Association between atopic dermatitis and extracutaneous bacterial and mycobacterial infections: A systematic review and meta-analysis

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Background: Atopic dermatitis (AD) is associated with increased bacterial colonization and infection of skin and multiple risk factors for extracutaneous infections. However, previous studies found conflicting results about whether AD is associated with increased extracutaneous infections.

Objective: To determine whether extracutaneous bacterial and mycobacterial infections are increased in AD.

Methods: A systematic review was performed of all published observational studies with controls in MEDLINE, EMBASE, Global Resource of EczemA Trials, Cochrane, and Web of Science that assessed extracutaneous infections in AD. Pooled meta-analysis was performed by using random-effects weighting.

Results: Overall, 7 studies met inclusion criteria. All 7 studies found an increased odds for at least 1 extracutaneous infection, including endocarditis, meningitis, encephalitis, bone and joint infections, and sepsis, in AD patients. In pooled meta-analysis, AD in children and adults was associated with a higher odds of ear infection (odds ratio [OR] 1.29, 95% confidence interval [CI] 1.16-1.43), strep throat (OR 2.31, 95% CI 1.66-3.22), and urinary tract infection (OR 2.31, 95% CI 1.66-3.22) but not pneumonia (OR 1.72, 95% CI 0.75-3.98). No publication bias was detected.

Limitations: Individual-level data were not available.

Conclusion: AD patients have higher odds of extracutaneous infections. Future studies are needed to confirm these associations and determine their mechanisms. (J Am Acad Dermatol 2019;80:904-12.)

Key words: atopic dermatitis; eczema; serious infection; severity; systematic review.

Atopic dermatitis (AD) is a chronic inflammatory skin disease associated with pruritus, skin pain,[1] sleep,[2,3] and mental health disturbances,[4] as well as considerable quality of life impairment.[5,6] The prevalence of AD ranges 15%-30% in children and 2%-10% in adults worldwide,[5,7] with an increase of 2-3 fold in industrialized countries since

Abbreviations used:

AD: atopic dermatitis
CI: confidence interval
OR: odds ratio
UTI: urinary tract infection

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1980.[8] AD is associated with increased bacterial colonization and infection of both lesional and nonlesional skin, especially with *Staphylococcus aureus* and *Streptococcus* spp.[9-12] Increased risk for cutaneous infections is a minor diagnostic criterion for AD.[13]

AD patients also have risk factors for increased extracutaneous infections, including skin-barrier dysfunction, immune dysregulation, lower antimicrobial peptides, increased bacterial colonization and infection of skin, and use of immunosuppressive agents.[14] Indeed, previous case reports[15,16] and recent studies[17-20] suggest that AD is associated with a higher odds of extracutaneous infections in children and adults. Yet, the relationship between AD and serious infections is not well established. We hypothesized that AD is associated with a higher likelihood of extracutaneous, multiorgan, and systemic infections. In the present study, we performed a systematic review to determine the risk for bacterial and mycobacterial extracutaneous infections in AD.

CAPSULE SUMMARY

- Atopic dermatitis was found to be associated with an increased odds of ear infection, strep throat, urinary tract infection, and multiple other extracutaneous infections.
- Risk for infection should be incorporated into clinical decision-making of atopic dermatitis patients.

METHODS

Literature search

This study was exempt from institutional review board approval at Northwestern University Feinberg School of Medicine as data were gathered from published literature. The following databases were searched for articles before May 01, 2018: Cochrane Library, MEDLINE, Embase, Global Resource of EczemA Trials, and Web of Science. The search strategy was modified from previous reviews of AD[21] and extracutaneous infection (Table I).[22,23]

Inclusion criteria were any retrospective or prospective studies that evaluated the relationship between AD and bacterial infections with a control group and included at least 20 AD patients (children or adults of male or female sex) published online, in print, or in press in any language before May 01, 2018. Title and abstract review were performed by 1 reviewer (Dr Serrano). Studies were excluded on the basis of the title or abstract if there was no clear indication they evaluated the relationship between AD and bacterial infections. The remaining articles progressed to full-text review and were completely reviewed for inclusion. If data were duplicated in >1 study, the most recent and complete study was included.

