

Association between obesity and atopic dermatitis in childhood: A case-control study

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Background: Obesity in children is associated with increased asthma and atopy.

Objective: We sought to determine whether obesity in childhood or adolescence increases the risk of atopic dermatitis.

Methods: This retrospective, practice-based, case-control study randomly sampled 414 children and adolescents (age, 1-21 years) with atopic dermatitis between January 2000 and December 2007 and 828 randomly sampled healthy control subjects. Information was obtained from an electronic medical record. Observations were made before the *a priori* hypothesis. **Results:** Obesity in children is associated with increased atopic dermatitis (conditional logistic regression: odds ratio, 2.00; 95% CI, 1.22-3.26; $P = .006$). These atopic dermatitis-predisposing effects are found when obesity started by less than 2 years of age (adjusted odds ratio [aOR], 15.10; 95% CI, 1.51-151.21; $P = .02$) and 2 to 5 years (aOR, 2.58; 95% CI, 1.24-5.41; $P = .01$) but not greater than 5 years (aOR, 1.32; 95% CI, 0.66-2.64; $P = .43$) and when obesity was prolonged for 2.5 to 5 years (aOR, 2.64; 95% CI, 1.13-6.18; $P = .03$) and greater than 5 years (aOR, 3.40; 95% CI, 1.34-8.63; $P = 0.01$). Obesity is associated with more severe atopic dermatitis (ordinal logistic regression: aOR, 2.37; 95% CI, 1.24-5.37; $P = .01$). Obese children who eventually have atopic dermatitis require more frequent pediatrician visits for the management of atopic dermatitis (ordinal logistic regression: aOR, 2.22; 95% CI, 1.12-4.50; $P = .03$).

Conclusion: Prolonged obesity in early childhood is a risk factor for atopic dermatitis. Weight loss might be an important approach for the prevention and treatment of atopic dermatitis in children. (J Allergy Clin Immunol 2011;■■■:■■■-■■■.)

Key words: Atopic dermatitis, obesity, overweight, body mass index, weight, eczema, atopy

Atopic dermatitis is a chronic, recurrent, pruritic inflammatory disorder of the skin that has reached epidemic proportions throughout the world. Atopic dermatitis is characterized by

Abbreviations used

aOR: Adjusted odds ratio
BMI: Body mass index
CDC: Centers for disease control and prevention
IQR: Interquartile range
OR: Odds ratio
WHO: World Health Organization

eczematous lesions, which can be intensely pruritic and a significant cause of morbidity. The prevalence of atopic dermatitis in childhood has increased from 2% to 3% before 1960, to 9% to 12% after 1970,¹ and to as high as 20%.^{2,3} The reasons for this increase are not well understood. However, at the same time, the rate of obesity has increased by more than double in children and adolescents between 1976 and 1980 and 2007 and 2008.^{4,5}

Obesity has been shown to have several effects on the immune system, including preferential activation and trafficking of leukocyte subsets⁶⁻¹¹ and proinflammatory immune responses^{7,8,12} that might modulate the severity of atopic disorders, such as atopic dermatitis or asthma. Multiple studies demonstrated an association between obesity and asthma in children and adolescents,¹³⁻²⁰ as well as wheeze.^{21,22} However, an association between obesity and atopic dermatitis has not been well established.

In this study we use a retrospective case-control study of a pediatric cohort to determine the effect of obesity in early and late childhood on the development of atopic dermatitis. The results of this study suggest that prolonged obesity beginning early in life is associated with increased risk for and severity of atopic dermatitis and more frequent atopic dermatitis-related pediatrician's office visits.

METHODS

Subjects and matching

The study was approved by the institutional review board for human subjects of the SUNY Downstate Medical Center, Brooklyn, New York. Patients with atopic dermatitis (International Classification of Diseases-ninth revision diagnostic code 691.8) and control subjects were randomly selected from the electronic medical record of outpatient pediatric practices in Brooklyn, New York, between January 2000 and December 2007 ($n =$ approximately 6000-patient pool). Selection for this retrospective case-control study was done by using a computerized random-number generator list provided by a statistician who was not involved in the data collection. Inclusion criteria were children who received primary care at these practices, male or female sex, and age of 1 to 18 years. Exclusion criteria included diagnosis of atopic dermatitis before diagnosis of overweight status or obesity, obesity at birth or during the first 6 months of life, history of autoimmune disorders or

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immunodeficiency, use of corticosteroids or immunotherapy, personal or family history of cigarette smoking, and incomplete follow-up. Control subjects were pairwise matched by age in years, with 2 control subjects per case. Cases and control subjects were linked by a blocking variable that was used for conditional logistic regression.

