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Title

Atopic dermatitis is more severe in children over the age of two who have an increased body mass index

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Short Title: Obesity and severity of atopic dermatitis

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Abstract

Aim: Childhood obesity increases the risk of developing atopic dermatitis, but no objective measuring tool has been used to determine if it also affects the severity. Our aim was to determine if an association existed between increased body mass index (BMI) or weight for length and severity of atopic dermatitis, as measured by the SCORing Atopic Dermatitis (SCORAD) index.

Methods: Children with atopic dermatitis that presented to the emergency department at an urban children's hospital (n=104) were assessed using the SCORAD index. We assessed the relationship between BMI percentile or weight for length percentile, based on age and atopic dermatitis severity, using single variable multinomial logistic regression with odds ratios.

Results: A significant association was found between BMI >24 and atopic dermatitis severity for children older than two years. When analysed separately, a significant association between BMI percentile and SCORAD severity was found in boys but not girls.

Conclusion: These data suggest that the severity of atopic dermatitis is associated with increased BMI percentile in children older than two years, although this association was not apparent in younger ages using weight for length. Our results indicate the need for new avenues in the prevention and treatment of these entities.

Keywords: Atopic dermatitis, body mass index, eczema, obesity, severity

Key Notes

- Childhood obesity increases the risk of developing atopic dermatitis, but no objective measuring tool has been used to determine if it also affects the severity.
- Our study showed that increased body mass index but not weight for length was associated with atopic dermatitis severity as measured by the SCORing Atopic Dermatitis index
- However, a significant association between the body mass index and atopic dermatitis severity was only found in boys

Introduction

Atopic dermatitis, a common debilitating skin condition characterised by intense itching and subsequent lichenification, affects nearly 13% of all children in the United States, with prevalence of more than 18% in some states (1, 2). Obesity also affects a significant number of children and a study showed that in 2009 and 2010 nearly 17% of children and adolescents in the United States were obese (3) with additional increases in children considered overweight (4). The United States Centers for Disease Control and Prevention (CDC) defines an overweight child as having a BMI between the 85th and the 95th percentiles compared to children of the same age and gender, while obesity is defined as a having a body mass index (BMI) at or above the 95th percentile (5). Although being overweight is not associated with an increased risk of atopic dermatitis, being obese increases the risk of developing atopic dermatitis and is associated with an increased number of visits to the paediatrician for atopic dermatitis (6). While sequela of obesity currently account for up to 2.8% of all healthcare-related costs in the United States, atopic dermatitis also causes significant familial and financial burdens (7, 8), suggesting a great need to reduce both the incidence and prevalence of these diseases. It has previously

been suggested that obesity is associated with increased severity of atopic dermatitis (6), however no objective measurement of atopic dermatitis severity testing has been utilised.

Over 20 different measurement tools exist for the objective scoring of atopic dermatitis, but the SCORing Atopic Dermatitis index (SCORAD), Patient-Oriented Eczema Measure (POEM), and the Eczema Area and Severity Index (EASI) have the most validity and are recommended for use in clinical practice (9). The SCORAD index was developed in 1990 by the European Task Force and consists of three measurable components: extent, intensity and functional impact of the patient's atopic dermatitis. This index has been the most utilised scoring tool in randomised controlled studies for measuring the severity of atopic dermatitis (10). Our study tests the hypothesis that there is an association between obesity and increased severity of atopic dermatitis using objective tools.

Patients and Methods

Study Population The project proposal was reviewed and approved by the Institutional Review Board at Drexel University College of Medicine. Data were collected from 1 December 2013 to 1 June 2014 at St Christopher's Hospital for Children, an urban children's hospital with approximately 70,000 Emergency Department visits a year from a predominantly inner-city population. Children under the age of 18 with atopic dermatitis were included, with verbal consent obtained from parents if the child was younger than seven-years-of-age and from the patient themselves if they were over that age. The sample was predominantly drawn from surrounding urban neighborhoods. There were 104 participants included in this study and 48 children were under two-years-old and 56 children were two to 18-years-old. Half (n=52) of the participants were male and half were female. The majority of participants were African American (33 females and 21 males) and Hispanic (12 females and 24 males) with less participants who were Caucasian (seven females and six males) and Asian (no females and one male).