Data extraction

The following data items, if available, were collected: first author; year of publication; study design; geographical region; number of persons with AD, bacterial infections, or both enrolled in the study; AD severity; age range; sex proportion; and AD and infection diagnostic criteria.

Study quality assessment

A modified version of the Newcastle-Ottawa Scale was used to assess study quality of cross-sectional studies in meta-analysis.[24] The scoring system summarized 7 aspects of each study: research design, recruitment strategy, response rate, representativeness of sample, objectivity/reliability of outcome determination, power calculation provided, and appropriate statistical analyses. The full score was 10 stars, and the high-quality study was defined as a study with ≥6 stars.

Statistical analysis

Statistical analyses were performed using MedCalc for Windows version 18.5 (Ostend, Belgium). Pooled meta-analyses were performed on all outcomes assessed in ≥3 studies. Prevalences, odds ratios (ORs), and 95% confidence intervals (CIs) were estimated. Random-effects estimates were generated owing to significant heterogeneity (I^2 >43% for all analyses). Forest plots were generated. Egger regression and Begg rank correlation were used to assess publication bias.

RESULTS

Study selection

Overall, 5592 nonduplicate citations were identified in the database search; 5166 were excluded during title and abstract review, and 419 were excluded after full-text review. In total, 7 publications met inclusion and exclusion criteria and were included in this meta-analysis as outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses[25] flow diagram (Fig 1).

Study characteristics

The 7 included publications were published in 1994-2018. These studies included 1 prospective observational study and 6 retrospective studies with survey data. Studies were conducted in North America (n = 5) and Europe (n = 2) and included children (n = 5) and adults (n = 2). The funding was

Table I. Search strategy in Ovid MEDLINE

1. Exp dermatitis, atopic/
2. Atopic dermatitis.mp.
3. Dermatitis atopic.mp.
4. Exp eczema/ or eczema.mp.
5. Childhood eczema.mp.
6. Infantile eczema.mp.
7. Neurodermatitis.mp. or exp neurodermatitis/
8. Besnier's prurigo.mp.
9. Or/1-8
10. Exp infection/
11. Exp soft tissue infections/
12. Exp meningitis/
13. Exp urinary tract infections/
14. Exp sepsis/
15. (Infected or infection* or infectious or infectious?disease* or (infect* adj disease*)).ab,ti.
16. (Sepsis or pneumonia* or mening*).ab,ti.
17. ((urine or urinary tract) adj3 infect*).ab,ti.
18. ((skin or soft tissue) adj3 infect*).ab,ti.
19. Exp orbital cellulitis/ or exp cellulitis/
20. Exp Mycobacterium kansasii/ or exp Mycobacterium fortuitum/ or exp Mycobacterium avium Complex/ or exp Mycobacterium smegmatis/ or exp Mycobacterium avium/ or exp Mycobacterium tuberculosis/ or exp Mycobacterium/ or exp Mycobacterium scrofulaceum/ or exp Mycobacterium lepraemurium/ or exp Mycobacterium chelonae/ or exp Mycobacterium avium-intracellulare Infection/ or exp Mycobacterium Infections/ or exp Mycobacterium leprae/ or exp Mycobacterium xenopi/ or exp Mycobacterium phlei/ or exp Mycobacterium marinum/ or exp Mycobacterium haemophilum/ or exp "Mycobacterium avium subsp. paratuberculosis"/ or exp Mycobacterium Infections, Nontuberculous/ or exp Mycobacterium ulcerans/ or exp Mycobacterium bovis/
21. Exp mycobacterium infections/
22. Exp "fever of unknown origin"/
23. Bacterial infection.mp. or exp bacterial infections/
24. Or/10-23
25. 24 and 9
26. Limit 25 to human

reported in all studies, with 1 (14%) funded federally, 4 (57%) by a foundation, and 2 (29%) unfunded. AD was diagnosed by the Hanifin and Rajka criteria (n = 1), self-reported AD (n = 4), and international classification of disease (ICD) codes (n = 2). All studies had modified Newcastle-Ottawa Scale scores ≥7 (Tables II and III).

