

Association between Atopic Dermatitis and Depression in US Adults

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TO THE EDITOR

Atopic dermatitis (AD) is associated with intense pruritus, high rates of sleep disturbance (Silverberg *et al.*, 2015b), stigma, increased healthcare costs (Silverberg, 2015) and poor quality of life (Silverberg *et al.*, 2015b). All of these might contribute toward higher rates of depression. Previous studies found that Taiwanese adolescents/adults with AD have a higher incidence of major depressive disorder than those without AD (1.42 vs. 0.20 per 1,000 person-years) (Cheng *et al.*, 2015), as well as a higher prevalence of depression in Korean males (10.4 vs. 5.3%) (Kim *et al.*, 2015). A recent study found that US children with AD had significantly higher prevalences of ever having depression (6.5%) and current depression (3.9%) compared with those without AD (3.4% and 1.8%, respectively) (Yaghmaie *et al.*, 2013). However, the prevalence of depression in US adults with AD is not known.

We studied participants from the 2005–2006 NHANES and 2012 National Health Interview Survey. Both surveys were sponsored and conducted by National Center for Health Statistics (NCHS) of Centers for Disease Control and Prevention. Households were selected through a stratified, randomized, multistage, and probability-cluster design. Health interviews were conducted in the home in either English or Spanish. The survey results were weighted to represent the population of non-institutionalized adults nationally and in each state using data from the U.S. Bureau of the Census, and to account for the complex survey

design, survey non-response and post-stratification. This study was approved by the institutional review board at the Northwestern University.

The questions used to assess for history of eczema and depression are shown in Supplementary Table 1 online. In NHANES, respondents were asked questions from the Patient Health Questionnaire (PHQ), a validated self-reported assessment based on the nine DSM-IV symptoms for depression (Spitzer *et al.*, 1999; Arroll *et al.*, 2010). A binary variable was also created based on the SIGECAPS criteria (acronym for depression symptoms), which are predictive of major depressive disorder when $\geq 4/8$ positive responses are combined with depressed mood for at least two week (Carlat, 1998). PHQ scores were classified as none (score 0–4), mild (score 5–9), moderate (score 10–14), and severe (score 15–27) depression.

All data processing and statistical analyzes were performed with SURVEY procedures in SAS version 9.4 (SAS Institute, Cary, NC). Complete data analysis was performed. Associations between AD and depression were tested via logistic regression models. In NHANES, the dependent variables included the nine PHQ9 questions, SIGECAPS, and total PHQ9 depression score. In NHIS, the dependents variables were self-reported history of depression ever or in the past year. The independent variable was history of AD. Multivariate models included age, gender, race/ethnicity, level of education, family poverty income ratio, history of asthma and hay fever. Crude

and adjusted prevalence odds ratios (OR) and 95% confidence intervals (CIs) were estimated.

A total of 5,555 adults (≥ 18 years) were included in NHANES 2005–2006. The prevalence of AD was 6.2% (95% CI: 5.6–6.8%). AD was associated with female gender, poverty income ratio ≥ 4 , greater than high school or GED equivalent education, history of asthma and hay fever (Supplementary Table 2 online). One hundred and nine adults (31.0%) with AD reported one or more symptoms of depression. In multivariate survey logistic regression models of NHANES data that controlled for socio-demographics, history of asthma and hay fever, AD was associated with higher odds of having little interest in doing things, feeling down, depressed or hopeless, feeling tired or having little energy, having a poor appetite, feeling bad themselves, having trouble concentrating and moving or speaking slowly or too fast and having thoughts of being better off dead (Table 1).

The prevalence of depression as judged by the SIGECAPS criteria was higher in adults with AD compared with adults who did not have eczema (17.5 vs. 10.5%; adjusted OR (95% CI): 1.89 (1.28–2.77)). Moreover, AD was associated with higher odds of moderate (2.24 (1.20–4.17)) and severe (5.64 (2.88–11.07)) depression as judged by the PHQ9 score.

