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Association between obesity and atopic dermatitis in children: A case-control study in a high obesity prevalence population

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Abstract

Background/Objective: Atopic dermatitis (AD) is a chronic inflammatory skin disease. Research suggests an association between obesity and AD, although evidence is lacking from Latin American populations. This study evaluated the association of obesity with AD in children from Chile, a country with high obesity prevalence.

Methods: A case-control study was performed in children with active AD (cases) and healthy controls (HCs) from Santiago, Chile. Body mass index was evaluated by z-score (z-BMI), with overweight defined as z-BMI ≥+1 and <+2, and obesity as z-BMI ≥+2. Abdominal obesity was defined by a waist circumference-to-height ratio (WHR) ≥0.5. AD severity was evaluated by Scoring AD (SCORAD) index.

Results: A total of 174 children with AD and 101 controls were included. AD patients had similar overweight (27% vs. 28%) and obesity (21% vs. 26%) rates as HCs ($p = .65$). Abdominal obesity rates were also comparable (64% vs. 62%, $p = .81$). In sex-specific analyses, girls with AD had higher abdominal obesity rates than HCs (71% vs. 53%, $p < .05$) while boys with AD had lower abdominal obesity rates than HCs (53% vs. 75%, $p = .03$). Among children with AD, higher z-BMI or WHR did not correlate with higher SCORAD, eosinophil counts or total IgE.

Conclusion: In our study, Chilean children with AD had high but similar rates of obesity as HCs, but showed sex-specific associations of abdominal obesity and AD. Further research is needed to evaluate these associations and the roles that weight excess and weight loss could play in the pathogenesis and treatment of AD.

KEYWORDS
abdominal obesity, atopic dermatitis, body mass index, obesity, overweight

Carolina Iturriaga and María Francisca Bustos are joint first author.

1 | INTRODUCTION

Atopic dermatitis (AD) is a chronic and relapsing inflammatory skin disease with a complex pathogenesis and multiple exacerbating factors.[1] In recent decades, an epidemiological transition from infectious diseases to chronic nontransmissible conditions has occurred in developing and developed countries, with a striking increase in prevalence of metabolic disorders such as obesity.[2] In parallel with the obesity epidemic, a concomitant rise in the prevalence of allergic diseases including AD has been observed, reaching as high as 20% in children and 10% in adults for the latter condition.[3,4] Weight excess has been associated with multiple non-communicable diseases such as cardiovascular illnesses and cancer,[5] but an association with allergic diseases, such as asthma and AD, has also been postulated.[6] Given the simultaneous increase of obesity rates and AD prevalence, several studies have evaluated an association between these two chronic conditions.

Research performed on children and adults, especially in North America and Asia, suggests that being overweight or obese is associated with AD.[7] Furthermore, the chronic itch characteristic of AD could lead to sleep disturbance, anxiety, and depression, all known factors that may influence obesity risk. In addition, patients with AD and inflamed skin tend to avoid physical exercise.[8] All these components could theoretically drive weight gain, an increase in cardiovascular risk, and obesity.[9–11]

Despite growing evidence of this important association, studies are lacking in Latin America.[7,12,13] In this region, and particularly in Chile, a steep increase has been observed in obesity rates over the last decades, with latest national surveys revealing an obesity rate of 24% in first grade children, 28% in fifth grade children and 34% in adults. Severe obesity prevalence was found to be 8% in preschool and first grade children in 2018.[14,15] The COVID-19 pandemic has further worsened the situation, with current rates of severe obesity in Chile exceeding 10% of preschool children.[16] Moreover, Latin America is described as a relatively high AD prevalence region in recent studies, with many knowledge gaps and challenges related to this condition.[17,18]

There are several potential mechanisms that could explain the hypothesized association between obesity and AD. AD pathophysiology involves a dysfunctional epidermal barrier, skin microbiome abnormalities, and a predominantly type-2 skewed immune dysregulation.[1] On the other hand, obesity could be associated with impaired skin barrier function,[19] resulting in a chronic inflammatory state that could trigger AD.[20] Obesity and AD are conditions that involve a complex interplay between genetic and environmental factors. Thus, it is important to determine their association because obesity is a comorbidity and a potentially modifiable factor for AD - and vice versa.

