

Letter to the Editor

Eczema is associated with osteoporosis and fractures in adults: A US population-based study

To the Editor:

Patients with eczema have multiple potential risk factors for decreased bone mineral density (BMD), including using large quantities of topical corticosteroids, systemic corticosteroids, and chronic inflammation. Furthermore, eczema is associated with distraction from itch, mental health comorbidities, and sleep disturbance,¹ all of which predispose to fractures and other injuries.^{2,3} However, previous studies examining BMD in adults with eczema found conflicting results⁴⁻⁶ and their risk of fractures has not been fully explored. In the present study, we analyzed data from a large-scale US-population-based study to assess the burden of fractures in adult eczema.

We used the 2005-2006 National Health and Nutrition Examination Survey. Household surveys were performed in-person in English and Spanish, as well as health examinations, blood collection, and dual-energy x-ray absorptiometry (DEXA) in mobile examination centers. Survey results were weighted to represent the population of US adults using data from the US Census Bureau. Approval by the Northwestern University institutional review board was waived.

Sociodemographic characteristics included age, sex, race, education level, and household income. Lifetime history of doctor-diagnosed osteoporosis and prednisone/cortisone use daily for at least 30 days were assessed. Daily tobacco and alcohol consumption habits were assessed. History of eczema was assessed by a positive response to the question, "Has a doctor or other health professional ever told (you/sample person) that (you have/sample person has) eczema?" To improve the specificity of self-reported eczema, subjects who reported a health care provider diagnosis of psoriasis were excluded from analyses. History of fractures was determined by asking "Has a doctor ever told (you/sample person) that (you/s/he) had broken or fractured ... (your/his/her) hip?", "... (your/his/her) spine?", "... (your/his/her) wrist?", "... any other bone after (you were/s/he was) 20 years of age?" A composite binary variable was created on the basis of the above responses.

The BMD (g/cm²) of the hip and spine was measured by using DEXA on all eligible participants. Total femur, femoral neck,

trochanter, and spine scans were performed with a Hologic QDR-4500A fan-beam densitometer (Hologic, Inc, Bedford, Mass) as previously described.⁷ BMD-for-age, sex, and race/ethnicity *t* scores were also determined on the basis of National Health and Nutrition Examination Survey reference standards.⁸ Physical examination was performed,⁹ body mass index was calculated, and blood samples were collected.

Bivariate and multivariate analyses were performed with SURVEY procedures in SAS (version 9.4; SAS Institute, Cary, NC). Bivariate associations between eczema, fracture, metabolic factors, and sociodemographic variables were tested via logistic regression models. Bivariate associations between eczema and BMD were tested via linear regression models. Complete data analysis was performed. Two-way interaction terms between eczema and age, sex, race, and household income were tested. Interactions were included in final models if *P* was less than .01 and modification of estimates was more than 20%. A 2-sided *P* value of less than .05 was taken to indicate statistical significance.

A total of 4972 people aged 20 to 85 years were included in this analysis. The prevalence (95% CI) of eczema was 7.4% (6.5% to 8.3%), of which 24.7% (18.8% to 30.5%) also had a lifetime history of asthma. The prevalence of any fracture was 32.3% (30.7% to 33.9%). Hip or spine fractures were described in 3.9% (3.3% to 4.6%), whereas 30.6% (29.0% to 32.2%) reported having "other" fractures. Associations with the prevalence of eczema and fractures are presented in Table E1 in this article's Online Repository at www.jacionline.org. Adult eczema was not associated with 25-OH vitamin D, calcium, parathyroid hormone, alkaline phosphatase, albumin, lactate dehydrogenase, C-reactive protein, or peripheral white blood cell counts compared with those without AD (see Table E2 in this article's Online Repository at www.jacionline.org).