Measurements The age of the participants was recorded in years and months. Weight was measured to the nearest 0.1 kilogram with clothes on for children greater than two-years-old and without clothes for children less than two-years-old. Length and height were measured without shoes and recorded to the nearest 0.1 centimetre. All participants were assessed for weight and height/length by the principle examiner, who also evaluated each participant using the three components of the SCORAD index: extent, intensity and functional impact of atopic dermatitis. An overall score of 0-24 was categorised as mild, 25-49 as moderate and 50-103 as severe. Waist circumference was not measured in this study.

Calculations BMI was determined using the standard formula $weight\ (kg) / [height\ (m)]^2$ and the online CDC Child and Teen BMI calculator tool. BMI percentile was determined using the online CDC BMI Percentile Calculator tool. Children less than the 5th BMI percentile were considered as group one, those between the 5th and 95th percentile were considered as group two, and those greater than the 95th percentile were considered as group three (Figures 1, 2).

For children of less than two-years-old, weight for length was determined using the online CDC/National Center for Health Statistics Infant Weight for Length Percentiles (<36 months) tool. Infants less than 5th weight for length percentile were considered as group one, those between the 5th-95th percentile were considered as group two, and those greater than the 95th percentile were considered as group three (Figure 3). Participants were also categorised according to gender and race, although ultimately we did not analyse race independently due to the predominance of African American and Hispanic participants. Data was analysed using single variable multinomial logistic regression to determine significant relationships between BMI percentile groupings and SCORAD severity categories for children greater than two-years-old and between weight for length percentile grouping and SCORAD severity categories for

children less than two-years-old. Odds ratios were calculated to determine the risk of more severe atopic dermatitis for each group.

Results

There was a significant association between BMI > 24 and SCORAD severity categories for children over the age of two years (Figure 1). The odds ratio was 1.299 with a 95% confidence interval (CI) of 1.124 to 1.502 ($p=0.0004$).

There were 56 participants (53.8%) older than two years included in this analysis, with 30 boys (53.6%) and 26 girls (46.4%). Of these participants, 12 had mild atopic dermatitis when evaluated with SCORAD (21.4%), 37 had moderate atopic dermatitis (66.1%) and seven had severe atopic dermatitis (12.5%). The mean SCORAD rating was 35.02 and the median SCORAD rating was 30.5.

When genders were analysed separately, a significant association was found between the BMI percentile for boys older than two years and dermatitis severity (odds ratio 1.039, 95% CI of 1.009 to 1.069 ($p=0.0098$)). Of these participants, seven had mild atopic dermatitis when evaluated with SCORAD (23.3%), 16 had moderate atopic dermatitis (53.3%) and seven had severe atopic dermatitis (23.3%). A significant association between BMI percentile grouping and atopic dermatitis severity was not seen in girls older than two years ($p=0.4541$). Of these participants, five had mild atopic dermatitis (19.2%), 21 had moderate atopic dermatitis (80.8%) and none had severe atopic dermatitis. For girls, the mean SCORAD rating was 33.88 and the median was 29.0. For boys, the mean SCORAD rating was 35.93 and the median was 32.0.

A significant association between weight for length percentile grouping and atopic dermatitis severity was not seen in children less than two-years-old ($p=0.1857$). Of these participants, there were 22 boys (45.8%) and 26 girls (54.2%). Overall, 20 participants had mild

atopic dermatitis when evaluated with SCORAD (41.7%), 28 had moderate atopic dermatitis (58.3%), and none had severe atopic dermatitis, which was a limitation to this study. The mean SCORAD rating was 25.63 and the median was 25.

Discussion

Obese children are more likely to develop atopic diseases such as atopic dermatitis and asthma (11, 12), and up to 70% of children with atopic dermatitis may develop subsequent atopic diseases in the phenomenon known as the atopic march (13). While obesity is associated with an increased risk for atopic diseases such as atopic asthma, there has been conflicting evidence of whether or not obesity is related to a more severe disease (14, 15). Likewise, obesity has been reported to correlate with more severe atopic dermatitis, although this was determined by parents' subjective rating of their child's atopic dermatitis as mild, moderate or severe in a questionnaire (6). A correlation using objective scoring measures has not been reported previously to the best of our knowledge. Our data suggest that there might be an association between obesity and the severity of atopic dermatitis as measured with the objective SCORAD index by one evaluator to eliminate inter-rater variability.

Possibly relating to these findings is the consideration that obese individuals have increased inflammatory markers including TNF- α , IL-6, and C-reactive protein within their adipose tissue along with increased numbers of macrophages, further propagating expression of the inflammatory markers (16). Other proteins known as adipokines, which are also involved in pro-inflammatory pathways, are increased in children with atopic dermatitis, although no difference has been shown between obese and normal weight children with atopic dermatitis (17).