In our study, we aimed to evaluate the association of obesity, overweight, and abdominal obesity with AD in Chilean children. We investigated the association, both overall and in sex-specific analyses.

2 | MATERIALS AND METHODS

2.1 | Study design

We conducted a prospective, case-control study of children with and without AD attending outpatient clinics at the Pontificia Universidad Católica de Chile and associated UC CHRISTUS health network. The scientific ethics committee of our institution approved this study. Informed consent was obtained from the parents and assents from children who were aged 7 years and older.

Inclusion criteria for the AD group were children aged 0 to 17 years and active AD (severity scoring of atopic dermatitis [SCORAD] >10). Children were excluded if systemic corticosteroids were used during the previous month, or if they had a known thyroid or autoimmune disease.

A pediatric immunologist or dermatologist diagnosed AD based on Hanifin and Rajka criteria.[21] AD severity was classified using the Severity Scoring of AD (SCORAD) and classified as mild (<25), moderate (25–50), or severe (≥50). Eosinophil blood counts and total IgE in serum were assessed as biomarkers of AD severity and atopy in children with AD.

Children of similar age and sex who attended the clinical centers for well-child visits were recruited as healthy controls (HCs). Nonatopic status of HCs was determined by questionnaire, and children with diagnosis of AD, asthma, allergic rhinitis, or food allergy were excluded.

2.2 | Growth parameters

Growth parameters were evaluated in all participants. Weight (in kilograms), length or height (in centimeters) and waist circumference (in centimeters) were measured. Waist circumference (WC) was measured at just above the uppermost border of the iliac crests using an inelastic measuring tape.[22]

Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Underweight was defined as BMI-for-age Z-score (z-BMI) <-2, normal weight as z-BMI ≥-2 and $<+1$, overweight as z-BMI $\geq+1$ and $<+2$, and obesity as z-BMI $\geq+2$ as per World Health Organization standard definitions. Abdominal obesity was assessed by evaluating waist circumference-to-height ratio (WHR) and defined as a WHR ≥0.5.[23]

2.3 | Statistical analysis

Patient characteristics with and without AD were examined. A normality analysis of continuous variables was performed with the Kolmogorov–Smirnov test ($p < .05$). In the case of a normal distribution, the data are presented as mean and standard deviation. In case of abnormal distribution, the data are presented as medians and interquartile ranges. To compare the clinical characteristics of cases and

TABLE 1 Characteristics of atopic dermatitis patients and healthy control children

Characteristic	Atopic dermatitis ($n = 174$)	Healthy controls ($n = 101$)	p Value
Age, mean ± SD, year	6.1 ± 4.5	6.3 ± 3.8	.70
Woman sex, *n* (%)	77 (44)	53 (53)	.19
BMI Z-score, median (IQR)	0.89 (0.22–1.79)	1.15 (0.31–2.04)	.42
WHR, median (IQR)	0.51 (0.47–0.57)	0.51 (0.47–0.55)	.56
SCORAD, median (IQR)	33.6 (23.8–44.5)	-	-

Abbreviations: BMI, body mass index; IQR, interquartile range; SCORAD, severity scoring of atopic dermatitis; SD, standard deviation; WHR, waist circumference-to-height ratio.