Atopic dermatitis

Criteria for the diagnosis of atopic dermatitis were based on the guidelines of Hanifin and Rajka.^{23,24} Characteristics of atopic dermatitis lesions typically vary with age, although chronic and recurrent pruritis is found in all age groups. Distribution of eczematous lesions shifts with age, affecting the cheeks and extensor surfaces of the extremities in infancy and flexural areas and dorsal extremities in childhood and adolescence. The children were routinely examined by a pediatrician, and physical signs of atopic dermatitis were documented. The date of diagnosis for atopic dermatitis was documented as the date of initial presentation of symptoms. The severity of atopic dermatitis was classified by a pediatrician as mild, moderate, or severe based on the extent and intensity of eczematous lesions, pruritis, and sleep disturbance, without the use of an established scoring system.

Growth parameters

Growth parameters were routinely measured by a physician at each well and sick visit. Weight while supine (in pounds), length from head to toe (in inches), and head circumference (in centimeters) were measured for patients 2 years of age or younger. Weight (in pounds) and height (in inches) while standing were measured for patients older than 2 years. Percentiles for weight for age, height for age, and head circumference for age were calculated according to standard curves of both the Centers for Disease Control and Prevention (CDC)²⁵ and the World Health Organization (WHO).²⁶

Body mass index (BMI) was calculated as follows:

$$(\text{Weight [lb]} * 703) / \text{height}^2.$$

CDC standards for BMI-for-age percentiles are used in clinical practice in the United States; however, these percentiles only exist for patients 2 years of age or older.²⁶ In contrast, WHO standards²⁵ for BMI for age are used outside the United States but exist for patients of all ages. Thus both CDC and WHO BMI-for-age standards were tested. BMI and BMI percentile showed nonmonotone curves when plotted against the end points of the study. Therefore an ordinal variable was encoded to represent normal weight, overweight, and obesity. Overweight was taken as a BMI percentile of 85% to less than 95%, and obese was taken as a BMI percentile of 95% or greater for both WHO and CDC percentiles.

It was hypothesized that long-term, rather than short-term, obesity is a stronger risk factor for atopic dermatitis. Therefore duration of overweight status and obesity was encoded as ordinal variables representing less than 0.5, 0.5 to 2.5, 2.5 to 5, and greater than 5 years. Earliest age of overweight status and obesity based on WHO BMI-for-age percentiles were encoded as ordinal variables representing 2 or less, 2 to 5, and greater than 5 years. Because CDC BMI percentiles start from 2 years of age, the earliest age of overweight status and obesity based on CDC BMI-for-age percentiles was modeled as ordinal variables representing 2 to 5 and greater than 5 years.

Minimum, maximum, and weighted means were determined for all growth parameters measured.

Sample size calculation

A priori power analysis was based on the Fisher exact test, assuming 85% power with the use of 2-sided tests and an α level of .01.²⁷ The nonexposure rate in the atopic dermatitis or "referent" group was predicted to be 83% based on recent National Health and Nutrition Examination Survey data demonstrating 16.9% obesity prevalence in children and adolescents in the United States.⁴ The odds ratio (OR) of having atopic dermatitis after obesity was predicted to be 2.0. With 2:1 control matching, the number of patients needed was estimated to be 1167, with 389 patients with atopic dermatitis and 778 control subjects.

Statistical analysis

The baseline characteristics of patients with atopic dermatitis and those without were examined. All continuous variables of patients' characteristics, including height, weight, BMI, head circumference, age at onset, duration of overweight status and obesity, and age at the time of the first atopic dermatitis episode were not normally distributed, as judged by analysis of normality with Shapiro-Wilk and Kolmogorov-Smirnov tests ($P < .01$).^{28,29} Therefore data are presented as medians, interquartile ranges (IQRs), and ranges. All data processing and statistics were done with SAS version 9.2 software (SAS Institute, Inc, Cary, NC).

A 2-sided P value of less than .05 was taken to indicate statistical significance for all estimates. However, the multiple dependent tests performed in this study ($k = 25$) increase the risk of falsely rejecting the null hypothesis. Therefore P values near .05 should be interpreted with caution.

Regression analysis

Conditional logistic regression for matched analysis was used to determine whether overweight status and obesity were associated with atopic dermatitis. Because atopic dermatitis is more common in early childhood, models were stratified by a blocking variable that represented age-matched pairs. Because subjects were age matched by current age (age on March 1, 2010), current age was included as a covariate in all parsimonious models. Additional matching by other demographic variables was not performed because it was deemed to decrease statistical efficiency and not eliminate confounding from other variables and even introduce unnecessary bias into the study design.³⁰ Sex; season of birth; comorbid asthma, allergic rhinoconjunctivitis, and food allergy; race/ethnicity; and immunization up-to-date status were all modeled as categorical variables. Age at the time of the study and at first diagnosis of atopic dermatitis, height, height for age, weight, weight for age, head circumference, head circumference for age, BMI, and BMI for age were modeled as continuous numerical variables. The OR for atopic dermatitis was calculated with the 95% CI. The adjusted OR (aOR) was calculated by including sex, season of birth, race/ethnicity, and immunization up-to-date status in the model.