In multivariate models, eczema was associated with a significantly lower BMD *t* score for the total femur, including trochanter and total lumbar spine, but not femoral neck (Table I). In particular, eczema was associated with osteopenia ($-2.5 < t$ score ≤ -1) and osteoporosis (t score ≤ -2.5) of the trochanter, but not of the total femur, femoral neck, or total spine (Table II). Adults with eczema had higher odds of any fracture, including hip/spine and other fracture. However, osteoporosis was self-reported in only 16.3% and 10.7% of the adults with eczema and a *t* score of -2.5 or less at the femoral neck or any site,

TABLE I. Association between eczema and lower BMD *t* score in adults (n = 3377)

Eczema	BMD <i>t</i> score (95% CI)	β (95% CI)	<i>P</i> value	Adjusted β (95% CI)	<i>P</i> value
Total femur					
No	0.04 (−0.01 to 0.10)	0.00 (ref)	—	0.00 (ref)	—
Yes	−0.25 (−0.44 to −0.06)	−0.29 (−0.49 to −0.10)	.004	−0.27 (−0.46 to −0.08)	.006
Trochanter					
No	−1.95 (−1.99 to 1.90)	0.00 (ref)	—	0.00 (ref)	—
Yes	−2.21 (−2.37 to −2.04)	−0.26 (−0.43 to −0.09)	.003	−0.25 (−0.42 to −0.08)	.004
Femoral neck					
No	−1.09 (−1.14 to −1.04)	0.00 (ref)	—	0.00 (ref)	—
Yes	−1.27 (−1.45 to −1.09)	−0.18 (−0.37 to 0.01)	.07	−0.13 (−0.31 to 0.04)	.14
Total lumbar spine					
No	0.58 (0.53 to 0.63)	0.00 (ref)	—	0.00 (ref)	—
Yes	0.40 (0.21 to 0.58)	−0.18 (−0.37 to 0.01)	.06	−0.22 (−0.41 to −0.03)	.02

Boldface indicates statistical significance (*P* < .05).

TABLE II. Association between eczema, osteopenia, osteoporosis, and fractures in adults (n = 4936)

Variable	No eczema		Frequency	Percent (95% CI)	Eczema			
	Frequency	Percent (95% CI)			OR (95% CI)	P value	aOR (95% CI)	P value
Osteopenia ($-2.5 < t \leq -1$)								
Total femur	586	18.8 (17.2-20.5)	43	22.7 (16.1-29.2)	1.31 (0.88-1.93)	.18	1.33 (0.85-2.07)	.21
Femoral neck	1302	41.6 (39.6-43.7)	85	41.1 (33.5-48.7)	1.06 (0.75-1.51)	.73	1.07 (0.74-1.55)	.74
Trochanter	1534	47.8 (45.7-49.9)	111	54.7 (47.0-62.4)	2.03 (1.24-3.33)	.005	2.08 (1.27-3.42)	.004
Total spine	278	8.3 (7.1-9.4)	19	10.4 (5.3-15.5)	1.29 (0.73-2.28)	.39	1.32 (0.74-2.36)	.34
Osteoporosis ($t \leq -2.5$)								
Total femur	101	2.6 (2.1-3.2)	11	4.9 (1.6-8.3)	2.04 (0.96-4.34)	.07	2.09 (0.93-4.70)	.08
Femoral neck	400	12.4 (11.1-13.8)	32	16.2 (10.4-21.9)	1.40 (0.88-2.25)	.16	1.42 (0.85-2.39)	.19
Trochanter	1015	32.4 (30.4-34.4)	67	34.1 (26.8-41.5)	1.86 (1.10-3.15)	.02	1.97 (1.14-3.41)	.02
Total spine	20	0.6 (0.3-0.9)	2	0.8 (0-2.0)	1.35 (0.29-6.3)	.71	1.23 (0.24-6.26)	.80
Fracture								
Any fracture	1327	31.60 (29.93-33.27)	118	40.77 (34.22-47.32)	1.49 (1.12-1.96)	.005	1.48 (1.10-1.99)	.01
Hip or spine fracture	175	3.70 (3.05-4.36)	17	6.47 (3.10-9.84)	1.80 (1.00-3.24)	.047	1.87 (1.02-3.43)	.04
Other fracture	1244	29.98 (28.33-31.63)	111	37.80 (31.36-44.25)	1.42 (1.07-1.89)	.016	1.40 (1.04-1.88)	.03

aOR, Adjusted odds ratio; OR, odds ratio.