TABLE 2 Association between nutritional status and abdominal obesity with atopic dermatitis

	Atopic dermatitis ($n = 174$)	Healthy controls ($n = 101$)	p Value
Nutritional status			.65
Underweight, *n* (%)	1 (0.6)	-	
Normal weight, *n* (%)	90 (52)	47 (47)	
Overweight, *n* (%)	47 (27)	28 (28)	
Obese, *n* (%)	36 (21)	26 (26)	
Abdominal obesity, *n* (%)	107 (62)	64 (64)	.81

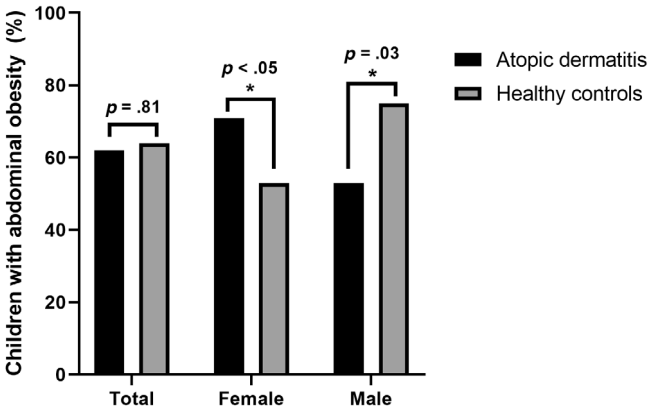

FIGURE 1 Total and sex-specific rates of abdominal obesity in children with atopic dermatitis and healthy controls. *$p < .05$

controls, we used the chi-square test for categorical variables. The independent Student *t*-test and Mann–Whitney *U* test were performed for continuous variables, depending on whether variables distributed normally or not, respectively. In patients with AD, the Spearman correlation coefficient was used to estimate the association of z-BMI and WHR with SCORAD, eosinophil count and total IgE. A two-sided *p*-value <.05 was considered statistically significant. All data processing and statistics were done with IBM SPSS Statistics Version 28.0 (IBM Corp).

3 | RESULTS

A total of 174 patients with AD (cases) and 101 HCs were evaluated. Patients with AD were similar to control subjects with respect to age, sex, z-BMI, and WHR (Table 1). AD patients had a median z-BMI of +0.89 and HCs had a median z-BMI of +1.15, with no significant differences between groups. Both groups had a median WHR of 0.51, corresponding to abdominal obesity.

Among patients with AD, 27% were overweight and 21% obese, while in HCs, 28% were overweight and 26% obese ($p = .65$). Abdominal obesity was observed in 62% of cases and 64% of controls ($p = .81$) (Table 2).

In the sex-specific analyses, girls with AD had higher rate of abdominal obesity than HCs (71% vs. 53%, $p < .05$), while boys with AD had lower rate of abdominal obesity than HCs (53% vs. 75%, $p = .03$) (Figure 1).

Among children with AD, higher z-BMI or WHR did not correlate with higher SCORAD, eosinophil counts or total IgE (Table 3). We then evaluated associations between z-BMI and WHR with specific body areas extracted from SCORAD evaluations. Of interest, children that had eczema on the trunk had higher z-BMI (+1.22 vs. +0.97, $p = .05$) and higher rates of abdominal obesity (58% vs. 38%, $p = .01$). No associations were observed of z-BMI and WHR with other body areas.

TABLE 3 Association of body mass index Z-score (z-BMI) and waist circumference-to-height ratio (WHR) with SCORAD, eosinophil count and total IgE in children with atopic dermatitis assessed by Spearman rank correlation

	SCORAD	Eosinophil count	Total IgE
z-BMI, rho (*p* value)	−0.03 (.38)	−0.06 (.57)	−0.12 (.25)
WHR, rho (*p* value)	0.07 (.38)	−0.04 (.69)	−0.15 (.13)

Abbreviations: BMI, body mass index; SCORAD, severity scoring of atopic dermatitis; WHR, waist circumference-to-height ratio.

4 | DISCUSSION

Our study is the first to evaluate the association between obesity and AD in a Latin American population. We observed that Chilean children

with AD were similar to healthy children, with high but comparable rates of overweight, obesity, and abdominal obesity. While overall results were null, girls with AD had higher rate of abdominal obesity than HCs, while boys with AD had lower abdominal obesity rates than controls. In patients with AD, severity was not associated with z-BMI or WHR.