Qualitative analysis

In a prospective Swedish birth cohort study (BAMSE study, n = 4089), significantly higher proportions of parent-reported recurrent pneumonias and acute otitis media and a higher usage of antibiotics were found in children with AD aged 0-2 years compared with healthy controls.[26] In particular, significantly higher rates of lower-respiratory symptoms provoked by furred animals, pollens, and antibiotic use more than twice a year were observed in boys but not girls. Whereas, girls with AD had significantly higher rates of rhinitis and pneumonia. Acute otitis media, pneumonia, and antibiotic use were more common in children with AD, even after stratification by asthma history. In a US population-based study (National Survey of Children's Health, n = 4957), a higher odds of caregiver-reported serious, recurrent ear infections was found in children with eczema than those without, and an even higher odds was found in children with severe eczema.[27] An other US population–based study (National Health Interview Survey, 9417 children) a higher odds of caregiver-reported strep throat, influenza and pneumonia, sinus infections, recurrent ear infections, and urinary tract infections (UTI) was found in children with eczema than those without eczema.[19] Further, there were even higher odds of recurrent ear infections and sinus infections among children with eczema and other AD compared with those with eczema alone.[19] Likewise, in the same cohort (National Health Interview Survey, 34,588 adults), adults with eczema alone compared with those without had a higher odds of self-reported influenza and pneumonia, strep throat, sinus infections, gastroenteritis, and infectious disease or immune problems.[20] Persons with eczema and atopic disease had even higher rates of multiple cutaneous infections than those with eczema alone.[20]

In a study of 72,108,077 hospitalized adults in the United States (National Inpatient Sample), a significantly higher prevalence of serious infections was found in those with AD (42.1%) than those without AD (25.4%), who were identified by ICD-9 codes.[28] In particular, AD was associated with 32 of 38 infections examined, including erysipelas, cellulitis, tuberculosis, infectious arthropathy, endocarditis, encephalitis, and methicillin-resistant *Staphylococcus aureus* infections. A study of 68,634,999 children from the same cohort (National Inpatient Sample) found significantly higher odds for 47 of 49 serious infections examined, including 8 cutaneous, 9 upper respiratory and 8 lower respiratory tract or lung infections, as well as cardiac, brain, gastrointestinal, and bone infections.[29]

In a retrospective study of infants aged 0-24 months with significant bacteriuria and leukocyturia, a significantly higher prevalence was found in children with AD (27.5%) than controls (3%).[30] Of note, significant bacteriuria and leukocyturia