Conditional logistic regression was also used to determine whether the duration and onset of overweight status and obesity was associated with atopic dermatitis. Models were stratified by a blocking variable that represented age-matched pairs, and current age was included as a covariate in all parsimonious models, as above. For duration of obesity, the independent variable was encoded as an ordinal variable from 0 to 4 representing normal weight and obesity (<0.5 , 0.5-2.5, 2.5-5.0, and >5.0 years). For earliest onset of obesity, the independent variable was encoded as an ordinal variable from 0 to 3, representing normal weight and obesity (≤ 2.0 , 2-5, and >5 years). The aOR was calculated by including sex, season of birth, race/ethnicity, and immunization up-to-date status in the model.

Ordinal logistic regression was used to determine whether overweight status and obesity were associated with increased severity of atopic dermatitis. The dependent variable was encoded as an ordinal variable from 1 to 3 representing mild, moderate, and severe, respectively. This approach was used because the models satisfied the proportional odds assumption as judged by using the score test ($P > .05$).

RESULTS

Population characteristics

Four hundred seventy-five patients with atopic dermatitis were randomly selected for the study; 10 were excluded because of incomplete follow-up, and 51 were excluded based on exclusion criteria. Eight hundred twenty-eight age-matched patients without a history of atopic dermatitis who had complete follow-up and met the exclusion criteria were randomly selected as control subjects. Conditional logistic regression models were constructed by using the blocking variable based on current age matching. Therefore current age was included as a covariate in all final

TABLE I. Patients' characteristics

Variable	Patients with atopic dermatitis (n = 414)	Control subjects (n = 828)	OR (95% CI)	P value†
Age (y)*	7.0 (6.6-18.7)	7.0 (6.6-18.9)	0.24 (0.15-0.37)	<.0001
Male sex, no. (%)	216 (52.2)	434 (52.4)	0.98 (0.77-1.25)	.88
Season of birth, no. (%)‡				
Winter	127 (30.7)	191 (23.1)	1.00	—
Spring	140 (33.8)	226 (27.3)	0.86 (0.63-1.17)	.34
Summer	49 (11.8)	194 (23.4)	0.48 (0.33-0.72)	.0003
Autumn	98 (23.7)	217 (26.2)	0.84 (0.60-1.17)	.30
Season of diagnosis (%)§				
Winter	119 (28.7)		—	
Spring	100 (24.2)			
Summer	103 (24.9)			
Autumn	92 (22.2)			
Age at first AD episode (y)*	2.8 (5.0-17.7)		—	
Atopic disease, no. (%)¶	136 (32.9)	15 (1.8)	73.74 (38.65-140.71)	<.0001
Asthma	45 (10.9)	4 (0.5)	24.16 (8.60-67.90)	<.0001
Allergic rhinoconjunctivitis	116 (28.0)	15 (1.8)	65.95 (35.46-122.66)	<.0001
Food allergy	38 (9.2)	3 (0.4)	24.39 (7.46-79.70)	<.0001
White (%)	408 (98.6)	819 (98.9)	1.53 (0.53-4.40)	.43
IUTD (%)	396 (98.3)	812 (98.1)	0.69 (0.24-1.92)	.47

Significant *P* values are indicated in boldface.

*Values are presented as medians (IQRs or ranges).

†*P* values for the comparison between the atopic dermatitis and control groups were calculated by using conditional logistic regression models stratified by the matching variable, including current age as a fixed covariate.

‡Season of birth.

§Season of diagnosis: winter = December through February; spring = March through May; summer = June through August; autumn = September through November.

||IUTD = all other immunizations up to date, including hepatitis A virus, hepatitis B virus, influenza, inactivated polio vaccine, measles-mumps-rubella, and varicella zoster according to the recommended vaccination schedule of the American Academy of Pediatrics.

¶Atopic disease = asthma and/or allergic rhinoconjunctivitis and/or food allergy.

models, and increasing age was associated with decreased odds of atopic dermatitis (OR, 0.24; 95% CI, 0.15-0.37; *P* < .0001). Patients with atopic dermatitis were similar to control subjects with respect to sex (52.2% vs 52.4%, *P* = .88), race/ethnicity (98.6% vs 98.9%, *P* = .43), and being up to date with other vaccinations (98.3% vs 98.1%, *P* = .47; Table I). Patients with atopic dermatitis were given diagnoses at a median age of 2.8 years (IQR, 5.0) evenly throughout all 4 seasons (22.2% to 28.7% per season). Patients with atopic dermatitis had significantly higher frequencies of atopic diseases, including asthma, rhinoconjunctivitis, and food allergies (*P* < .0001). Interestingly, patients born during the summer had significantly lower odds of atopic dermatitis compared with those born in winter (OR, 0.48; 95% CI, 0.33-0.72; *P* = .0003).

