Dermatol Ther (Heidelb) (2017) 7:111–121
DOI 10.1007/s13555-017-0172-7

ORIGINAL RESEARCH

Adult Atopic Dermatitis with Comorbid Atopic Disease is Associated with Increased Risk of Infections: A Population-Based Cross-Sectional Study

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Received: December 15, 2016 / Published online: January 30, 2017

ABSTRACT

Introduction: Atopic dermatitis (AD) is related to other atopic diseases asthma and allergic rhinitis. It is known that those with asthma or allergic rhinitis have impaired immune responses that may predispose them to infections. This study sought to determine whether adult AD is associated with systemic infections, and whether association is strengthened in those with AD plus another atopic disease.
Methods: This cross-sectional study obtained information from adults in the 2010 and the 2012 National Health Interview Survey (NHIS). The primary exposure was history of AD without or with an additional atopic disease, asthma or allergic rhinitis. Self-reported systemic infections were the primary outcomes. Survey logistic regression was performed and adjusted odds ratios (aOR) reported.

Results: AD in NHIS 2010 was associated with increased risk of sinusitis [aOR (95% CIs): 1.65 (1.42, 1.91), $P < 0.001$], head or chest cold [1.31 (1.12, 1.52), $P < 0.001$], and gastrointestinal illness [2.39 (1.97, 2.89), $P < 0.001$], and in NHIS 2012, pneumonia/influenza [1.73 (1.54, 1.95), $P < 0.001$], strep throat/tonsillitis [1.72 (1.54, 1.92), $P < 0.001$], sinusitis [1.77 (1.54, 2.02), $P < 0.001$], head or chest cold [1.49 (1.33, 1.67), $P < 0.001$], and infectious disease [2.66 (2.20, 3.21), $P < 0.001$]. An increase in atopic disease mirrored an increase in number of infectious outcomes and was statistically significant in the combined dataset ($P < 0.001$).
Conclusion: The associations between AD and AD plus another atopic disease with systemic infections suggest that an underlying immune defect may be contributing to microbial susceptibility. Further studies are warranted to understand the burden of infectious disease in this population.

Keywords: Allergic rhinitis; Atopic dermatitis; Asthma; Infection

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Electronic supplementary material The online version of this article (doi:10.1007/s13555-017-0172-7) contains supplementary material, which is available to authorized users.

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INTRODUCTION

Atopic dermatitis (AD), also known as eczema, is a chronic inflammatory skin disease characterized by pruritic, scaly, and crusted lesions, typically on flexor surfaces. Symptoms usually develop in childhood and follow a chronic

relapsing course over a person's lifetime [1]. A significant proportion of the United States population is affected by AD, with a prevalence ranging from 8.7% to 18.1% in children [2]. While it was previously thought that AD resolves as one reaches adulthood, a recent US population estimate of 10% in adults [3] suggests that the prevalence may be higher than expected [4]. AD is associated with significant comorbidities, including high blood pressure [5], mental health disorders [6], and sleep disturbance [7]. The incidence of AD is actually increasing in industrialized countries, representing a major healthcare cost [8].

A multitude of factors are implicated in the pathogenesis of AD, including a skin barrier defect due to filaggrin mutations, environmental sensitization, decreased production of antimicrobial peptides [9], and alterations in the balance of the skin microbiome [1]. It is well-established that patients with AD have increased susceptibility to skin infections, including *Staphylococcus aureus*, molluscum contagiosum, and herpes simplex [10, 11]. This predisposition to pathogenic colonization has been linked to a defective skin barrier, but it is being recognized that defective innate and cell-mediated immunity may also be a significant factor.

Studies have demonstrated aberrant T-helper-2 (Th2) lymphocyte predominance over T-helper-1 (Th1) lymphocyte immune responses in patients with AD. Th2 lymphocytes secrete factors that downregulate anti-inflammatory cytokines, inhibit Toll-like 2 receptor-mediated signal transduction, and ultimately inhibit the ability to mount an immune response against bacteria and viruses [12, 13]. Similar immune system skewing is seen in other atopic diseases such as asthma and allergic rhinitis [14]. The triad of asthma, allergic rhinitis, and atopic dermatitis share common genetic and pathophysiologic characteristics, and 50% of AD patients develop one of these other atopic disorders [8, 15]. Many studies have found an increased risk for infections, particularly respiratory, in those with asthma [14]. These explorations even led to the implementation of national ACIP guidelines to give a single dose of the pneumococcal vaccine to adult patients with asthma [16].