When gender was analysed independently, the association of increased BMI with increased severity of atopic dermatitis was seen in boys greater than two-years-old but not in girls greater than two-years-old. One limitation to our study was that due to a small sample size, there were no females older than two-years-old with severe atopic dermatitis as measured by the SCORAD index, so a significant association for girls only could not be fully assessed. However, intrinsic gender differences, gender-related behaviours or both may still relate to the discrepancy found between boys and girls. For example, while gender differences in hormone levels in patients with atopic dermatitis have been reported in adults (18), it is unclear whether such findings can be extended to our study, which includes both pre-pubertal and pubertal children. However, boys with chronic atopic dermatitis, have been reported to be sensitised to Immunoglobulin E more often than girls, suggesting a gender-related difference in intrinsic risk for developing atopic diseases (19). Another study observed that, in general, pre-adolescent girls were more likely to be affected by atopic dermatitis than pre-adolescent boys (20), although prevalence seemed to equalise after puberty (21). Interestingly, while girls and boys have been shown to use topical corticosteroids with the same frequency, girls also used moisturisers more frequently than boys (20). Skin barrier function in children with atopic dermatitis is compromised and permits increased trans-epithelial water loss, suggesting the importance of adequate skin hydration (22), and moisturising immediately after bathing improves atopic dermatitis (23). Simple daily practices such as increased moisturiser use could help explain why obese girls have less severe atopic dermatitis than their male counterparts.

The majority of participants in this study were African American or Hispanic and from urban communities. Children within urban communities may have a higher risk of eczema than those from rural communities (24). Increased severity of atopic dermatitis, although subjectively reported by the patients and parents, has been reported in African American and Hispanic populations, multi-race populations, urban populations, people residing in poor living conditions

and people with low income (25, 2). Therefore, while this study may be generalised to children living in urban areas such as Philadelphia, it is unclear whether these results can be extended to non-urban populations, non-African American, and non-Hispanic populations. Future measures could include more equal representation amongst African American, Caucasian, Hispanic, and Asian American children, as well as more equal representation of both urban and non-urban populations.

Our data also showed that increased weight for length in children less than two-years-old was not associated with increased atopic dermatitis severity. Interestingly, obesity has previously been shown to increase the overall risk of developing atopic dermatitis in children younger than two-years-old (6). The severity of the atopic dermatitis in very young children, therefore, may be more heavily influenced by factors other than obesity, such as the genetic and behavioural factors discussed previously. As these young patients grow older, however, their BMI status does begin to correlate to the severity of their disease. Of note, the history of the participant's obesity and atopic dermatitis was not recorded and so no assessment can be made on the chronicity of either disease. It is possible, however, that the chronicity of atopic dermatitis may be of significance in children older than two-years-of-age and may contribute to the severity of their disease. Given the significant social and family burden as well as financial cost, it is of great importance from both a healthcare and economic standpoint to continue finding ways to reduce the incidence and prevalence of atopic dermatitis. Children who are obese for more than two-and-a-half-years are at increased risk of developing atopic dermatitis (6), suggesting that early identification of obesity with early intervention in weight control may prevent the development of atopic dermatitis in children who have not yet been affected. Clinical and family education about the associations of childhood obesity with increased incidence and severity of atopic dermatitis could potentially motivate achievement of appropriate body weights and should be discussed at both well child visits and visits for atopic dermatitis.

management. Future insight into whether there is improvement of atopic dermatitis with achievement of target BMI would be of great clinical value for patients suffering from the effects of both atopic dermatitis and obesity.

CONCLUSION

In summary, our study showed that in children older than two years, increased BMI percentile correlated to increased severity of atopic dermatitis. In children younger than two years, increased weight for length did not correlate to the severity of atopic dermatitis. These findings will hopefully help guide clinicians in the education and treatment of their paediatric patients with both atopic dermatitis and obesity.

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References

1. Silverberg JI, Simpson EL. Associations of childhood eczema severity: a US population-based study. *Dermatitis* 2014; 25:107-114.
2. Shaw TE, Currie GP, Koudelka CW, Simpson EL. Eczema prevalence in the United States: data from the 2003 National Survey of Children's Health. *J Invest Dermatol* 2011; 131:67-73.
3. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of childhood and adult obesity in the united states, 2011-2012. *JAMA* 2014; 311:806-814.
4. Ogden CL, Carroll MD, Curtin LR, McDowell MA, Tabak CJ, Flegal KM. Prevalence of overweight and obesity in the united states, 1999-2004. *JAMA* 2006; 295:1549-1555.