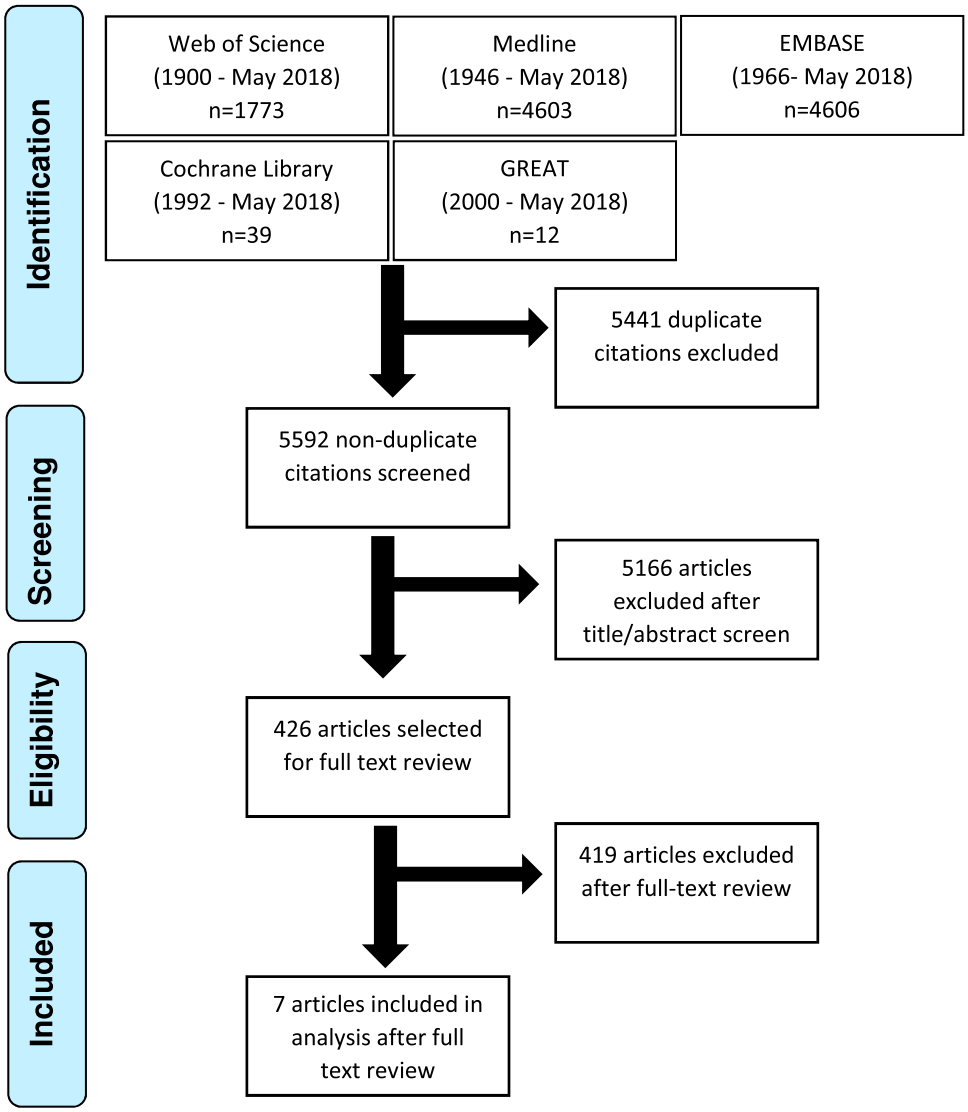

Fig 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses diagram. *GREAT*, Global Resource of EczemA Trials.

occurred more commonly in male patients with AD (72.2%) than controls (42.5%). *Escherichia coli* was the most commonly isolated organism, but *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Klebsiella oxytoca*, and *Enterococcus* sp. were also present in some urine cultures of children with AD. The control group grew *E. coli*, *P. aeruginosa*, *Klebsiella* sp., and *Proteus* sp. in their urine cultures.[30]

Pooled meta-analysis

In pooled random-effects meta-analysis, AD in children and adults was associated with a higher prevalence and odds of ear infection (3 studies, 26.6% vs 21.9%, OR 1.29, 95% CI 1.16-1.43; $P < .0001$), strep throat (4 studies, 8.4% vs 3.1%, OR 2.31, 95% CI 1.66-3.22; $P < .0001$), and UTI (4 studies, 8.4% vs 3.1%, OR 2.31, 95% CI 1.66-3.22; $P < .0001$) but not pneumonia (5 studies, 8.8% vs 5.4%, OR 1.72, 95% CI 0.75-3.98; $P = .20$) compared with controls (Fig 2).

Publication bias

Publication bias was not detected among studies that provided sufficient data for inclusion in the meta-analysis of AD and ear infection, strep throat, UTI or pneumonia, as judged by nonsignificant Egger regression ($P \geq .24$) and Begg rank correlation ($P \geq .36$).

