allergic disease, gender, breastfeeding duration, birth weight, maternal age at baseline, and maternal smoking during pregnancy and/or at baseline.
[b] $P < .05$.

that disease-related modification of exposure had no major influence on our results.

An increased risk of asthma in overweight children was observed in several earlier prospective studies.[9–17] There are also some published studies that have not found any association between asthma and overweight in children.[19,27] These studies have a cross-sectional design in common; a prospective design is much more suitable for suggesting risk and direction of causation. Our finding that only late and persistent high BMI were associated with asthma corresponds with results from the Dutch cohort showing that children with a current high BMI are at increased risk for having asthma symptoms at 8 years of age.[17] The results from our study and the Dutch cohort[17] do not give convincing support to the hypothesis that overweight causes asthma in children. These findings might reflect a cross-sectional association between high BMI and asthma, because no significant association could be seen among children who had previously been overweight but whose weight later became normal. Nevertheless, we cannot exclude a casual association between obesity and asthma.

Among children with no parental history of allergic disease, an association between high BMI and asthma was observed at all ages. No associations between high BMI and asthma were observed among children whose parents had a history of allergic disease. A possible explanation for this difference can be that parental history of allergic disease in itself entails such a great risk of developing asthma[28] that overweight does not additional increase that risk, whereas for a child with no parental history of allergic disease, overweight is a risk factor. The clinical implication of this may be substantial, but before any recommendations can be given, our data need to be verified by others.

We observed an increased risk of sensitization to inhalant allergens among children with a high BMI at 7 years. However, no such associations were observed for food allergens. The results from previous studies on BMI and allergic sensitization are inconclusive. Some studies showed an increased risk of sensitization,[19–21] mostly to inhalant allergens,[19,20] and sometimes the risk is restricted to certain subgroups of the population.[19,20] In contrast, other studies showed no association between BMI

TABLE 3 Adjusted Associations Between Change in BMI Status During Childhood and Asthma at 8 Years of Age, Stratified on Parental History of Allergic Disease

	No Parental History of Allergic Disease				Parental History of Allergic Disease			
	Asthma at 8 y of age				Asthma at 8 y of age			
	N	*n*	Adjusted OR[a]	95% CI	*N*	*n*	Adjusted OR[a]	95% CI
Change in BMI status between 1–1.5 and 7 y								
Persistent normal	941	25	1.00		405	43	1.00	
Early high	217	14	2.70[b]	1.35–5.40	90	3	0.31	0.09–1.05
Late high	107	11	4.59[b]	2.15–9.78	63	8	1.42	0.62–3.25
Persistent high	86	7	3.49[b]	1.32–9.24	34	4	1.09	0.36–3.32
Change in BMI status between 4 and 7 y								
Persistent normal	1078	35	1.00		472	42	1.00	
Early high	101	5	1.60	0.61–4.24	39	3	0.78	0.23–2.71
Late high	82	7	3.03[b]	1.28–7.16	46	5	1.37	0.50–3.72
Persistent high	103	11	3.75[b]	1.73-8.10	48	6	1.55	0.61-3.97

[a] Adjusted for gender, breastfeeding duration, birth weight, maternal age at birth, and maternal smoking during pregnancy and/or at baseline.
[b] $P < .05$.

TABLE 4 Adjusted Associations Between High BMI at 1, 1.5, 4, and 7 Years and Change in BMI Status During Childhood, and Sensitization to Inhalant Allergens at Age 8

		Sensitization to Inhalant Allergens		
	N	*n*	Adjusted OR[a]	95% CI
BMI status at 1 y				
Normal	1362	328	1.00	
High	250	74	1.43[b]	1.04–1.96
BMI status at 1.5 y				
Normal	1269	318	1.00	
High	228	59	1.10	0.78–1.55
BMI status at 4 y				
Normal	1306	317	1.00	
High	234	63	1.25	0.90–1.75
BMI status at 7 y				
Normal	1384	335	1.00	
High	228	67	1.42[b]	1.02–1.97
Change in BMI status between 1–1.5 and 7 y				
Persistent normal	1052	250	1.00	
Early high	243	67	1.25	0.90–1.74
Late high	135	43	1.59[b]	1.06–2.39
Persistent high	93	24	1.30	0.77–2.19
Change in BMI status between 4 and 7 y				
Persistent normal	1202	286	1.00	
Early high	120	30	1.12	0.71–1.76
Late high	104	31	1.44	0.91–2.28
Persistent high	114	33	1.50	0.95–2.36

[a] Adjusted for parental history of allergic disease, gender, breastfeeding duration, birth weight, maternal age at baseline, and maternal smoking during pregnancy and/or at baseline.
[b] $P < .05$.

and allergic sensitization.[8,17,18] One explanation for the discrepancy between the various studies on BMI and allergic sensitization might be differences in the range of allergens tested or in the methods used.

An association between overweight and asthma is biologically plausible and most likely multifactorial. One factor that might play a role is leptin. Leptin is an adipocyte-derived hormone and has been suggested to upregulate inflammatory immune responses[29]; asthma is recognized as a chronic inflammatory disease of the airways. A study by Mai and colleagues supports this theory; they observed higher levels of serum leptin in overweight children than in children of normal weight, and in addition, the levels of leptin in overweight children with current asthma were higher (albeit not significantly) than levels in children without current asthma despite similar BMI.[30] However, our study does not allow us to draw any conclusions regarding the biological mechanisms underlying the association between overweight and asthma.

CONCLUSION

In conclusion, our study among 2075 Swedish boys and girls followed from birth up to age 8 years indicates that high BMI during the first 4 years of life does not increase the risk of asthma at school age among children who have reached normal weight. However, high BMI at age 7 years is associated with an increased risk of asthma and sensitization to inhalant allergens in school age.

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