The association of obesity and AD has been described in multiple studies. A systematic review of observational studies, with 35 studies in children until 2017, described that most research has found a positive association between obesity/overweight and AD. Of note, the more recent prospective studies found a positive association, whereas this was not observed in the older cross-sectional studies, many of which were based on retrospective chart reviews or surveys, which can be misleading.[12] Another meta-analysis that included 24 studies of children with AD found that children who were overweight or obese had higher odds ratio (OR) of AD; with an OR of 1.24 (95% CI: 1.08–1.43) for overweight and an OR of 1.44 (95% CI: 1.12–1.86) for obesity. When analyzed by geographical region, this association was significant in North America and Asia but not Europe, whereas no studies were found in Latin America.[7] In our study, we did not find an overall association between obesity and AD. This discrepancy with other reports might be explained by ethnic and socioeconomic differences in the study population, study design, or varied definitions of overweight, obesity, and abdominal obesity.

Different mechanisms have been proposed for the association between obesity and AD. Obesity could alter the skin barrier function, alter leptin activity leading to an immune imbalance, and produce chronic low-grade inflammation.[1,19,20] On the other hand, reverse causality is also possible. The symptoms of AD could contribute to obesity; chronic itch can lead to sleep disturbance[11] and to avoidance of physical exercise to avoid the discomfort caused by sweating onto inflamed skin,[24] two situations that can promote weight gain. A recent study investigated the association of obesity and AD longitudinally in a birth cohort of 4898 children across the United States.[25] This research found that overweight or obesity at age 5 years among those without AD was associated with AD at ages 9 or 15 years, but AD at age 5 years was not associated with overweight or obesity at ages 9 or 15 years, suggesting that obesity is a risk factor for developing AD and not vice versa.

Although the BMI z-scores were not related to AD overall, our data showed that biological sex had opposite associations between abdominal obesity and AD: girls with AD had higher rate of abdominal obesity than HC girls while boys with AD had lower rates of abdominal obesity than controls. A systematic literature review found two studies that described a positive association between central obesity and AD.[13] A study with 5202 young Korean adults found that women with abdominal obesity (WC ≥80 cm) had higher prevalence of AD, and obesity with abdominal obesity showed synergistic effects in AD for women (OR 3.29).[26] In pediatric patients, Silverberg et al. also found that central obesity defined as a WC in the 85th percentile or greater and a WHR in the 5th percentile or greater were associated with AD, with OR of 3.92 and 2.22. respectively.[27] The association between abdominal adiposity and AD could be explained by the fact that visceral adipose tissue produces adipokines that in turn produce inflammatory mediators (TNF, IL-6) related to the etiology of AD. The female sex-specific association of abdominal obesity we observed in our study may be because, in obese persons, estrogens may enhance leukocyte survival and could contribute to an increase in chronic inflammation.[13] These important questions merit further investigation.

In our study, z-BMI and WHR did not correlate with AD severity evaluated by higher SCORAD index and eosinophil blood counts. Some studies have found an association between obesity and AD severity[28–32] but this remains controversial, and may depend on age, sex, or race/ethnicity. For example, the previously mentioned study by Silverberg et al that assessed the association of central obesity with AD, found no association between WHR and AD severity.[27]

The present study has several strengths, including the evaluation in a Latino population with high prevalence of obesity and AD, diagnosis of AD and anthropometric characterization performed by a trained physician,[33] reducing parental interpretation and recall bias. Limitations of this study include its case-control design, which limits causal inferences, as well as the study's relatively small sample size ($n = 275$ children).

In conclusion, this study provides evidence that Chilean children with AD have a prevalence of overweight and obesity similar to control subjects. In addition, there were sex-specific associations of abdominal obesity with AD, with girls having a higher rate of abdominal obesity than HCs and the opposite finding in boys. Additional studies are warranted to confirm sex differences in the association of abdominal obesity and AD and further evaluate this topic in Latino populations.

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CONFLICT OF INTEREST

Written informed consent was obtained from all participants.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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