Table II. Study characteristics

No.	Study	Location	Infection type	No AD N	No AD n (%) with infections	AD N	AD n (%) with infections	Age, y	Sex, %	Study design	Assessment of AD	Assessment of infections	Newcastle Ottawa Scale score
1	Bohme, 2002[26]	Sweden	Pneumonia	2834	223 (7.9)	950	77 (8.1)	0-2	M, 65 (with AD)	Cross-sectional survey	Parental report	Physician diagnosed	9
			Recurrent pneumonia	2832	23 (0.8)	950	16 (1.7)						
			Acute otitis media	2827	1385 (49.0)	949	528 (55.6)						
2	Silverberg and Simpson, 2013[27]	United States	Recurrent ear infections	3849	770 (20.0)	1108	259 (23.34)	<18	F, 47.9	Cross-sectional; 2007-2008 National Survey of Children's Health	Caregiver report	Caregiver report	7
3	Oggero, 1994[30]	Italy	Urinary tract infection	1327	40 (3)	131	36 (27.5)	0-1	M, 48.6	Retrospective case-control study	Hanifin and Rajka criteria	Significant bacteruria and leukocyturia	8
4	Silverberg and Silverberg, 2014[19]	United States					Without atopic disease / With atopic disease	<18	M, 51.6	Cross-sectional; 2007 National Health Interview Survey	Caregiver report	Caregiver report	8
			Strep throat	8556	855 (9.9)	460/395	65 (14.2) / 81 (20.5)						
			Sinus Infection	8556	526 (6.1)	460/396	40 (8.7) / 97 (24.5)						
			Recurrent ear infection	8556	412 (4.8)	460/396	34 (7.4) / 38 (9.6)						
			Urinary tract infection	8556	102 (1.2)	460/396	11 (2.4) / 12 (3.0)						
			Pneumonia or influenza	8556	487 (5.6)	460/396	37 (8.0) / 47 (11.9)						
5	Strom, 2017[20]	United States	Strep throat	32100	963 (3.0)	2488	160 (6.4)	≥18		Cross-sectional; 2012 National Health Interview Survey	Caregiver report	Caregiver report	7
			Pneumonia or influenza	32100	1156 (3.6)	2488	204 (8.1)						
			Sinus infection	32100	3627 (11.3)	2488	575 (23.1)						
			Gastroenteritis past 2 wk	32100	1252 (3.9)	2488	231 (9.3)						
			Infection and immune problem in past year	32100	899 (2.8)	2488	219 (8.8)						
6	Narla and Silverberg, 2017[17]	United States	Acute sinusitis	507,135,000	507,135 (0.1)	882,000	1764 (0.2)	≥18	F, 60.5	Cross-sectional; 2002-2012 Nationwide Inpatient Sample	ICD-9 codes 691.8 and 692.9	Specific ICD-9 codes	10
			Acute pharyngitis	508,126,000	508,126 (0.1)	813,000	2439 (0.3)						
			Acute tonsillitis	340,373,333	102,112 (0.03)	750,000	225 (0.03)						
			Bronchitis	353,104,833	2,118,629 (0.6)	838,750	6710 (0.8)						
			Pneumonia	343,684,513	24,745,285 (7.2)	791,644	60,165 (7.6)						
			Tuberculosis	312,748,500	625,497 (0.2)	738,666	2216 (0.3)						
			Abscess of lung or mediastinum	363,700,000	181,850 (0.05)	771,667	463 (0.06)						
			Empyema	376,096,000	376,096 (0.1)	865,000	865 (0.1)						
			Meningitis	275,395,000	550,790 (0.2)	920,000	1840 (0.2)						
			Encephalitis	329,405,714	230,584 (0.07)	790,909	870 (0.11)						
			Endocarditis	359,146,000	718,292 (0.2)	687,667	2063 (0.3)						
			Infectious arthropathy	297,707,500	595,415 (0.2)	743,250	2973 (0.4)						
			Infection of bone	323,133,714	2,261,936 (0.7)	811,222	7301 (0.9)						
			Enterocolitis	341,290,714	4,778,070 (1.4)	733,055	13,915 (1.8)						
			Clostridium difficile	345,632,888	3,110,696 (0.9)	768,846	9995 (1.3)						
			Diverticulitis	331,631,500	3,316,315 (1.0)	812,500	6500 (0.8)						
			Peritonitis and intestinal abscess	371,491,600	1,857,458 (0.5)	811,750	3247 (0.4)						
			Urinary tract infection	344,075,191	30,622,692 (8.9)	787,613	83,487 (10.6)						
			Pyelonephritis	349,270,142	2,444,891 (0.7)	746,666	4480 (0.6)						
			MSSA	343,240,769	4,462,130 (1.3)	786,545	25,956 (3.3)						
			MRSA	324,789,500	2,598,316 (0.8)	775,730	20,169 (2.6)						
			Streptococcal infection	331,438,363	3,645,822 (1.1)	784,222	14,116 (1.8)						
			Pseudomonas infection	329,228,166	1,975,369 (0.6)	800,000	8000 (1.0)						
			Mycobacterial infection	340,816,000	170,408 (0.05)	764,000	764 (0.1)						
			Septicemia	344,972,800	13,798,912 (4)	797,020	39,851 (5.0)						
			Any serious infection	342,560,712	87,010,421 (25.4)	789,864	332,533 (42.1)						