Although the underlying immune defect is similar in asthma and AD, only a few studies have investigated infectious complications in AD on a systemic level. Many of the studies were in the pediatric population [17–21], while the same risk in adult AD patients has not been thoroughly examined [14, 22, 23]. This study seeks to determine whether adult AD alone or AD with comorbid atopic disease is associated with higher odds of systemic infections compared to the general adult population in two large population-based observational surveys.

METHODS

National Health Interview Survey

This population-based cross-sectional study extracted pre-existing, publically available data from participants of the 2010 and 2012 National Health Interview Survey (NHIS), a database collected by the National Center for Health Statistics. The NHIS annually samples households based on the Bureau of the Census to provide an accurate representation of the civilian non-institutionalized population. One adult 18 years of age or older from each household was randomly selected to complete the questionnaire. Trained United States Census Bureau interviewers conducted NHIS interviews, which consisted of in-person household interviews, as well as telephone follow-up or computer-assisted personal interviewing. The population was weighted based on age, sex, and race/ethnicity using United States Bureau of the Census data. All numeric population counts represent raw values, and prevalence estimates and statistical analyses include population weights. This study was approved by the Institutional Review Board at the University of California, San Diego. This article does not contain any new studies with human or animal subjects performed by any of the authors. The NHIS questions corresponding to the study variables of interest are shown in Table S1.

Statistical Analysis

Statistical analyses were performed using R Statistical Software v.3.2.2. Complete data analysis was performed, meaning those with missing values were excluded. All analyses were performed using the survey design package to assign population weights. The primary aim was to determine the risk of infections in participants with AD versus those without AD. The secondary aim was to analyze the subset of individuals with AD to determine the risk of systemic infections in those with AD alone versus those with AD plus another atopic disease. Survey logistic regression was performed with those with a 1-year history of AD and AD plus other atopic disease as the independent variables, and the following binary outcomes as the dependent variables: history of pneumonia/influenza, history of strep throat/tonsillitis, 1-year history of sinusitis, 1-year history of head/chest cold, 2-week history of gastrointestinal (GI) illness, and 1-year history of overall infectious disease. One-year history of overall infectious disease was a separate variable in the questionnaire (Table S1). Multivariable survey logistic regression was performed using backwards model selection for the following potential confounders or independent predictors: age, gender, race/ethnicity, Hispanic origin, smoking status, body mass index (BMI), history of asthma, 1-year history of allergic rhinitis, diabetes, hypertension, chronic obstructive pulmonary disease (COPD), and history of malignancy. Two-way interactions between AD, asthma, and allergic rhinitis were also tested for significance and included in the multivariable analysis if the P value <0.05. Unadjusted odds ratios (OR) and adjusted odds ratios (aORs) with 95% confidence intervals were calculated using the multivariable logistic regression models. Two-sided P values less than 0.05 were considered statistically significant.

For NHIS 2010, a response of "don't know" or refusal to answer the question was seen in the following cases: 18 for AD (0.07%), 20 for asthma (0.07%), 22 for allergic rhinitis (0.08%), 16 for head/chest cold (0.06%), 23 for sinusitis (0.09%), 13 for GI illness (0.04%), 185 for smoking status (0.68%), 16 for diabetes (0.06%), 46 for hypertension (0.17%), 28 for COPD (0.10%), and 20 for malignancy (0.08%). For NHIS 2012, a response of "don't know" or refusal to answer the question was seen in the following cases: 25 for AD (0.07%), 20 for asthma (0.05%), 25 for allergic rhinitis (0.07%), 46 for head/chest cold (0.13%), 33 for infectious diseases (0.12%), 29 for sinusitis (0.09%), 43 for pneumonia/influenza (0.13%), 86 for strep throat/tonsillitis (0.25%), 258 for smoking status (0.75%), 25 for diabetes (0.07%), 12 for hypertension (0.09%), 34 for COPD (0.10%), and 20 for malignancy (0.06%).