Patients' weight, height, head circumference, and BMI

Patients with atopic dermatitis were similar to control subjects with respect to birth weight (median ± IQR, 7.2 ± 1.1 vs 7.4 ± 1.0 lbs; *P* = .37) and birth-weight percentiles (*P* = .18-.37, see Table E1 in this article's Online Repository at www.jacionline.org). None of the subjects were obese at birth or during the first 6 months of life. Patients with atopic dermatitis had significantly higher maximum lifetime weight-for-age WHO percentiles (80.4% ± 49.3% vs 67.4% ± 52.2%, *P* < .0001) and maximum lifetime BMI-for-age WHO percentiles (90.0% ± 25.6% vs 81.3% ± 34.1%, *P* < .0001; Table E1). Otherwise, there were no significant differences of minimum, maximum, or weighted mean weight-for-age, height-for-age, head-circumference-for-age, or BMI-for-age CDC or WHO percentiles between patients

with atopic dermatitis and control subjects when modeled as continuous variables (*P* = .20-.99, see Table E1).

Obesity increases odds of atopic dermatitis

Obesity was associated with increased odds of atopic dermatitis (conditional logistic regression; CDC: OR, 2.00; 95% CI, 1.22-3.26; *P* = .006; WHO: OR, 1.91; 95% CI, 1.19-3.09; *P* = .008; Table II). The association between obesity and atopic dermatitis remained significant in multivariate models that included sex, ethnicity, season of birth, and being up to date with other immunizations (*P* = .003-.006, Table II). In contrast, there was no significant association between overweight status by CDC or WHO standards and atopic dermatitis (*P* = .12-.17, Table II).

Prolonged obesity increases odds of atopic dermatitis

The effect of duration of obesity on the OR of atopic dermatitis was determined by constructing conditional logistic regression models using dummy variable coding of intervals for years of obesity (<0.5, 0.5-2.5, 2.5-5, and >5 years). The effects of obesity, as determined by CDC criteria, were only significant when ongoing for 2.5 to 5 years (aOR, 2.64; 95% CI, 1.13-6.18; *P* = .03) and greater than 5 years (aOR, 3.40; 95% CI, 1.34-8.63; *P* = .01) but not at less than 0.5 years (aOR, 0.95; 95% CI, 0.27-3.29; *P* = .93) or 0.5 to 2.5 years (aOR, 1.98; 95% CI, 0.72-5.40; *P* = .18; Table III). The effect of obesity, as determined by WHO standards, was significant in a parsimonious model when ongoing for 0.5 to 2.5 years (OR, 3.90; 95% CI, 1.12-13.54; *P* = .03) but not at less than 0.5 years (*P* = .78), 2.5 to

TABLE II. Conditional logistic regression analysis of the effects of overweight status and obesity on the development of atopic dermatitis

BMI classification	No. of patients (%)		Atopic dermatitis			
	Patients with atopic dermatitis	Control subjects	OR (95% CI)*	P value	Adjusted OR (95% CI)†	P value
CDC‖						
Normal weight	348 (84.1)	713 (85.7)	1.00	—	1.00	—
Overweight‡	30 (7.3)	78 (9.4)	0.74 (0.47-1.16)	.18	0.69 (0.43-1.10)	.12
Obese§	36 (8.7)	11 (4.9)	2.00 (1.22-3.26)	.006	2.15 (1.29-3.56)	.003
WHO¶						
Normal weight	330 (79.7)	671 (80.7)	1.00	—	1.00	—
Overweight‡	46 (11.1)	119 (14.3)	0.78 (0.54-1.12)	0.17	0.77 (0.53-1.12)	.17
Obese§	38 (9.2)	12 (5.1)	1.91 (1.19-3.09)	.008	1.97 (1.21-3.21)	.006

Significant *P* values are indicated in boldface.

*All conditional logistic regression models were stratified by blocking (matching) variable, and age was included as a covariate.

†Adjusted ORs are from conditional logistic regression models including age, sex, race/ethnicity, season of birth, and immunizations up to date.

‡Overweight is defined as 85% < BMI percentile ≤ 95%.

§Obese is defined as BMI percentile > 95%.

‖CDC percentiles for BMI begin at 24 months of age. Thus the earliest age of onset for CDC-based models is 24 months.