7	Narla and Silverberg, 2018[18]	United States	Necrotizing fasciitis	68,320,218	2440 (0.004)	314,781	38 (0.01)	<18	F, 48.9	Cross-sectional; 2002-2012 Nationwide Inpatient Sample	ICD-9 code 691.8 or 692.9	Specific ICD-9 codes	10
			Acute nasopharyngitis	68,320,218	15,451 (0.02)	314,781	357 (0.1)						
			Acute sinusitis	68,320,218	73,332 (0.1)	314,781	1017 (0.3)						
			Acute pharyngitis	68,320,218	169,002 (0.2)	314,781	1965 (0.6)						
			Acute tonsillitis	68,320,218	78,786 (0.1)	314,781	1017 (0.3)						
			Strep throat	68,320,218	147,570 (0.2)	314,781	2112 (0.7)						
			Acute laryngitis, tracheitis, or both and laryngopharyngitis	68,320,218	70,438 (0.1)	314,781	819 (0.3)						
			Acute epiglottitis	68,320,218	3679 (0.005)	314,781	49 (0.02)						
			Bronchitis	68,320,218	1,750,687 (2.6)	314,781	29,171 (9.2)						
			Acute bronchiolitis not due to RSV	68,320,218	745,348 (1.1)	314,781	14,478 (4.6)						
			Strep pneumonia	68,320,218	51,275 (0.08)	314,781	681 (0.2)						
			Pneumonia	68,320,218	2,304,214 (3.4)	314,781	38,079 (12.2)						
			Abscess of lung or mediastinum	68,320,218	13,602 (0.02)	314,781	250 (0.08)						
			Empyema	68,320,218	34,910 (0.05)	314,781	544 (0.2)						
			Meningitis	68,320,218	229,753 (0.3)	314,781	1715 (0.5)						
			Encephalitis	68,320,218	38,837 (0.06)	314,781	387 (0.1)						
			Endocarditis	68,320,218	10,191 (0.01)	314,781	120 (0.04)						
			Infectious arthropathy	68,320,218	46,395 (0.07)	314,781	917 (0.3)						
			Infection of bone	68,320,218	75,313 (0.1)	314,781	1686 (0.5)						
			Enterocolitis	68,320,218	720,277 (1.1)	314,781	8988 (2.9)						
			Clostridium difficile	68,320,218	83,900 (0.1)	314,781	1126 (0.4)						
			Peritonitis and intestinal abscess	68,320,218	56,159 (0.08)	314,781	314 (0.1)						
			Appendicitis	68,320,218	873,224 (1.3)	314,781	1684 (0.5)						
			Urinary tract infection	68,320,218	933,825 (1.4)	314,781	7701 (2.5)						
			Pyelonephritis	68,320,218	334,466 (0.5)	314,781	2385 (0.8)						
			Septicemia	68,320,218	855,892 (1.3)	314,781	7614 (2.4)						
			MSSA	68,320,218	366,598 (0.5)	314,781	13,659 (4.4)						
			MRSA	68,320,218	156,611 (0.2)	314,781	6609 (2.1)						
			Any strep infection	68,320,218	401,841 (0.6)	314,781	6818 (2.2)						
			Pseudomonas infection	68,320,218	136,429 (0.2)	314,781	1422 (0.5)						
			Mycobacterial infection	68,320,218	5250 (0.008)	314,781	57 (0.02)						
			Tuberculosis	68,320,218	10,035 (0.01)	314,781	93 (0.03)						
			Any serious infection	68,320,218	9,952,691 (14.6)	314,781	151,941 (48.3)						

AD, Atopic dermatitis; *ICD-9*, International Classification of Disease, Ninth Revision; *MRSA*, methicillin-resistant *Staphylococcus aureus*; *MSSA*, methicillin-sensitive *Staphylococcus aureus*; *RSV*, respiratory syncytial virus.