RESULTS

Population Demographics

This study analyzed data from 26,815 adults in NHIS 2010 and 33,918 adults in NHIS 2012, representing all ages, genders, and races. The 1-year prevalence of atopic dermatitis was 10.1% (9.7–10.6%) in the NHIS 2010 population and 7.2% (6.8–7.6%) in the NHIS 2012 population. The prevalence of asthma was 12.6% (12.1–13.2%) and 12.6% (12.1–13.1%) and allergic rhinitis was 7.8% (7.4–8.2%) and 7.5% (7.1–7.8%) in NHIS 2010 and NHIS 2012, respectively.

In both datasets, individuals with AD had higher prevalence of many comorbid medical conditions, including hypertension (2010: 36.0% vs. 29.6%, $P < 0.001$; 2012: 36.5% vs. 29.1%, $P < 0.001$), COPD (2010: 3.1% vs. 1.7%, $P < 0.001$; 2012: 6.2% vs. 2.6%, $P < 0.001$), and history of malignancy (2010: 13.9% vs. 7.8%, $P < 0.001$; 2012: 11.5% vs. 8.2%, $P < 0.001$). Additionally, individuals with AD had a greater prevalence of asthma (2010: 25.0% vs. 11.6%, $P < 0.001$; 2012: 25.0% vs. 11.6%, $P < 0.001$) and allergic rhinitis (2010: 15.7% vs. 6.9%, $P < 0.001$; 2012: 14.0% vs. 7.0%, $P < 0.001$) (Tables S2, S3).

Prevalence of Infectious Outcomes

In NHIS 2010, the prevalence of 1-year history of sinusitis was 13.0% (12.4–13.5%), 2-week

history of head or chest cold was 11.1% (10.7–11.7%), and 2-week history GI illness was 5.0% (4.7–5.3%). In NHIS 2012, the prevalence of pneumonia/influenza was 23.7% (22.9–24.6%), strep throat/tonsillitis was 33.8% (33.0–34.7%), 1-year history of sinusitis was 12.1% (11.6–12.6%), 1-year history of head or chest cold was 42.9% (42.1–43.7%), and 1-year history of any infectious disease was 3.1% (2.9–3.4%).

Association Between AD and Systemic Infections

In NHIS 2010, history of AD in the past year was associated with significantly higher odds of all infectious outcomes in univariate models. This association remained significant in multivariate survey logistic regression models that adjusted for age, sex, race, Hispanic origin, BMI, diabetes, hypertension, COPD, and history of malignancy. AD was associated with higher odds of sinusitis [aOR (95% CIs): 1.65 (1.42, 1.91), $P < 0.001$], head or chest cold [1.31 (1.12, 1.52), $P < 0.001$], and GI illness [2.39 (1.97, 2.89), $P < 0.001$] (Table 1).

Similarly, AD for the past year in the NHIS 2012 dataset was associated with higher odds of all infectious outcomes in multivariate models. AD was associated with higher odds of sinusitis [1.77 (1.54, 2.02), $P < 0.001$], head or chest cold [1.49 (1.33, 1.67), $P < 0.001$], pneumonia/influenza [aOR (95% CIs): 1.73 (1.54, 1.95), $P < 0.001$], strep throat/tonsillitis [1.72 (1.54, 1.92), $P < 0.001$], and infectious disease [2.66 (2.20, 3.21), $P < 0.001$] (Table 2).

Association Between AD Subgroups and Systemic Infections

Participants with a 1-year history of AD were stratified into three categories of atopic disease severity: (1) no other atopic disease, (2) at least one other atopic disease, defined as current diagnosis of asthma or allergic rhinitis, and (3) both asthma and allergic rhinitis. In both datasets, there was parallel increase in odds of infectious disease with increasing atopic disease (Tables 3, 4). All adjusted odds ratios in those with additional atopic disease were significantly higher than AD alone, except for GI illness in NHIS 2010 [one atopic disease: 1.33 (0.97, 1.84), $P = 0.08$; two atopic diseases: 1.30 (0.72, 2.35), $P = 0.39$] (Table 3) and strep throat/tonsillitis in NHIS 2012 [one atopic disease: 1.09 (0.84, 1.41), $P = 0.51$] (Table 4).