¶WHO percentiles for BMI begin at birth. Thus the earliest age of onset for WHO-based models is 0 months.

TABLE III. Conditional logistic regression analysis of the effects of duration and age of onset of obesity on the development of atopic dermatitis

Variables	No. of obese patients‡ (%)		Atopic dermatitis			
	Patients with atopic dermatitis	Control subjects	OR (95% CI)*	P value	Adjusted OR (95% CI)†	P value
CDC§						
Duration (y)						
<0.5	4 (1.0)	10 (1.2)	0.84 (0.26-2.73)	.77	0.95 (0.27-3.29)	.93
0.5-2.5	9 (2.2)	9 (1.1)	2.33 (0.87-6.29)	.09	1.98 (0.72-5.40)	.18
2.5-5.0	12 (2.9)	12 (1.4)	2.56 (1.11-5.89)	.03	2.64 (1.13-6.18)	.03
>5.0	11 (2.7)	10 (1.2)	2.63 (1.08-6.39)	.03	3.40 (1.34-8.63)	.01
Age of onset (y)						
2.0-5.0	24 (5.8)	17 (2.0)	3.48 (1.75-6.95)	.0004	4.40 (2.10-9.22)	<.0001
>5.0	12 (2.9)	24 (2.9)	1.16 (0.56-2.38)	.69	1.13 (0.54-2.34)	.75
WHO						
Duration (y)						
<0.5	4 (1.0)	7 (0.8)	1.20 (0.34-4.19)	.78	1.0 (0.28-3.59)	.99
0.5-2.5	8 (1.9)	4 (0.5)	3.90 (1.12-13.54)	.03	3.32 (0.96-11.52)	.06
2.5-5.0	13 (3.1)	16 (1.9)	1.95 (0.91-4.16)	.09	2.10 (0.96-4.57)	.06
>5.0	13 (3.1)	15 (1.8)	1.94 (0.90-4.20)	.09	2.23 (1.01-4.96)	.04
Onset (y)						
≤2.0	7 (1.7)	1 (0.1)	12.90 (1.44-115.30)	.02	15.10 (1.51-151.21)	.02
2.0-5.0	17 (4.1)	16 (1.9)	2.54 (1.23-5.22)	.01	2.58 (1.24-5.41)	.01
>5.0	14 (3.4)	25 (3.0)	1.27 (0.64-2.50)	.49	1.32 (0.66-2.64)	.43

Significant *P* values are indicated in boldface.

*All conditional logistic regression models were stratified by blocking (matching) variable, and age was included as a covariate.

†Adjusted ORs are from conditional logistic regression models including age, sex, race/ethnicity, season of birth, and immunizations up to date.

‡Obese is defined as a BMI percentile greater than 95%.

§CDC percentiles for BMI begin at 24 months of age. Thus the earliest age of onset for CDC-based models is 24 months.

||WHO percentiles for BMI begin at birth. Thus the earliest age of onset for WHO-based models is 0 months.

5 years, or greater than 5 years ($P = .09$, Table III). However, in a multivariate model obesity was only significant at greater than 5 years (aOR, 2.23; 95% CI, 1.01-4.96; $P = .04$; Table III). These data suggest that prolonged obesity increases atopic dermatitis.

Obesity in early childhood increases odds of atopic dermatitis

The effect of age of onset of obesity on the OR of atopic dermatitis was determined by constructing conditional logistic regression models using dummy variable coding of intervals for age of obesity (<2, 2-5, and >5 years) compared with nonobesity.

The effects of obesity, as determined by CDC standards, were only significant when starting by age 2 to 5 years (aOR, 4.40; 95% CI, 2.10-9.22; $P < .0001$) but not at greater than 5 years (aOR, 1.13; 95% CI, 0.54-2.34; $P = .75$; Table III); onset before 2 years of age was not tested because CDC BMI-for-age percentiles were not available. The effect of obesity, as determined by WHO standards, was significant when starting at less than 2 years (aOR, 15.10; 95% CI, 1.51-151.21; $P = .02$) and 2 to 5 years (aOR, 2.58; 95% CI, 1.24-5.41; $P = 0.01$) but not at greater than 5 years (aOR, 1.32; 95% CI, 0.66-2.64; $P = .43$; Table III). These data suggest that obesity early in childhood increases atopic dermatitis.