A total of 34,613 adults were included in NHIS 2012. The US prevalence (95% CI) of eczema in adults was 7.2% (6.9–7.6%). The associations of adult eczema in NHIS 2012 were previously described (Silverberg *et al.*, 2015b). The lifetime prevalence of health-care diagnosed depression was higher in adults with AD compared with adults who did not have AD (26.9 vs.

Abbreviations: AD, atopic dermatitis; CI, confidence interval; NHANES, National Health and Nutrition Examination Survey; NHIS, National Health Interview Survey; OR, odds ratio; PHQ, Patient Health Questionnaire; SIGECAPS, depression acronym for disturbances in at least 4/8 symptoms with depressed mood: sleep, interest, guilt, energy, concentration, appetite, psychomotor disturbance

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Table 1. Association between depression and eczema in US adults from NHANES 2005–2006 (*n* = 5,555)

Variable	Outcomes	Eczema					
		No			Yes		
		Freq.	Percent (95% CI)	Freq.	Percent (95% CI)	Crude OR (95% CI)	P-value
Little interest in doing things	None	3,616	81.34 (79.93, 82.75)	232	74.59 (68.78, 80.41)	1.00	—
	Several days	620	13.61 (12.35, 14.87)	51	16.51 (11.45, 21.57)	1.32 (0.90, 1.94)	0.15
	More than half the days	160	3.03 (2.44, 3.62)	20	5.98 (2.92, 9.04)	2.17 (1.21, 3.89)	0.009
	Nearly every day	114	2.02 (1.57, 2.48)	10	2.92 (0.77, 5.07)	1.57 (0.71, 3.47)	0.27
Feeling down depressed, or hopeless	None	3,542	80.22 (78.79, 81.66)	225	72.86 (66.99, 78.72)	1.00	—
	Several days	715	15.09 (13.79, 16.40)	52	16.10 (11.25, 20.95)	1.19 (0.82, 1.73)	0.37
	More than half the days	157	2.89 (2.32, 3.45)	22	6.25 (3.09, 9.41)	2.39 (1.34, 4.26)	0.003
	Nearly every day	99	1.80 (1.35, 2.24)	15	4.79 (1.93, 7.65)	2.91 (1.48, 5.73)	0.002
Trouble sleeping or sleeping too much	None	2,957	65.20 (63.43, 66.97)	192	61.99 (55.61, 68.36)	1.00	—
	Several days	997	23.23 (21.64, 24.82)	73	23.82 (18.22, 29.43)	1.09 (0.79, 1.52)	0.59
	More than half the days	265	5.91 (5.04, 6.78)	21	5.62 (2.62, 8.62)	1.01 (0.56, 1.83)	0.98
	Nearly every day	293	5.66 (4.85, 6.48)	27	8.57 (4.96, 12.17)	1.58 (0.97, 2.59)	0.07
Feeling tired or little energy	None	2,298	51.43 (49.58, 53.29)	129	39.31 (32.92, 45.70)	1.00	—
	Several days	1,585	35.47 (33.69, 37.25)	119	40.59 (34.08, 47.10)	1.50 (1.11, 2.04)	0.009
	More than half the days	331	7.07 (6.13, 8.00)	39	11.57 (7.39, 15.74)	2.13 (1.35, 3.37)	0.001
	Nearly every day	299	6.03 (5.20, 6.87)	27	8.53 (4.82, 12.25)	1.86 (1.10, 3.13)	0.02
Poor appetite or overeating	None	3,582	80.53 (79.08, 91.98)	227	75.55 (66.67, 78.43)	1.00	—
	Several days	640	13.65 (12.38, 14.92)	51	14.24 (9.85, 18.63)	1.16 (0.79, 1.69)	0.46
	More than half the days	143	3.24 (2.58, 3.90)	17	5.56 (2.31, 8.80)	1.89 (0.98, 3.63)	0.06
	Nearly every day	149	2.58 (2.06, 3.11)	19	7.65 (4.01, 11.29)	3.28 (1.88, 5.73)	<0.0001
Feeling bad about yourself	None	3,887	86.60 (85.35, 87.84)	244	77.84 (72.45, 83.27)	1.00	—
	Several days	467	10.41 (9.29, 11.54)	45	15.03 (10.31, 19.76)	1.63 (1.10, 2.40)	0.02
	More than half the days	81	1.57 (1.12, 2.02)	14	4.30 (1.69, 6.92)	3.08 (1.53, 6.18)	0.002
	Nearly every day	79	1.42 (1.00, 1.83)	10	2.83 (0.82, 4.83)	2.22 (1.01, 4.88)	0.048
Trouble concentrating	None	3,831	85.58 (84.30, 86.86)	237	77.11 (71.58, 82.64)	1.00	—
	Several days	497	10.58 (9.45, 11.70)	46	15.16 (10.29, 20.03)	1.60 (1.08, 2.39)	0.02
	More than half the days	98	2.14 (1.60, 2.68)	20	5.13 (2.39, 7.86)	2.69 (1.44, 5.03)	0.002
	Nearly every day	88	1.70 (1.26, 2.14)	11	2.60 (0.75, 4.45)	1.69 (0.78, 3.65)	0.19
Moving or speaking slowly or too fast	None	4,092	91.93 (90.96, 92.90)	267	85.57 (81.00, 90.15)	1.00	—
	Several days	302	5.83 (4.99, 6.66)	39	11.87 (7.67, 16.07)	2.19 (1.42, 3.36)	0.0004
	More than half the days	74	1.59 (1.15, 2.04)	5	1.64 (0.00, 3.42)	1.16 (0.36, 3.69)	0.81
	Nearly every day	42	0.65 (0.39, 0.91)	3	0.92 (0.00, 2.00)	1.52 (0.43, 5.42)	0.52
							0.28

