

ONLINE FIRST

RESEARCH LETTER

Association Between Vitiligo and Atopic Disorders: A Pilot Study

Vitiligo is an autoimmune disorder characterized by melanocyte destruction and loss of pigmentation. Vitiligo has a higher prevalence of autoimmune disorders.¹ Little is known about the atopic comorbidities associated with vitiligo. We hypothesized that the proinflammatory state in vitiligo may contribute toward atopic disorders.

We previously reported a high prevalence of skin symptoms in vitiligo, such as itching or burning.¹ We hypothesized that a subset of symptomatic patients may actually have a history of eczema and atopy. We conducted a prospective epidemiological study to elucidate these points.

Methods. This prospective online-questionnaire based study was approved by the institutional review board at St Luke's-Roosevelt Hospital Center. The survey validation and distribution were performed as previously described.¹ Two distinct questionnaires were created for adults with vitiligo and parents of children and adolescents with vitiligo (eTable; <http://www.jamaderm.com>). Questionnaire items were developed to determine novel risk and prognostic factors for vitiligo. The a priori aims of the questionnaire included identification of comorbid atopic disease in vitiligo.

Data processing and statistical analysis were performed with SAS statistical software (version 9.2; SAS Institute Inc). Current age and duration of vitiligo were divided into quartiles for statistical analysis owing to wide skewing.

Logistic regression models were constructed to examine associations between clinical parameters and atopic disease, with specific etiologies as dependent variables. The independent variables were self-reported body surface area (BSA), duration of vitiligo and itching or burning of skin. Adjusted odds ratios (aORs) were calculated by including sex, age, and race/ethnicity in multivariate models. Linear interaction terms were tested and only included in final models if significant ($P < .05$). Correction for multiple dependent tests ($k = 38$) with the approaches of Benjamini and Hochberg² yielded a critical P value of .03.

Results. A total of 2848 patients started the survey, of whom 2763 completed it (a 97.0% completion rate). There were 2645 diagnosed as having vitiligo by a physician, including 2273 adults and 371 children and adolescents. The patient characteristics are listed in **Table 1**.

A total of 1635 patients (61.8%) reported a history of at least 1 atopic disease. The most common etiology was hay fever (48.2%), followed by atopic dermatitis (AD)

(24.0%), food allergy (18.2%), and asthma (17.8%). A history of any atopic disease was more common in those older than 40 years ($P \leq .03$) and patients who were multiracial or of "other" race/ethnicity ($P = .03$), but was less common in Indians ($P < .001$). There was no association between sex and history of atopic disease ($P = .44$).

Atopic disease was associated with vitiligo involving a BSA of at least 76% (aOR, 1.47 [95% CI, 1.10-1.97]; $P = .009$) and itching or burning of skin (aOR, 1.64 [95% CI, 1.38-1.96]; $P < .001$) but not duration of vitiligo ($P \geq .04$). Among patients who had an atopic disease involving a BSA of 76% (aOR, 1.57 [95% CI, 1.12-2.18]; $P = .008$) and itching or burning (aOR, 1.48 [95% CI, 1.20-1.83]; $P < .001$) were associated with higher odds of multiple disorders compared with those who had only 1 atopic disease.

Table 1. Characteristics of 2645 Patients^a

Variable	No. (%)
Age, median (IQR), y	40.0 (24.4-85.1)
Duration of vitiligo, median (IQR), y	13.0 (19.0-65.0)
Female sex	1828 (69.9)
Race/ethnicity	
African American	110 (4.2)
Hispanic	202 (7.6)
White	1019 (38.6)
Indian	101 (3.8)
Asian	57 (2.2)
Southeast Asian	30 (1.1)
Native American/Pacific Islander	11 (0.4)
Multiracial/other	1113 (42.1)
BSA	
0-25	1516 (57.7)
26-50	577 (22.0)
51-75	272 (10.4)
76-100	264 (10.0) ^d
Lesions	
Bilateral	2386 (91.2)
Acrofacial ^b	2404 (90.9)
Central ^c	1843 (75.6)
Itch from lesions	880 (35.9)
Atopic disorders	
Atopic dermatitis	604 (24.0)
Asthma	441 (17.8)
Hay fever	1227 (48.2)
Food allergy	452 (18.2)
Any disorder	1635 (61.8)
Multiple disorders	678 (25.6)
All 4 disorders	67 (2.5)

Abbreviations: BSA, body surface area; IQR, interquartile range.

^aThe questionnaire was validated, uploaded to <http://www.surveymonkey.com>, and members of nonprofit support groups for vitiligo vulgaris were invited to participate by responding to the survey. Responses from initiation of the study in June 2010 through November 2012 were reviewed.

^bAcrofacial lesions include face, scalp, axillae, arms, hands, legs, and feet.

^cCentral lesions include chest, stomach, back, hips, and buttocks.

^dA relatively high percentage of patients had a BSA of 76% to 100%. This was likely because the invitation to participate in this study was sent to vitiligo support groups, which included patients with more severe disease.