Association Between Atopic Disease and Multiple Infections

The NHIS 2010 and 2012 datasets were combined, and the cumulative number of infectious outcomes was calculated for participants in the following subgroups of atopic disease: (1) no atopic disease, (2) AD alone, (3) AD plus one other atopic disease (asthma or allergic rhinitis), (4) all three atopic diseases. Using a multivariate generalized linear model controlling for the same confounders as in the previous analysis, the means and 95% CI for each group were generated: (1) 0.62 (0.62, 0.63), (2) 0.85 (0.82, 0.87), (3) 1.25 (1.21, 1.30), (4) 1.68 (1.59, 1.77). An increase in atopic disease mirrored an increase in number of infectious outcomes and was statistically significant in the combined dataset (Fig. 1; $P < 0.001$).

DISCUSSION

In this population-based study, atopic dermatitis was associated with increased odds of systemic infections including pneumonia/influenza, strep throat/tonsillitis, sinusitis, overall infectious disease, head or chest cold, and GI illness. This risk remained significant after adjusting for other atopic diseases, asthma and allergic rhinitis, and controlling for comorbidities commonly associated with risk of infection. Stratification of AD into participants with one or two atopic diseases revealed an increased risk of all infections with increased atopic comorbidity. As the number of comorbid atopic diseases increased, participants reported a parallel increase in cumulative number of infections.

It is well-established that patients with AD are susceptible to skin infections by several microorganisms, but significance beyond the

Table 1 Association between atopic dermatitis and infections in NHIS 2010

Outcome	No AD (n = 24,208)		AD (n = 2607)					
	No.	% Prev (95% CI)	No.	% Prev (95% CI)	OR (95% CI)	*P* value	aOR (95% CI)	*P* value
Sinusitis								
No	21,355	88.0 (87.4, 88.6)	2008	78.3 (76.3, 80.3)	1.00 (ref)		1.00 (ref)	
Yes	2853	12.0 (11.4, 12.6)	599	21.7 (19.7, 23.7)	2.03 (1.78, 2.32)	<0.001	1.65 (1.42, 1.91)	<0.001
Head or chest cold								
No	21,619	89.2 (88.8, 89.7)	2202	85.2 (83.4, 87.0)	1.00 (ref)		1.00 (ref)	
Yes	2589	10.8 (10.3, 11.2)	405	14.8 (13.0, 16.6)	1.44 (1.25, 1.68)	<0.001	1.31 (1.12, 1.52)	<0.001
GI illness								
No	23,123	95.6 (95.3, 96.0)	2314	89.6 (88.2, 90.9)	1.00 (ref)		1.00 (ref)	
Yes	1085	4.4 (4.0, 4.7)	293	10.4 (9.1, 11.8)	2.55 (2.16, 3.02)	<0.001	2.39 (1.97, 2.89)	<0.001

Univariable survey-weighted logistic regression models were created with the infectious disease as the dependent variable and a 1-year history of atopic dermatitis as the independent variable. Unadjusted OR and 95% CI were calculated. Multivariable survey-weighted logistic regression models were performed that included current asthma, allergic rhinitis, age, race, Hispanic origin, BMI, smoking status history of diabetes, COPD, malignancy, and hypertension. Two-way interactions between AD, asthma, and allergic rhinitis were tested and included if significant ($P < 0.01$). Adjusted OR and 95% CI were calculated *AD* atopic dermatitis, *aOR* adjusted odds ratio, *CI* confidence interval, *GI* gastrointestinal, *no.* number, *OR* odds ratio, *prev* prevalence, *ref* reference

skin is not as well understood. Increased risk of systemic infections has been demonstrated in pediatric patients with atopic dermatitis [17–21]. In adults, one small-scale study did find an increased risk of serious invasive pneumococcal disease in adults with AD [22]. Other small studies examining outcomes of strep pharyngitis and pneumonia failed to ascertain a significant difference, perhaps due to limited sample size [23]. Our results are consistent with a recent publication examining the risk of infections in adult AD [24]. However, we have expanded on this study by including one more year of data and controlling for several important comorbidities that also increase infection risk, decreasing the possibility of confounding. Additionally, we have examined the relationship between comorbid atopic disease and infection.