Boldface indicates statistical significance ($P < .05$).

respectively. In multivariate models, osteoporosis was associated with ever using oral corticosteroids daily for a month or longer (adjusted odds ratio [95% CI], 1.44 [1.05-1.99]; $P = .02$) but not associated with lifetime or 1-year history of asthma, peripheral eosinophil counts of more than 1000 cells/uL, or IgE level of more than 100 kU/L (data not shown).

The results of this study confirm and expand on previous studies that found a higher risk of fractures and other injuries among patients with eczema.^{2,3} Other studies of BMD in adults with AD/eczema found conflicting results. One found lower lumbar spine BMD only in patients using moderate to high potency topical corticosteroids,⁵ whereas another found that adults with moderate to severe AD had high rates of osteopenia and osteoporosis.⁴ The present study suggests that AD in adults is associated with lower BMD overall and osteoporosis of the trochanter.

In the present study, only a small proportion of adults with eczema and t scores of -2.5 or less reported a physician diagnosis of osteoporosis. This pattern was also seen in adults without eczema, suggesting that osteoporosis in the general population is underdiagnosed. These data suggest that adults with eczema have a higher risk for osteoporosis and would benefit from increased surveillance via DEXA. Patient education and intervention for osteoporosis risk factors appears warranted, including smoking cessation, reduced alcohol consumption, increased weight-bearing activity, vitamin D and calcium supplementation, and even bisphosphonates.

Corticosteroid use in patients with eczema might contribute to decreased BMD. However, only a small number of subjects in our study reported current topical or oral corticosteroid use. Furthermore, 2 recent studies suggested that topical corticosteroids have no effect on BMD in moderate to severe AD.^{6,10} Last, comorbid psychological and behavioral disorders and sleep disturbance likely play a role in the risk for all types of injury,^{2,3} and therefore likely influence fracture risk as well. Future studies are needed to determine the mechanisms of increased fracture risk in adults with AD.

In conclusion, eczema in adults is associated with decreased BMD at the femur and spine, osteoporosis of the trochanter, and increased risk for fractures. Most adults with eczema and osteoporosis were not diagnosed with osteoporosis, suggesting that greater surveillance for osteoporosis is warranted in this

high-risk population. Further studies are needed to confirm these associations and determine effective strategies for fracture risk reduction.

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TABLE E1. Determinants of eczema and fracture in adults*