In a subset analysis, a BSA of least 76% was associated with AD (aOR, 1.71 [95% CI, 1.26-2.31]; $P < .001$), hay fever (aOR, 1.35 [95% CI, 1.03-1.79]; $P = .03$), and food allergy (aOR, 1.35 [95% CI, 1.03-1.79]; $P = .03$) but not asthma (aOR, 1.21 [95% CI, 0.85-1.71]; $P = .30$) (**Table 2**). Itching or burning was associated with all 4 atopic diseases ($P < .001$).

Discussion. The present study found higher prevalences of atopic disease in vitiligo compared with previously established prevalences in the general adult population (AD, 3%³; asthma, 8%⁴; hay fever, 24%⁵; food allergy, 5%⁶). These results are consistent with those of a previous study of 59 patients with vitiligo that found increased rates of asthma, hay fever, and positive results from skin prick and radioallergen testing.⁷ Similarly, a Chinese study of 6516 patients with vitiligo found a higher prevalence of asthma in familial probands.⁸

History of atopic disease may be helpful to predict which patients with vitiligo will experience progression to extensive disease. There are several possible explanations for the association of vitiligo involving a BSA of at least 76% and itching or burning with atopic diseases. The proinflammatory state of AD may predispose toward melanocyte destruction, while scratching of pruritic AD lesions may koebnerize vitiligo. Alternatively, there may be a common genetic mutation(s) that predisposes to both AD and vitiligo. One such example might be vitamin D receptor polymorphisms that are associated with generalized vitiligo and severe AD.⁹ Filaggrin mutations are thought to mediate severity for patients with alopecia areata and with AD and should be explored in vitiligo.¹⁰ This raises an important question: does atopy predispose toward vitiligo or do the 2 diseases merely coexist?

This study has several strengths, including being prospective with a validated survey instrument for vitiligo. However, it is limited by the lack of a control group without vitiligo. A large randomized sample of healthy patients with minimization of bias should be used for controls. However, that is a very ambitious undertaking, beyond the scope of this pilot study, and will be the subject of future studies.

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Accepted for Publication: February 22, 2013.

Published Online: June 5, 2013. doi:10.1001/jamadermatol.2013.4228

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Author Contributions: Both authors had full access to all the data in the study and take responsibility for the integrity of the data and accuracy of the data analysis. *Study concept and design:* J. I. Silverberg. *Acquisition of data:* J. I. Silverberg. *Analysis and interpretation of data:* Both authors. *Drafting of the manuscript:* J. I. Silverberg. *Critical revision of the manuscript for important intellectual content:* Both authors. *Statistical analysis:* J. I. Silverberg. *Administrative, technical, and material support:* N. B. Silverberg. *Study supervision:* N. B. Silverberg.

Conflict of Interest Disclosures: None reported.

Online-Only Material: The eTable is available at <http://www.jamaderm.com>.

Trial Registration: clinicaltrials.gov Identifier: NCT01401374

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Supplementary Online Content

Silverberg JI, Silverberg NB. Association between vitiligo and atopic disorders: a pilot study. JAMA Dermatol. Published online June 5, 2013.
doi:10.1001/jamadermatol.2013.4228

eTable. Questions used in the study

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable. Questions used in the study

Questions	Response (%)
Adult survey	
What is your sex? (male/female)	99.5
What is your age in years? (numeric)	99.9
Have you ever been diagnosed with vitiligo by a doctor? (yes/no)	99.9
Does the vitiligo affect both sides of the body? (yes/no)	98.2
How much body surface area does the vitiligo affect? (1-25%, 26-50%, 51-75%, 75-99%, 100%)	98.7
How old were you when your vitiligo started? (numeric)	98.0
How long did/do you have vitiligo? (numeric)	97.8
On which parts of the body is your vitiligo located? (yes/no) scalp, grey hair, eyelids, lips, in the mouth, chest, stomach, back, underarms, arms, elbows, wrists, hands, fingers, hips, genitals, buttocks, legs, knees, ankles, feet, toes, face, neck	87.1
Over the last week, how itchy, sore, painful or stinging has your skin been?	93.5
Do you have or have you ever had (yes/no): asthma, eczema or atopic dermatitis, food allergies or seasonal allergies	93.3–96.0
Pediatric survey	
What is your child's sex? (male/female)	99.1
What is your child's age in years? (numeric)	100.0
Has your child ever been diagnosed with vitiligo by a doctor? (yes/no)	98.0
Does the vitiligo affect both sides of the body? (yes/no)	99.2
How much body surface area does the vitiligo affect? (1-25%, 26-50%, 51-75%, 75-99%, 100%)	99.1
How old was your child when their vitiligo started? (numeric)	98.0
How long has your child had vitiligo? (numeric)	98.0
On which parts of the body is your child's vitiligo located? (yes/no) scalp, grey hair, eyelids, lips, in the mouth, chest, stomach, back, underarms, arms, elbows, wrists, hands, fingers, hips, genitals, buttocks, legs, knees, ankles, feet, toes, face, neck	96.1
Over the last week, how itchy, sore, painful or stinging has your child's skin been?	80.7
Does your child have or have they ever had (yes/no): asthma, eczema or atopic dermatitis, food allergies or seasonal allergies	96.8–97.1