TABLE IV. Ordinal logistic regression analysis of the effects of overweight status and obesity on the severity of atopic dermatitis

BMI classification	Severity of atopic dermatitis						
	No. of patients (%)			OR (95% CI)*	P value	Adjusted OR (95% CI)†	P value
	Mild	Moderate	Severe				
CDC							
Normal weight	53 (15.7)	249 (73.9)	35 (10.4)	1.00	—	1.00	—
Overweight‡	6 (20.7)	21 (72.4)	2 (6.9)	0.66 (0.29-1.51)	.32	0.52 (0.23-1.17)	.11
Obese§	4 (13.3)	18 (60.0)	8 (26.7)	2.38 (1.05-5.39)	.03	2.37 (1.24-5.37)	.01
WHO¶							
Normal weight	51 (16.0)	235 (73.7)	33 (10.3)	1.00	—	1.00	—
Overweight‡	8 (17.8)	33 (73.3)	4 (8.9)	0.82 (0.41-1.61)	.56	0.57 (0.29-1.11)	.10
Obese§	4 (12.5)	20 (62.5)	8 (25.0)	2.28 (1.03-5.05)	.04	2.23 (1.11-4.95)	.02

Significant *P* values are indicated in boldface.*Proportional odds assumption was met in all ordinal logistic regression models ($P > .05$, score test).

†Adjusted ORs are from conditional ordinal logistic regression models including age, sex, race/ethnicity, season of birth, and immunizations up to date.

‡Overweight is defined as 85% < BMI percentile ≤ 95%.

§Obese is defined as a BMI percentile of greater than 95%.

||CDC percentiles for BMI begin at 24 months of age. Thus the earliest age of onset for CDC based models is 24 months.

¶WHO percentiles for BMI begin at birth. Thus the earliest age of onset for WHO based models is 0 months.

TABLE V. Ordinal logistic regression analysis of the effects of overweight status and obesity on the frequency of pediatrician's office visits for atopic dermatitis

	No. of office visits (%)						
BMI classification	1	2-5	5-8	OR (95% CI)*	P value	Adjusted OR (95% CI)†	P value
CDC							
Normal weight	230 (84.6)	114 (85.1)	2 (50.0)	1.00	—	1.00	—
Overweight‡	18 (6.6)	12 (9.0)	0 (0.0)	1.53 (0.74-3.16)	.26	1.47 (0.70-3.07)	.31
Obese§	24 (8.8)	8 (6.0)	2 (50.0)	2.22 (1.08-4.59)	.03	2.22 (1.12-4.50)	.03
WHO¶							
Normal weight	222 (81.6)	106 (79.1)	2 (50.0)	1.00	—	1.00	—
Overweight‡	23 (8.5)	21 (15.8)	0 (0.0)	1.12 (0.62-2.03)	.70	0.81 (0.44-1.50)	.50
Obese§	27 (9.9)	7 (5.2)	2 (50.0)	2.80 (1.33-5.87)	.007	2.20 (1.04-4.67)	.03

Significant *P* values are indicated in boldface.*Proportional odds assumption was met in all ordinal logistic regression models ($P > .05$, score test).

†Adjusted ORs are from conditional ordinal logistic regression models including age, sex, race/ethnicity, season of birth, and immunizations up to date.

‡Overweight is defined as 85% < BMI percentile ≤ 95%.

§Obese is defined as a BMI percentile of greater than 95%.

||CDC percentiles for BMI begin at 24 months of age. Thus the earliest age of onset for CDC-based models is 24 months.

¶WHO percentiles for BMI begin at birth. Thus the earliest age of onset for WHO based models is 0 months.

Obesity increases severity of atopic dermatitis

Obesity was associated with increased odds of more severe atopic dermatitis (ordinal logistic regression; CDC: aOR, 2.37; 95% CI, 1.24-5.37; $P = .01$; WHO: aOR, 2.23; 95% CI, 1.11-4.95; $P = .02$; Table IV). In contrast, overweight status was not significantly associated with more severe atopic dermatitis ($P = .10$ -.11).

Obesity increases number of pediatrician visits for atopic dermatitis

Obesity was associated with increased odds of more frequent pediatrician's office visits for atopic dermatitis (ordinal logistic regression; CDC: aOR, 2.22; 95% CI, 1.12-4.50; $P = .03$; WHO: aOR, 2.20; 95% CI, 1.04-4.67; $P = .03$; Table V). In contrast, overweight status was not significantly associated with more frequent pediatrician's office visits for atopic dermatitis ($P = .26$ -.71).

DISCUSSION

The present study demonstrates an association between obesity and increased atopic dermatitis. We found that obesity in children

is associated with increased odds of atopic dermatitis and that these atopic dermatitis-predisposing effects are found when obesity started before 5 years of age, with the highest odds in the first 2 years, and when obesity was prolonged for greater than 2.5 years. Obesity is associated with increased odds of more severe atopic dermatitis and more frequent pediatrician's office visits devoted to atopic dermatitis.