Variable, n (%)	Eczema (n = 4972)				History of any fracture (n = 4963)			
	No	Yes	OR (95% CI)	P value	No	Yes	OR (95% CI)	P value
Age (y)				.17				<.0001
20-29	91.6 (89.5-93.8)	8.4 (6.2-10.5)	—	—	78.6 (75.4-81.8)	21.4 (18.2-24.6)	1.00	—
30-49	94.1 (92.7-95.5)	5.9 (4.5-7.3)	—	—	71.3 (68.7-73.9)	28.7 (26.1-31.3)	1.48 (1.18-1.86)	.0009
50-69	92.5 (90.7-94.4)	7.5 (5.6-9.3)	—	—	60.7 (57.4-63.9)	39.3 (36.1-42.6)	2.38 (1.89-3.01)	<.0001
≥70	93.6 (91.7-95.5)	6.4 (4.5-8.3)	—	—	54.8 (51.1-58.6)	45.1 (41.3-48.9)	3.02 (2.37-3.86)	<.0001
Sex								
Male	94.6 (93.5-95.7)	5.4 (4.3-6.5)	1.00	—	64.0 (61.7-66.4)	36.0 (33.6-38.3)	1.00	—
Female	91.8 (90.4-93.1)	8.2 (6.9-9.6)	1.56 (1.17-2.06)	.002	71.1 (68.9-73.3)	28.9 (26.7-31.1)	0.73 (0.63-0.84)	<.0001
Race				<.0001				<.0001
White	92.2 (91.0-93.3)	7.8 (6.7-9.0)	1.00	—	62.6 (60.5-64.7)	37.4 (35.3-39.5)	1.00	—
Black	93.3 (91.8-94.9)	6.7 (5.1-8.2)	0.84 (0.62-1.14)	.26	81.1 (78.6-83.5)	18.9 (16.5-21.4)	0.39 (0.33-0.47)	<.0001
Mexican American	98.4 (97.5-99.2)	1.6 (0.8-2.5)	0.20 (0.11-0.35)	<.0001	80.3 (77.6-83.0)	19.7 (17.0-22.4)	0.41 (0.34-0.50)	<.0001
Other Hispanic	97.0 (94.0-100)	3.0 (0-6.0)	0.37 (0.13-1.04)	.06	89.5 (84.5-94.5)	10.5 (5.5-15.5)	0.20 (0.11-0.34)	<.0001
Multiracial/other	95.0 (91.5-98.4)	5.0 (1.6-8.5)	0.62 (0.30-1.31)	.21	75.6 (68.9-82.2)	24.4 (17.8-31.1)	0.54 (0.37-0.79)	.001
Household income (×\$1000)								
<20	94.5 (92.9-96.1)	5.5 (3.9-7.1)	1.00	—	66.9 (63.3-70.4)	33.1 (29.6-36.7)	1.00	—
≥20	92.7 (91.7-93.8)	7.3 (6.2-8.3)	1.36 (0.96-1.91)	.08	67.9 (66.1-69.7)	32.1 (30.3-33.9)	0.95 (0.80-1.14)	.60
Highest level of education				.02				.08
<High school	95.1 (93.5-96.8)	4.9 (3.2-6.5)	1.00	—	70.0 (66.8-73.1)	30.0 (26.9-33.2)	—	—
High school or GED	93.3 (92.1-94.4)	6.7 (5.6-7.9)	1.41 (0.95-2.10)	.09	66.1 (63.9-68.4)	33.9 (31.6-36.1)	—	—
>High school	91.6 (89.6-93.5)	8.4 (6.5-10.4)	1.80 (1.17-2.78)	.008	69.5 (66.2-72.8)	30.5 (27.2-33.8)	—	—
Body mass index				.06				.74
<18.5	96.9 (93.2-100)	3.1 (0-6.7)	—	—	67.3 (55.0-79.6)	32.7 (20.4-45.0)	—	—
18.5-24.9	91.6 (89.7-93.4)	8.4 (6.6-10.3)	—	—	69.2 (66.2-72.2)	30.8 (27.8-33.8)	—	—
25-29.9	94.4 (93.0-95.8)	5.6 (4.2-7.0)	—	—	67.7 (64.8-70.5)	32.3 (29.5-35.2)	—	—
30-34.9	93.2 (91.2-95.1)	6.8 (4.9-8.8)	—	—	65.5 (61.6-69.3)	34.5 (30.7-38.4)	—	—
35-39.9	94.0 (91.0-97.0)	6.0 (3.0-9.0)	—	—	67.8 (62.3-73.3)	32.2 (26.7-37.7)	—	—
≥40	90.1 (85.5-94.7)	9.9 (5.3-14.5)	—	—	65.3 (58.4-72.3)	34.7 (27.7-41.6)	—	—
Osteoporosis (self-report)								
No	90.9 (86.6-95.2)	6.8 (5.9-7.7)	1.00	—	69.0 (67.4-70.7)	31.0 (29.3-32.6)	1.00	—
Yes	90.9 (86.6-95.2)	9.1 (4.8-13.4)	1.38 (0.81-2.36)	.23	42.5 (35.4-49.5)	57.5 (50.5-64.6)	3.02 (2.24-4.08)	<.0001
Daily prednisone use (>1 mo)								
No	93.1 (92.2-94.0)	6.9 (6.0-7.8)	1.00	—	68.8 (67.1-70.5)	31.2 (29.5-32.9)	1.00	—
Yes	92.3 (88.2-96.5)	7.7 (3.5-11.8)	1.13 (0.62-2.05)	.70	51.9 (44.5-59.4)	48.1 (40.6-55.5)	2.04 (1.50-2.77)	<.0001

GED, General educational development; OR, odds ratio.