The association between AD and systemic infections suggests that the immunological defects contributing to skin disease may also be contributing on a deeper level. Extensive study of the immunologic basis of AD consistently identifies an expansion of Th2, Th17, and Th22 cells and concomitant decreased Th1 cell frequency in AD versus control skin [25–27]. The expression of Th2/Th22 cytokines such as Interleukin (IL)-4, IL-13, IL-25, and IL-33 can directly impair expression of barrier proteins [28] and also increase serine protease activity [29, 30], both of which contribute to a defective skin barrier. These cytokines inhibit antimicrobial peptide production and impair innate immune cell activation at the epidermis [4]. In addition, the relative deficiency of interferon gamma producing T cells can inhibit viral immunity [31]. These consequences of Th2 lymphocyte skewing help explain the increased susceptibility to skin infections. However, how these immune mechanisms function at other epithelial sites is largely unknown. Increased

Table 2 Association between atopic dermatitis and infections in NHIS 2012

Outcome	No AD (n = 31,493)		AD (n = 2425)					
	No.	% Prev (95% CI)	No.	% Prev (95% CI)	OR (95% CI)	*P* value	aOR (95% CI)	*P* value
Sinusitis								
No	27,945	88.7 (88.3, 89.2)	1832	76.9 (74.8, 79.0)	1.00 (ref)		1.00 (ref)	
Yes	3548	11.3 (10.8, 11.7)	593	23.1 (21.0, 25.2)	2.37 (2.11, 2.66)	<0.001	1.77 (1.54, 2.02)	<0.001
Head or chest cold								
No	18,928	58.0 (57.2, 58.9)	1079	44.9 (42.4, 47.4)	1.00 (ref)		1.00 (ref)	
Yes	12,565	42.0 (41.1, 42.8)	1346	55.1 (52.6, 57.6)	1.70 (1.53, 1.89)	<0.001	1.49 (1.33, 1.67)	<0.001
Pneumonia/influenza								
No	24,469	77.4 (76.5, 78.2)	1499	62.1 (59.5, 64.6)	1.00 (ref)		1.00 (ref)	
Yes	7024	22.6 (21.8, 23.5)	926	37.9 (35.4, 40.5)	2.09 (1.87, 2.33)	<0.001	1.73 (1.54, 1.95)	<0.001
Strep throat/tonsillitis								
No	21,755	67.3 (66.4, 68.2)	1273	50.9 (48.6, 53.2)	1.00 (ref)		1.00 (ref)	
Yes	9738	32.7 (31.8, 33.6)	1152	49.1 (46.8, 51.4)	1.99 (1.80, 2.20)	<0.001	1.72 (1.54, 1.92)	<0.001
Infectious disease								
No	30,632	97.3 (97.1, 97.5)	2211	91.3 (90.0, 92.7)	1.00 (ref)		1.00 (ref)	
Yes	861	2.7 (2.5, 2.9)	214	8.7 (7.3, 10.0)	3.41 (2.85, 4.07)	<0.001	2.66 (2.20, 3.21)	<0.001

Univariable survey-weighted logistic regression models were created with the infectious disease as the dependent variable and a 1-year history of atopic dermatitis as the independent variable. Unadjusted OR and 95% CI were calculated. Multivariable survey-weighted logistic regression models were performed that included current asthma, allergic rhinitis, age, race, Hispanic origin, BMI, smoking status history of diabetes, COPD, malignancy, and hypertension. Two-way interactions between AD, asthma, and allergic rhinitis were tested and included if significant ($P < 0.01$). Adjusted OR and 95% CI were calculated
AD atopic dermatitis, *aOR* adjusted odds ratio, *CI* confidence interval, *no.* number, *OR* odds ratio, *prev* prevalence, *ref* reference

circulating levels or induction of these cytokines at other epithelial surfaces in the body can theoretically induce similar suppression of barrier proteins and antimicrobial defense.

Additionally, behavioral changes related to atopic disease may contribute to this phenomenon. Epidemiology studies have shown that severe atopic disease, including AD, is associated with reduced physical activity and sports participation in children [32]. Some may also avoid outdoor activities due to irritation from airborne allergens and sun exposure, resulting in low vitamin D levels. Given that exercise and adequate vitamin D levels are powerful stimuli of immune function, these behavioral changes may partially explain the risk of infections in atopic patients [33–36].