Table 1. (Continued)

Variable	Outcomes	Eczema					
		No			Yes		
		Freq.	Percent (95% CI)	Freq.	Percent (95% CI)	Crude OR (95% CI)	P-value
Thought better off dead	None	4,365	97.16 (96.58, 97.74)	299	96.23 (93.91, 98.55)	1.00	—
	Several days	113	2.19 (1.69, 2.71)	8	1.85 (0.21, 3.48)	0.86 (0.34, 2.18)	0.76
	More than half the days	26	0.45 (0.21, 0.69)	6	1.70 (0.09, 3.32)	3.79 (1.27, 11.37)	0.02
	Nearly every day	12	0.20 (0.05, 0.34)	1	0.22 (0.00, 0.64)	1.13 (0.14, 9.24)	0.91
Difficulty these problems have caused	None at all	2,177	73.97 (71.49, 75.96)	153	71.16 (64.21, 78.12)	1.00	—
	Somewhat difficult	678	22.41 (20.53, 24.29)	58	24.25 (17.69, 30.81)	1.12 (0.77, 1.63)	0.56
	Very difficult	71	2.73 (1.97, 3.49)	8	3.67 (0.64, 6.70)	1.36 (0.55, 3.37)	0.51
	Extremely difficult	26	0.89 (0.48, 1.29)	4	0.92 (0.00, 1.84)	1.09 (0.36, 3.31)	0.88
SIGECAPS criteria	No	3,977	89.5 (88.4, 90.6)	508	82.5 (77.6–87.4)	1.00	—
	Yes	250	10.5 (9.4–11.6)	61	17.5 (12.6–22.4)	1.81 (1.26–2.59)	0.001
PHQ9 score	None (0–4)	3,860	87.0 (85.0–88.2)	242	77.9 (72.4–83.4)	1.00	—
	Mild (5–9)	404	8.6 (7.6–9.6)	33	10.9 (6.6–15.2)	1.41 (0.89–2.25)	0.14
	Moderate (10–14)	161	3.1 (2.5–3.7)	22	5.4 (2.7–8.2)	1.97 (1.10–3.51)	0.02
	Severe (15–27)	77	1.4 (1.0–1.8)	16	5.8 (2.7–8.8)	4.64 (2.46–8.75)	<0.0001