Table III. Modified Newcastle-Ottawa Scale for atopic dermatitis and infection studies included in the review

	Selection					Outcome		
Study	Representativeness of the sample	Sample size	Nonrespondents	Ascertainment of the exposure	Comparability	Assessment of the outcome	Statistical test	Total quality scores
Bohme, 2002[26]	*	*	*	*	**	**	*	9
Silverberg and Simpson, 2013[27]	*	*	*	*	*	*	*	7
Oggero, 1994[30]	*	*	*	*	*	**	*	8
Silverberg and Silverberg, 2014[19]	*	*	*	*	**	*	*	8
Strom, 2017[20]	*	*	*	*	*	*	*	7
Narla and Silverberg, 2017[17]	*	*	*	**	**	**	*	10
Narla and Silverberg, 2018[18]	*	*	*	**	**	**	*	10

Selection (Maximum 5 stars)

1) Representativeness of the sample:
   a) truly representative of the average in the target population* (all subjects or random sampling);
   b) somewhat representative of the average in the target population* (nonrandom sampling);
   c) selected group of users;
   d) no description of the sampling strategy.
2) Sample size:
   a) justified and satisfactory*;
   b) not justified.
3) Nonrespondents:
   a) comparability between respondents and nonrespondents characteristics is established, and the response rate is satisfactory*;
   b) the response rate is unsatisfactory, or the comparability between respondents and nonrespondents is unsatisfactory;
   c) no description of the response rate or the characteristics of the responders and the nonresponders.
4) Ascertainment of the exposure (risk factor):
   a) validated measurement tool**;
   b) nonvalidated measurement tool, but the tool is available or described*;
   c) no description of the measurement tool. Comparability: (Maximum 2 stars)
5) The subjects in different outcome groups are comparable, based on the study design or analysis. Confounding factors are controlled.
   a) The study controls for the most important factor (select one).*
   b) The study control for any additional factor.* Outcome: (Maximum 3 stars)
6) Assessment of the outcome:
   a) independent blind assessment**;
   b) record linkage**;
   c) self report*;
   d) no description.
7) Statistical test:
   a) The statistical test used to analyze the data is clearly described and appropriate, and the measurement of the association is presented, including confidence intervals and the probability level (*P* value).*
   b) The statistical test is not appropriate, not described or incomplete.

DISCUSSION

This systematic review found higher prevalence of numerous extracutaneous infections identified across multiple studies. In only 1 study, infection rates were stratified by AD severity, and this study showed that severe childhood AD was associated with an even higher odds of ear infections than mild-moderate childhood AD. These associations