Table 3 Association between atopic dermatitis with atopic comorbidity and infections in NHIS 2010

Outcome	AD alone (n = 1796)		AD plus one atopic disease (n = 664)				AD plus two atopic diseases (n = 147)			
	No.	% Prev (95% CI)	No.	% Prev (95% CI)	aOR (95% CI)	P value	No.	% Prev (95% CI)	aOR (95% CI)	P value
Sinusitis										
No	1532	86.0 (84.0, 88.1)	427	66.3 (62.0, 70.5)	1.00 (ref)		49	37.7 (27.8, 47.5)	1.00 (ref)	
Yes	264	14.0 (11.9, 16.0)	237	33.7 (29.5, 38.0)	3.04 (2.36, 3.93)	<0.001	98	62.3 (52.5, 72.2)	9.48 (6.14, 14.62)	<0.001
Head or chest cold										
No	1559	87.2 (85.3, 89.1)	533	81.7 (77.9, 85.5)	1.00 (ref)		110	75.6 (66.6, 84.6)	1.00 (ref)	
Yes	237	12.8 (10.9, 14.7)	131	18.3 (14.5, 22.1)	1.39 (1.04, 1.87)	0.03	37	24.4 (15.4, 33.4)	1.77 (1.41, 2.21)	0.006
GI illness										
No	1617	90.5 (89.0, 92.0)	567	87.4 (84.4, 90.5)	1.00 (ref)		130	87.4 (80.9, 93.8)	1.00 (ref)	
Yes	179	9.5 (8.0, 11.0)	97	12.6 (9.5, 15.6)	1.33 (0.97, 1.84)	0.08	17	12.6 (6.2, 19.1)	1.30 (0.72, 2.35)	0.39

Participants with a 1-year history of AD were stratified into three categories of atopic disease severity: (1) AD alone: no other atopic disease, (2) one atopic disease: defined as current diagnosis of asthma or allergic rhinitis, (3) two atopic diseases: both asthma and allergic rhinitis. Multivariable survey-weighted logistic regression models were performed that included including age, race, Hispanic origin, BMI, smoking status, history of diabetes, COPD, malignancy, and hypertension. Adjusted OR and 95% CI were calculated

AD atopic dermatitis, *aOR* adjusted odds ratio, *CI* confidence interval, *GI* gastrointestinal, *no.* number, *OR* odds ratio, *prev* prevalence, *ref* reference

Our findings demonstrate that multiple comorbid atopic diseases directly correlate with increased infections. While this is purely an observational study, this suggests that increased atopic sensitization may lead to greater immune dysregulation. Further epidemiologic in vitro and in vivo studies investigating the differences between subgroups of atopic patients may help to understand the pathophysiology. If indeed there is a significant difference, those with multiple atopic conditions may benefit from stricter monitoring for infectious disease.

This study has several strengths, including the use of two large, randomly sampled US population surveys. The survey respondents represent diverse geographic and demographic variables, making them generalizable to the entire population. In addition, there was a sufficiently large population to control for a large number of potential confounders in logistic regression analyses. The use of a survey dataset also has limitations. Ascertainment of exposure and outcome variables was based on self-report of disease status and was not verified by clinical or laboratory measures. However, the self-report questions used to determine AD in this survey have been validated as adequately sensitive and specific for epidemiologic research [37]. Selection bias is also possible given that

Table 4 Association between atopic dermatitis with atopic comorbidity and infections in NHIS 2012

Outcome	AD alone ($n = 1623$)		AD plus one atopic disease ($n = 649$)				AD plus two atopic diseases ($n = 153$)			
	No.	% Prev (95% CI)	No.	% Prev (95% CI)	aOR (95% CI)	*P* value	No.	% Prev (95% CI)	aOR (95% CI)	*P* value
Sinusitis										
No	1367	85.2 (83.0, 87.4)	407	64.4 (59.5, 69.3)	1.00 (ref)		58	40.5 (29.7, 51.2)	1.00 (ref)	
Yes	256	14.8 (12.6, 17.0)	242	35.6 (30.7, 40.5)	3.04 (2.31, 3.99)	<0.001	95	59.5 (48.8, 70.3)	7.64 (4.57, 12.77)	<0.001
Head or chest cold										
No	796	49.6 (46.5, 52.7)	233	35.9 (30.7, 41.0)	1.00 (ref)		50	32.9 (23.1, 42.6)	1.00 (ref)	
Yes	827	50.4 (47.3, 53.5)	416	64.1 (59.0, 69.2)	1.70 (1.31, 2.20)	<0.001	103	67.1 (57.4, 76.9)	2.15 (1.33, 3.46)	0.002
Pneumonia/influenza										
No	1078	65.9 (63.1, 68.7)	346	55.5 (50.4, 60.5)	1.00 (ref)		75	48.8 (38.2, 59.4)	1.00 (ref)	
Yes	545	34.1 (31.3, 36.9)	303	44.5 (39.5, 49.6)	1.53 (1.20, 1.96)	<0.001	78	51.2 (40.6, 61.8)	2.07 (1.25, 3.42)	0.005
Strep throat/tonsillitis										
No	890	52.5 (49.7, 55.4)	318	50.0 (44.7, 55.4)	1.00 (ref)		65	36.2 (27.0, 45.5)	1.00 (ref)	
Yes	733	47.5 (44.6, 50.3)	331	50.0 (44.6, 55.3)	1.09 (0.84, 1.41)	0.51	88	63.8 (54.5, 73.0)	1.84 (1.21, 2.81)	0.005
Infectious disease										
No	1511	92.9 (91.4, 94.4)	571	89.2 (86.3, 92.2)	1.00 (ref)		129	83.6 (76.4, 90.8)	1.00 (ref)	
Yes	112	7.1 (5.6, 8.6)	78	10.8 (7.8, 13.7)	1.53 (1.04, 2.25)	0.03	24	16.4 (9.1, 23.6)	2.37 (1.31, 4.28)	0.005