Abbreviations: CI, confidence interval; Freq, frequency; OR, odds ratio; PHQ9, patient health questionnaire; SIGECAPS, depression acronym for disturbances in at least 4/8 symptoms with depressed mood: sleep, interest, guilt, energy, concentration, appetite, psychomotor, suicidal.

Binary survey logistic regression models were constructed for individual PHQ9 questions, PHQ9 depression score (none (score 0–4), mild (score 5–9), moderate (score 10–14), severe (15–27)) and SIGECAPS depression criteria (no, yes (at least 4/8 criteria with depressed mood)) as the independent variables and history of eczema as the dependent variable. Multivariate models included age, gender, race/ethnicity, education, poverty income ratio, history of hay fever and asthma as the dependent variables. Crude and adjusted prevalence ORs and 95% CIs were estimated.

13.1%; adjusted OR (95% CI): 2.29 (2.02–2.61) (Table 2). In addition, AD was associated with higher odds of depression in the past year (2.31 (2.00–2.66)). There were no significant statistical interactions between history of AD and other covariates as predictors of depression.

These results confirm and expand on previous international studies that have found a higher rates of depression among adults with AD (Gupta and Gupta, 1998; Cheng *et al.*, 2015; Kim *et al.*, 2015). We were unable to assess the direction of association between AD and depression; however, it is likely bidirectional. That is, AD increases the risk for depression (Gupta and Gupta, 1998; Cheng *et al.*, 2015; Kim *et al.*, 2015), whereas stress may trigger AD (Oh *et al.*, 2010). Either way, the results of the present study and prior studies suggest that adults with AD are at higher risk for depression and would benefit from increased screening for depression.

This study has several strengths, including similar results using two large-scale, randomly sampled, diverse databases using sampling weights that allow for generalizability to the entire adult US population. PHQ9 and SIGECAPS are extensively validated screening questionnaires for depression. We previously performed a multicenter validation study and found that the question used in NHANES for eczema has excellent sensitivity, specificity, positive and negative predictive values (Silverberg *et al.*, 2015a). Previous studies also found good concordance between self-reported eczema and AD diagnosed by medical examination (Susitaival *et al.*, 1995; Flohr *et al.*, 2009). However, the question used in NHIS did not specify healthcare-diagnosed AD, which may decrease its specificity. It is possible that some of the higher rates of depression observed in NHIS may be attributable to other inflammatory skin disorders. However, the similar prevalences of depression in the past year in NHIS and SIGECAPS in NHANES suggest that the higher prevalence observed are in fact from depression. We were able to control for many potentially confounding factors in multivariate regression models. This study also has several limitations. Questions pertaining to history of depression in NHIS were based on self-report and not

Table 2. Association between depression and eczema in US adults from NHIS 2012 (n = 34,613)

Variable	Eczema							
	No				Yes			
	Freq	Percent (95% CI)	Freq	Percent (95% CI)	Crude OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
<i>Ever history of depression</i>								
No	27,412	86.9 (86.4–87.3)	1,745	73.1 (70.8–75.4)	1.00	—	1.00	—
Yes	4,671	13.1 (12.7–13.6)	741	26.9 (24.6–29.2)	2.44 (2.15–2.76)	<0.0001	2.29 (2.02–2.61)	<0.0001
<i>1-year history of depression</i>								
No	28,750	90.7 (90.3–91.1)	1,923	80.1 (78.0–82.1)	1.00	—	1.00	—
Yes	3,329	9.3 (8.9–9.7)	563	19.9 (17.9–22.0)	2.44 (2.12–2.80)	<0.0001	2.31 (2.00–2.66)	<0.0001

Abbreviations: CI, confidence interval; OR, odd ratio.