*For multinomial predictors, *P* values for overall test results are presented. If the overall *P* value is significant, then individual pairwise tests are also presented.

TABLE E2. Lack of association between eczema, metabolic factors, and inflammatory factors in adults (n = 4438)

Variable	No eczema		Eczema			P value
	Frequency	Percent (95% CI)	Frequency	Percent (95% CI)	OR (95% CI)	
Vitamin D (ng/mL)						
Deficient (<20)	1867	35.6 (33.8-37.3)	110	36.1 (29.5-42.7)	1.19 (0.80-1.78)	.40
Insufficient (20-29)	1582	42.0 (40.1-43.8)	111	44.8 (37.8-51.7)	1.25 (0.84-1.86)	.27
Adequate (≥30)	752	22.5 (20.8-24.1)	48	19.1 (13.7-24.7)	1.00	—
Calcium (mg/dL)						
Low (<8.5)	20	0.3 (0.1-0.5)	1	0.6 (0-1.9)	2.05 (0.26-16.12)	.49
Normal (8.5-10.2)	4069	97.9 (97.3-98.4)	258	96.5 (93.9-99.0)	1.00	—
High (>10.2)	81	1.8 (1.3-2.3)	9	2.9 (0.7- 5.1)	1.61 (0.71-3.68)	.26
Parathyroid hormone (pg/mL)						
Low (<10)	13	0.2 (0-0.4)	0	0	<0.0001 (<0.0001)	<.0001
Normal (10-55)	3214	80.1 (78.6-81.5)	204	76.9 (71.0-82.7)	1.00	—
High (>55)	957	19.7 (18.3-21.1)	64	23.1 (17.3-29.0)	1.22 (0.87-1.72)	.23
Albumin (g/dL)						
Low (<3.5)	279	2.5 (2.0-2.9)	15	3.9 (1.3-6.5)	1.59 (0.78-3.29)	.21
Normal (3.5-5.4)	3891	97.5 (97.1-98.0)	253	96.1 (93.5-98.7)	1.00	—
High (>5.4)	0	0	0	0	—	—
Alkaline phosphatase (U/L)						
Low (<30)	17	0.6 (0.3-0.9)	4	0.9 (0-1.8)	1.60 (0.51-4.99)	.42
Normal (30-130)	4045	98.0 (97.5-98.5)	256	96.1 (93.5-98.6)	1.00	—
High (>130)	108	1.4 (1.1-1.8)	8	3.0 (0.6-5.4)	2.17 (0.92-5.13)	.08
Lactate dehydrogenase (U/L)						
Low (<140)	2895	74.0 (72.4-75.6)	183	73.1 (67.0-79.3)	—	—
Normal (140-280)	1203	25.9 (24.3-27.5)	76	26.7 (20.5-32.8)	1.04 (0.48-37.58)	.81
High (>280)	5	0.1 (0.0-0.1)	1	0.2 (0-0.6)	4.25 (0.48-37.58)	.19
CRP (mg/dL)						
Normal (<1.0)	3679	89.8 (88.7-90.9)	233	86.5 (81.6-91.3)	—	—
High (≥1.0)	519	10.2 (9.1-11.3)	36	13.5 (8.7-18.4)	1.38 (0.90-2.12)	.14
WBC (×1000 cells/uL)						
Low	242	5.0 (4.2-5.7)	15	5.1 (2.1-8.0)	1.03 (0.55-1.94)	.93
Normal	3508	85.2 (83.9-86.6)	227	84.2 (79.1-89.4)	—	—
High	462	9.8 (8.7-10.9)	29	10.7 (6.2-15.2)	1.10 (0.68-1.81)	.67

CRP, C-reactive protein; OR, odds ratio; WBC, white blood cell.