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5. Barlow SE. Expert committee recommendations regarding the prevention, assessment, and treatment of child and adolescent overweight and obesity: summary report. *Pediatrics* 2007; 120 Suppl 4:164-192.
 6. Silverberg JI, Kleiman E, Lev-Tov H, Silverberg NB, Durkin HG, Joks R, et al. Association between obesity and atopic dermatitis in childhood: a case-control study. *J Allergy Clin Immunol* 2011; 127:1180-1186.
 7. Su JC, Kemp AS, Varigos GA, Nolan TM. Atopic eczema: its impact on the family and financial cost. *Arch Dis Child* 1997; 76:159-162.
 8. Claessen H, Brenner H, Drath C, Arndt V. Repeated measures of body mass index and risk of health related outcomes. *Eur J Epidemiol* 2012; 27:215-224.
 9. Schmitt J, Langan S, Williams HC. What are the best outcome measurements for atopic eczema? A systematic review. *J Allergy Clin Immunol* 2007; 120:1389-1398.
 10. Charman C, Chambers C, Williams H. Measuring atopic dermatitis severity in randomized controlled clinical trials: what exactly are we measuring? *J Invest Dermatol* 2003; 120:932-941.
 11. Baumann S, Lorentz A. Obesity - A Promoter of Allergy? *International Archives of Allergy and Immunology* 2013; 162:205-213.
 12. van der Hulst AE, Klip H, Brand PL. Risk of developing asthma in young children with atopic eczema: a systematic review. *J Allergy Clin Immunol* 2007; 120:565-569.
 13. Spergel JM, Paller AS. Atopic dermatitis and the atopic march. *J Allergy Clin Immunol* 2003; 112:118-127.
 14. Quinto KB, Zuraw BL, Poon KY, Chen W, Schatz M, Christiansen SC. The association of obesity and asthma severity and control in children. *J Allergy Clin Immunol* 2011; 128:964-969.

15. Forte GC, Grutcki DM, Menegotto SM, Pereira RP, Dalcin PT. Prevalence of obesity in asthma and its relations with asthma severity and control. *Rev Assoc Med Bras* 2013; 59:594-599.
16. Weisberg SP, McCann D, Desai M, Rosenbaum M, Leibel RL, Ferrante AW. (2003). "Obesity is associated with macrophage accumulation in adipose tissue." *J Clin Invest* 2003; 112:1796-1808
17. Machura E, Szczepanska M, Ziora K, Ziora D, Swietochowska E, Barc-Czarnecka M, et al. Evaluation of Adipokines: Apelin, Visfatin, and Resistin in Children with Atopic Dermatitis. *Mediators of Inflammation* 2013; 2013:8.
18. Ebata T, Itamura R, Aizawa H, Niimura M. Serum sex hormone levels in adult patients with atopic dermatitis. *J Dermatol* 1996; 23:603-605.
19. Bohme M, Svensson A, Kull I, Nordvall SL, Wahlgran CF. Clinical features of atopic dermatitis at two years of age: a prospective, population-based case-control study. *Acta Derm Venereol* 2001; 81:193-197.
20. Ballardini N, Kull I, Soderhall C, Lilja G, Wickman M, Wahlgran CF. Eczema severity in preadolescent children and its relation to sex, filaggrin mutations, asthma, rhinitis, aggravating factors and topical treatment: a report from the BAMSE birth cohort. *Br J Dermatol* 2013; 168:588-594.
21. Chen W, Mempel M, Schober W, Behrendt H, Ring J. Gender difference, sex hormones, and immediate type hypersensitivity reactions. *Allergy* 2008; 63:1418-1427.
22. Gupta J, Grube E, Ericksen MB, Stevenson MD, Lucky AW, Sheth AP, et al. Intrinsically defective skin barrier function in children with atopic dermatitis correlates with disease severity. *J Allergy Clin Immunol* 2008; 121:725-730.
23. Boguniewicz M, Schmid-Grendelmeier P, Liung DYM. Atopic dermatitis. *J Allergy Clin Immunol* 2006; 118:40-43.