Binary survey logistic regression models were constructed with ever and 1-year history of depression as the binary dependent variables and history of eczema as the independent variable. Multivariate models included age, gender, race/ethnicity, education, poverty income ratio, history of hay fever and asthma as the dependent variables. Crude and adjusted prevalence ORs and 95% CIs were estimated.

confirmed clinically through physician report or billing. However, the similarity between prevalence estimates from self-report of healthcare diagnosis in NHIS and SIGECAPS in NHANES suggests the results of both studies are valid.

In conclusion, approximately one in three US adults with AD reported any symptoms of depression and one in three adults with AD met diagnostic criteria for major depressive disorder. Future research is needed to determine whether improved treatment of AD might prevent or mitigate depressive symptoms in adults.

CONFLICT OF INTEREST

The authors state no conflict of interest.

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Author contributions

JIS had full access to all the data in the study and takes responsibility for the integrity of the data and accuracy of the data analysis. JIS contributed to study concept and design; SHY and JIS helped in acquisition of data; SHY and JIS analyzed and interpreted data, and drafted the manuscript; and SHY and JIS provided critical revision of the manuscript for important intellectual content and helped in statistical analysis.

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SUPPLEMENTARY MATERIAL

Supplementary material is linked to the online version of the paper at <http://www.nature.com/jid>

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Supplemental Table 1. Questions used in the study.

Disorder	Question	Study assessed
Eczema	Has a doctor or other healthcare professional ever told you that you have eczema? [yes or no]	NHANES 2005-2006
	During the past 12 months, have you had eczema or any kind of skin allergy? [yes or no]	NHIS 2012
Asthma	Has a doctor or other healthcare professional ever told you that you have asthma? [yes or no]	NHANES 2005-2006
	Have you ever been told by a doctor or other health professional that you had asthma? [yes or no]	NHIS 2012
Hay fever	During the past 12 months, have you had an episodes of hay fever? [yes or no]	NHANES 2005-2006
	During the past 12 months, have you been told by a doctor or other health professional that you had hay fever? [yes or no]	NHIS 2012
Depression	Over the last two weeks, how often have you been bothered by the following problems: Feeling down, depressed, or hopeless? [“not at all”, “several days”, “more than half the days” or “nearly every day”]	NHANES 2005-2006
	Over the last two weeks, how often have you been bothered by the following problems: Little interest or pleasure in doing things? [“not at all”, “several days”, “more than half the days” or “nearly every day”]	NHANES 2005-2006
	Over the last two weeks, how often have you been bothered by the following problems: Trouble falling or staying asleep, or sleeping too much? [“not at all”, “several days”, “more than half the days” or “nearly every day”]	NHANES 2005-2006
	Over the last two weeks, how often have you been bothered by the following problems: Feeling tired or having little energy? [“not at all”, “several days”, “more than half the days” or “nearly every day”]	NHANES 2005-2006
	Over the last two weeks, how often have you been bothered by the following problems: Poor appetite or overeating? [“not at all”, “several days”, “more than half the days” or “nearly every day”]	NHANES 2005-2006
	Over the last two weeks, how often have you been bothered by the following problems: Feeling bad about yourself or that you are a failure or have let yourself or your family down? [“not at all”, “several days”, “more than half the days” or “nearly every day”]	NHANES 2005-2006
	Over the last two weeks, how often have you been bothered by the following problems: Trouble concentrating on things, such as reading the newspaper or watching TV? [“not at all”, “several days”, “more than half the days” or “nearly every day”]	NHANES 2005-2006
	Over the last two weeks, how often have you been bothered by the following problems: Moving or speaking so slowly that other people have noticed? Or the opposite- being so fidgety or restless that you have been moving around a lot more than usual? [“not at all”, “several days”, “more than half the days” or “nearly every day”]	NHANES 2005-2006
	Over the last two weeks, how often have you been bothered by the following problems: Thoughts that you would be better off dead or of hurting yourself in some way? [“not at all”, “several days”, “more than half the days” or “nearly every day”]	NHANES 2005-2006
	How difficult have these problems made it for you to do your work, take care of things at home, or get along with people? [“not at all”, “several days”, “more than half the days” or “nearly every day”]	NHANES 2005-2006
	Have you ever been told by a doctor or other health professional that you had depression? [yes or no]	NHIS 2012
	During the past 12 months have you had depression? [yes or no]	NHIS 2012