These results are consistent with prior studies that reported associations between obesity in children and adolescents with asthma¹³⁻²⁰ and atopy.^{16,22,31} Some of those studies found no association between obesity and atopic dermatitis,^{15,32,33} whereas others found a significantly higher risk of atopic dermatitis with increased BMI.³⁴ However, none of those studies were primarily powered to examine the association between obesity and atopic dermatitis.

The findings of the present study suggest that the epidemic of obesity in the United States might be contributing to the increased prevalence of atopic dermatitis. It is estimated that the prevalence of atopic dermatitis has more than doubled over the past 5 decades.¹ Similarly, obesity has increased by more than double in children and adolescents between 1976 and 1980 and 2007 and

2008.^{4,5} Our results indicate that obesity might be a contributing factor to the increased prevalence of atopic dermatitis. However, the cause of atopic dermatitis is likely multifactorial. Our group recently reported an association between a single episode of chickenpox in early or late childhood compared with varicella vaccine and significant protection against atopic dermatitis.³⁵ It is possible that other factors, such as infectious exposures, genetics, or diet, might be common to both obesity and atopic dermatitis.

These findings also indicate that there is increased health care use by patients with atopic dermatitis who are obese. Obese patients are more likely to have atopic dermatitis, and obese patients with atopic dermatitis have more frequent pediatrician's office visits devoted to their atopic dermatitis. Obesity is a major public health burden that is already shown to cause increased asthma,¹³⁻²⁰ diabetes and secondary complications,^{36,37} cardiovascular disease,^{38,39} and impaired academic and psychosocial functioning.⁴⁰ This study reveals atopic dermatitis as yet another harmful consequence of obesity.

It is particularly interesting that prolonged obesity (>2.5 years), but not short-term obesity, was associated with atopic dermatitis. This suggests that reversal of obesity, if caught early, by means of aggressive weight loss intervention might be an important strategy for the prevention and treatment of atopic dermatitis. This is consistent with previous studies by others who found that asthmatic patients exhibited significant improvement of lung function and decreased asthma symptoms with weight loss.⁴¹⁻⁴³ Further studies are warranted to determine whether reversal of obesity can improve atopic dermatitis symptoms.

We found a significant association between obesity occurring within the first 2 years of life and increases in atopic dermatitis symptoms, suggesting a possible effect on the immature immune system found in the first year of life. This study is consistent with previous studies that demonstrated that obesity is associated with a variety of immune sequelae, including accumulation of macrophages⁴⁴ and cytotoxic T cells⁴⁵ in adipose tissue and production of TNF- α and IL-6.⁴⁴ Leptin, which is produced by adipocytes, has numerous proinflammatory effects on the immune system, including proliferation and activation of circulating monocytes⁶ and CD4⁺ and CD8⁺ T cells,⁷ polarization of T cells toward a T_H1 response,⁸ development and activation of natural killer cells,⁹ promotion of neutrophil chemotaxis,^{10,11} and upregulation of numerous cytokines, including TNF- α , IL-6,¹² IFN- γ , and IL-2.^{7,8} In addition, adipose tissue produces and systemically releases a variety of other adipokines, including adiponectin, resistin, and visfatin.⁴⁶ Indeed, studies by Nagel et al⁴⁷ found associations between high leptin levels and asthma and between low adiponectin levels and atopic dermatitis. As of yet, the mechanism behind the association of obesity early in childhood and atopic dermatitis remains unclear. However, these studies do indicate that the immunomodulatory effects of obesity might be most profound during the first 2 years of life.

This study has several strengths, including a well-powered sample size of cases and control subjects and the use of multiple statistical methodologies. Statistical modeling of both CDC and WHO BMI-for-age percentiles allowed determination of the effects of obesity during infancy. The data used in this study are less likely to be affected by subjective parental interpretation and recall bias because diagnoses and other clinical information were obtained by a physician during a clinical encounter and were not parent or questionnaire based.

This study has potential limitations. Selection bias might be more prone in a retrospective/observational study and was addressed by using a computerized random-number generator list for patient selection. Because this study was retrospective, several important clinical factors were not collected, including stress and irritant exposures and food and/or environmental histories. Moreover, results of atopic dermatitis scoring systems, such as SCORAD or the Eczema Area and Severity Index,^{48,49} were not recorded by the pediatrician during evaluation.

In conclusion, this study provides evidence that obese children are at higher risk for atopic dermatitis. These observations suggest that early intervention for weight loss by pediatricians might decrease the risk of atopic dermatitis. Furthermore, intervention for weight loss might be an important strategy for the treatment of children with atopic dermatitis in addition to conventional therapy. Further studies might identify underlying pathways involved in the pathogenesis of atopic dermatitis and further elucidate the role of obesity in patients with atopic dermatitis.