Participants with a 1-year history of AD were stratified into three categories of atopic disease severity: (1) AD alone: no other atopic disease, (2) one atopic disease: defined as current diagnosis of asthma or allergic rhinitis, (3) two atopic diseases: both asthma and allergic rhinitis. Multivariable survey-weighted logistic regression models were performed that included including age, race, Hispanic origin, BMI, smoking status, history of diabetes, COPD, malignancy, and hypertension. Adjusted OR and 95% CI were calculated

AD atopic dermatitis, *aOR* adjusted odds ratio, *CI* confidence interval, *no.* number, *OR* odds ratio, *prev* prevalence, *ref* reference

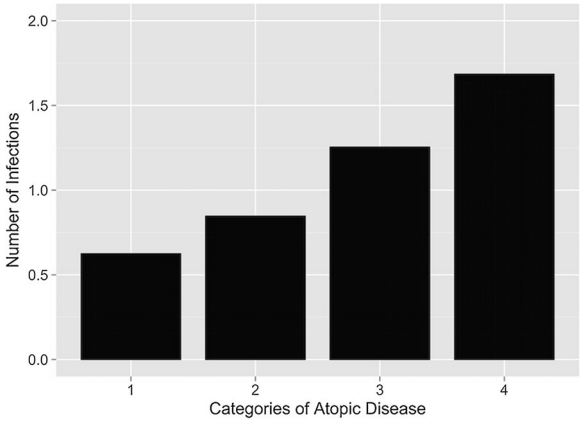

Fig. 1 Association between atopic disease and number of infections in NHIS 2010 and 2012. The number of infectious outcomes was calculated for *1* no atopic disease, *2* AD alone, *3* AD plus one other atopic disease, and *4* all three atopic diseases. The increased number of infections was significant in a multivariable linear regression model ($P < 0.001$)

those with AD may be more likely to remember and report illness.

CONCLUSIONS

In conclusion, adult atopic dermatitis is associated with increased risk of pneumonia/influenza, sinusitis, strep pharyngitis, head or chest cold, gastrointestinal illness, and infectious disease overall. Atopic dermatitis plus increasing atopic comorbidity confers significantly increased risk for these systemic infections compared to atopic dermatitis alone. Little is known about the morbidity and mortality of this increased susceptibility in this population. Further studies are warranted to characterize the burden of infectious disease in atopic dermatitis.

ACKNOWLEDGEMENTS

No funding or sponsorship was received for this study or publication of this article. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this manuscript, take responsibility for the integrity of the work as a whole, and have given final approval to the version to be published. This work was presented at the American Academy of Dermatology Summer Meeting in July 2016.

Disclosures. Saisindhu Narala and Tissa R. Hata declare no conflicts of interest.

Compliance with Ethics Guidelines. This study was approved by the Institutional Review Board at the University of California, San Diego. This article does not contain any new studies with human or animal subjects performed by any of the authors.

Data Availability. The datasets generated during and/or analyzed during the current study are available in the National Health Interview Survey repository, https://www.cdc.gov/nchs/nhis/data-questionnaires-documentation.htm.

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