Supplemental Table 2. Associations with eczema in US adults in NHANES 2005-2006 (n=5,555).

Variable	Eczema					
	No (n = 5211)		Yes (n= 344)			
	Freq	Prev (95% CI)	Freq	Prev (95% CI)	Crude OR (95% CI)	P-value
Age (yr)						
18-39	2341	93.5 (92.5–94.5)	163	6.51 (5.54–7.48)	1.00	-
40-59	1383	93.2 (91.9–94.5)	101	6.81 (5.52–8.09)	1.06 (0.79–1.43)	0.70
≥60	1487	94.9 (93.8–96.0)	80	5.11 (4.02–6.20)	0.83 (0.60–1.14)	0.24
Sex						
Male	2534	94.8 (94.0–95.6)	139	5.20 (4.36–6.04)	1.00	-
Female	2677	92.9 (92.0–93.8)	205	7.11 (6.17–8.05)	1.50 (1.15–1.96)	0.003
Race/ethnicity						
White	2307	91.5 (90.3–92.7)	206	8.5 (7.3–9.7)	1.00	-
Black	1202	92.8 (91.2–94.4)	94	7.2 (5.6–8.8)	0.84 (0.63–1.11)	0.23
Hispanic	1114	98.4 (97.5–99.2)	18	1.6 (0.8–2.5)	0.18 (0.10–0.31)	<0.0001
Other	369	95.5 (93.0–98.0)	16	4.5 (2.0–7.0)	0.51 (0.28–0.92)	0.03
Poverty Income Ratio (PIR)						
≤4.0	3670	93.2 (92.1–94.3)	216	6.8 (5.7–7.9)	1.00	-
≥4.0	1256	91.2 (89.5–92.9)	120	8.8 (7.1–10.5)	1.32 (1.01–1.73)	0.046
Highest level of education						
<HS or GED	1276	94.8 (93.1–96.5)	51	5.2 (3.5–6.9)	1.00	-
HS or GED	1072	93.0 (91.1–94.9)	64	7.0 (5.1–8.9)	1.35 (0.87–2.11)	0.18
≥HS or GED	2112	91.7 (90.4–93.0)	184	8.3 (7.0–9.6)	1.65 (1.13–2.41)	0.01
Asthma						
No	4544	94.6 (94.0–95.3)	259	5.39 (4.8–6.0)	1.00	-
Yes	658	88.6 (86.3–90.9)	85	11.44 (9.2–13.7)	2.15 (1.57–2.94)	<0.0001
Hay Fever						
No	4746	94.5 (93.9–95.1)	276	5.50 (4.9–6.1)	1.00	-
Yes	453	87.1 (84.2–90.0)	67	12.88 (10.0–15.8)	2.44 (1.76–3.39)	<0.0001

Abbreviations: CI, confidence interval; OR, odds ratio; Prev, prevalence; HS or GED, High school or graduate equivalence degree.

Refusal to answer a particular question or a response of “don’t know” occurred for the questions pertaining to ever being told by a doctor that you have eczema in 18 (5.3%), age in 0 (0.0%), gender in 0 (0.0%), race in 0 (0.0%), education in 9 (0.2%), poverty-income ratio in 294 (5.3%), hay fever in 9 (0.2%), and asthma in 9 (0.2%).