Clinical implications: This study suggests that aggressive intervention for weight loss early in childhood might be an important strategy for the prevention and management of atopic dermatitis and other atopic diseases.

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TABLE E1. Birth weight, weight, height, head circumference, and BMI

Variable	Patients with atopic dermatitis (n = 414)	Control subjects (n = 828)	OR (95% CI)	P value†
Birth weight (%)	7.2 (1.1-8.8)	7.4 (1.0-3.1)	0.69 (0.31-1.54)	.37
CDC*	34.0 (22.0-73.0)	41.0 (38.0-76.0)	0.98 (0.95-1.01)	.18
WHO*	50.0 (22.0-83.3)	56.3 (41.6-87.3)	0.99 (0.96-1.01)	.27
Minimum weight (% for age)				
CDC*	19.0 (39.0-95.0)	24.0 (43.0-94.0)	0.99 (0.99-1.03)	.33
WHO*	25.0 (52.3-98.0)	30.9 (44.9-98.0)	1.00 (0.99-1.01)	.72
Maximum weight (% for age)				
CDC*	72.5 (50.0-94.0)	64.0 (48.0-94.0)	1.00 (0.99-1.01)	.70
WHO*	80.4 (49.3-98.0)	67.4 (52.2-98.0)	1.01 (1.01-1.02)	<.0001
Weighted mean weight (% for age)				
CDC*	47.7 (47.6-94.0)	42.0 (42.4-93.0)	1.00 (0.99-1.01)	.66
WHO*	48.0 (58.2-97.8)	49.1 (43.2-97.2)	1.00 (1.00-1.00)	.91
Minimum height (% for age)				
CDC*	25.6 (30.4-60.0)	27.0 (32.0-61.2)	1.29 (<0.001->999.9)	.98
WHO*	24.1 (50.9-59.5)	25.0 (52.6-58.9)	1.27 (<0.001->999.9)	.98
Maximum height (% for age)				
CDC*	63.8 (42.8-93.0)	64.0 (42.5-92.4)	1.00 (1.00-1.00)	.3
WHO*	85.1 (57.5-94.0)	89.3 (58.1-96.0)	0.52 (<0.001->999.9)	.98
Weighted mean height (% for age)				
CDC*	42.1 (50.7-92.0)	42.3 (45.8-92.5)	1.00 (1.00-1.00)	.99
WHO*	25.0 (49.3-98.0)	27.3 (49.3-98.0)	1.00 (0.99-1.01)	.71
Minimum head circumference (% for age)				
CDC*	28.0 (31.0-93.0)	27.0 (32.0-86.0)	1.00 (0.99-1.03)	.37
WHO*	23.0 (55.3-98.0)	25.0 (52.6-92.8)	1.00 (0.99-1.01)	.97
Maximum head circumference (% for age)				
CDC*	61.0 (38.0-92.0)	61.0 (48.0-89.5)	1.00 (0.99-1.001)	.42
WHO*	86.3 (45.9-98.0)	85.0 (51.2-98.0)	1.01 (0.99-1.01)	.20
Weighted mean head circumference (% for age)				
CDC*	45.3 (28.4-93.2)	45.9 (39.1-89.9)	1.00 (0.99-1.002)	.41
WHO*	45.0 (87.8-98.0)	36.1 (59.9-98.0)	1.00 (0.99-1.02)	.62
Minimum BMI (% for age)				
CDC*‡	26.0 (47.2-94.1)	36.0 (46.2-94.0)	1.00 (0.99-1.01)	.79
WHO*§	22.4 (43.1-98.0)	31.3 (43.9-98.0)	1.00 (0.99-1.003)	.33
Maximum BMI (% for age)				
CDC*‡	76.0 (56.0-94.0)	70.0 (48.0-94.0)	1.00 (0.99-1.01)	.48
WHO*§	90.0 (25.6-98.0)	81.3 (34.1-97.7)	1.01 (1.01-1.02)	<.0001
Weighted mean BMI (% for age)				
CDC*‡	52.9 (64.6-93.2)	54.5 (50.7-94.0)	1.00 (0.99-1.01)	.33
WHO*§	63.0 (49.5-98.0)	57.8 (43.7-98.0)	1.00 (1.00-1.00)	.96

Significant *P* values are indicated in boldface.

*Values are presented as medians (IQRs and ranges).

†*P* values for the comparison between the atopic dermatitis and control groups were calculated by using conditional logistic regression models stratified by the matching variable, including current age as a fixed covariate.

‡CDC percentiles for BMI are available only for 2 years of age and older and therefore do not include BMI values for ages 0 to 2 years.

§WHO percentiles for BMI are available only from birth and on and therefore include BMI values for ages 0 to 2 years.