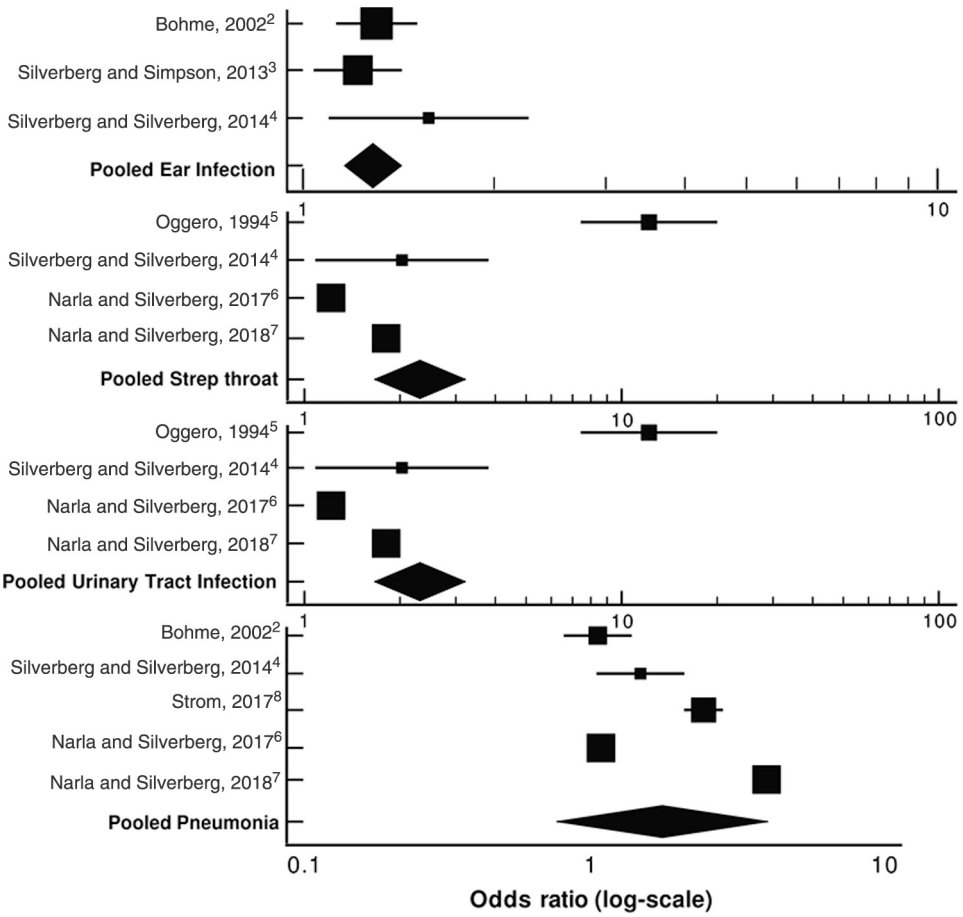

Fig 2. Forest plot of the odds of extracutaneous bacterial infections in persons with versus without atopic dermatitis. Individual (*squares*) and pooled random-effects (*diamond*) odds ratios with 95% confidence intervals are presented.

were similarly observed in studies that included physician diagnosis or self-reported and caregiver-reported AD and infections. In pooled meta-analysis, AD was found to have a significantly higher odds of ear infections, strep throat, and UTI. Together, these results suggest that AD is associated with a significantly higher likelihood of developing a variety of extracutaneous infections. There was no evidence of publication bias. However, many of the infections found to be increased in some studies still require confirmation in further clinical and epidemiologic studies.

It is well established that AD is associated with bacterial skin infections; in fact, this association is one of the minor diagnostic criterion of Hanifin and Rajka that were published in 1980.[13] However, the association between AD and extracutaneous infections has not been examined until fairly recently. Remarkably, AD was associated with a significantly higher odds of infectious endocarditis in 2 studies, which is consistent with previous case reports suggesting a connection between endocarditis and AD (or its treatments).[31-33] Moreover, AD was associated with higher rates of meningitis in 2 studies, which is consistent with a prior case report suggesting the association.[34]

These associations are clinically relevant, given that many of the infections identified can cause significant pain and discomfort, lost school and work productivity, and might even be life threatening. In addition, use of topical or oral antibiotics for the treatment of AD without infections might contribute to higher rates of antibiotic-resistant organisms that were identified in some studies, eg, methicillin-resistant *S aureus* and vancomycin-resistant *Enterococcus*. Moreover, use of systemically immunosuppressing medications for the treatment of AD (eg, systemic corticosteroids) might contribute to increased infectious risk in AD.[35] These potential risks should be factored into therapeutic decision-making in AD.

The exact mechanisms of association between AD and extracutaneous infection are unknown.

However, skin-barrier dysfunction, immune dysregulation, systemic atopy, lower antimicrobial peptides, increased bacterial colonization and infection of skin, and use of immunosuppressive agents might be contributing factors.[14] Future translational studies are needed to determine the mechanisms of increased infection in AD.

In conclusion, AD is associated with increased likelihood of extracutaneous infections, particularly ear infections, strep throat, and UTI. In addition, some studies suggested that AD is also associated with multiple potentially life-threatening infections, including endocarditis, meningitis, and septicemia. Future research is needed to confirm some of these associations and identify causal mechanisms.

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