24. Schram ME, Tedja AM, Spijker R, Bos JD, Williams HC, Spuls PI.. Is there a rural/urban gradient in the prevalence of eczema? A systematic review. *Br J Dermatol* 2010; 162:964-973.
25. Silverberg JI, Simpson EL. Associations of childhood eczema severity: a US population-based study. *Dermatitis* 2014; 25:107-114.

Table 1

SCORAD Category	BMI Category			
	<5 th Percentile	5-95 th Percentile	>95 Percentile	Total
Mild	1	10	1	12
Moderate	0	17	20	37
Severe	0	1	6	7
Total	1	28	27	56

Table 2

SCORAD Category	WFL Category			
	<5 th Percentile	5-95 th Percentile	>95 Percentile	Total
Mild	1	11	8	20
Moderate	0	10	18	28
Severe	0	0	0	0
Total	1	21	26	48

Table 1: Children older than 2 years, categorized into group 1 (<5th BMI percentile), group 2 (5th-95th percentile), or group 3 (>95th percentile). AD severity was measured using SCORAD and categorized mild (n=7), moderate (n=16), or severe (n=7).

Table 2: Children younger than 2 years old, categorized into group 1 (<5th WFL percentile), group 2 (5th-95th WFL percentile), or group 3 (>95th WFL percentile). AD severity was measured using SCORAD and categorized mild (n=20), moderate (n=28), or severe (n=0).

Figure 1

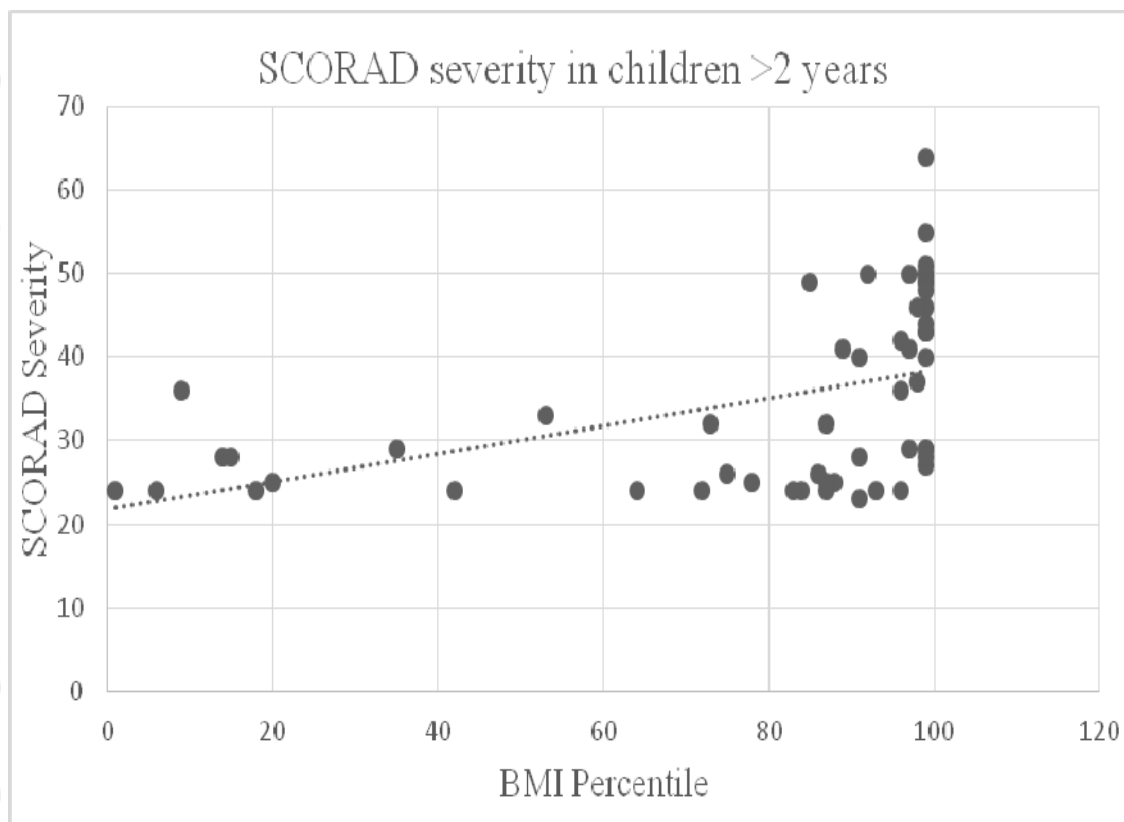


Figure 1: SCORAD severity (raw score) vs. BMI percentile in children older than 2 years.