Title

Alopecia areata clinical trial enrollment and retention outcome factors among underrepresented ethnic and racial groups: A cross-sectional study

Journal

Journal of the American Academy of Dermatology, 89(6)

ISSN

0190-9622

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Publication Date

2023-12-01

DOI

10.1016/j.jaad.2023.07.003

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Funding sources: None.

IRB approval status: Reviewed and approved by Ethical Committee - Fondazione Policlinico Universitario Agostino Gemelli IRCCS - Università Cattolica del Sacro Cuore, Prot N.: 4434.

Patient consent: Obtained by all patients according to IRB requirements.

Key words: alopecia areata; atopic dermatitis; eczema; JAK inhibitors; SALT score; upadacitinib.

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Conflicts of interest

None declared for the authors with the exception of Ketty Peris who has served on advisory board, received honoraria for lectures and/or research grants for AbbVie, Almirall, Lilly, Galderma, Leo Pharma, Pierre Fabre, Novartis, Sanofi, Sun Pharma, Janssen; Andrea Chiricozzi who served as advisory board member and consultant and has received fees and speaker's honoraria or has participated in clinical trials for AbbVie, Almirall, Leo Pharma, Lilly, Janssen, Novartis, Pfizer, and Sanofi Genzyme; Maria Concetta Fargnoli has served on advisory boards, received honoraria for lectures and research grants from AMGEN, Almirall, Abbvie, BMS, Galderma, Kyowa Kyrin, Leo Pharma, Pierre Fabre, UCB, Lilly, Pfizer, Janssen, MSD, Novartis, Sanofi-Regeneron, Sunpharma; Maria Esposito who served as advisory board member, speaker and consultant and has participated in clinical trials for AbbVie, Almirall, Leo Pharma, Eli Lilly, Janssen, Novartis, and Sanofi Genzyme, UCB; Cataldo Patruno who served as advisory board member and consultant and has received fees and speaker's honoraria or has participated in clinical trials for AbbVie, Amgen, Eli Lilly, Leo Pharma Novartis, Pfizer, Pierre Fabre, Sanofi.

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Alopecia areata clinical trial enrollment and retention outcome factors among underrepresented ethnic and racial groups: A cross-sectional study

To the Editor: Although Hispanic and Black patients have greater lifetime incidence of alopecia areata (AA) compared with White patients in the United States, the etiology and pathology of this disparity are not well characterized, likely due to lack of inclusion in clinical trials.[1,2] Furthermore, data on enrollment and retention rates across underserved groups are limited.[1] Therefore, we sought to examine enrollment

Table I. Demographics, enrollment outcomes, and clinical features of alopecia areata of study participants

	White (*n* = 52)	Hispanic (*n* = 28)	Asian (*n* = 19)	Black (*n* = 14)	Pacific Islander (*n* = 2)
Patient characteristics					
Female, *n* (%)	23 (44.2)	15 (53.6)	9 (47.4)	11 (78.6)	1 (50)
Male, *n* (%)	29 (55.8)	13 (46.4)	10 (52.6)	3 (21.4)	1 (50)
Age at enrollment, mean (SD)	41.4 (16.7)	35.4 (14.3)	32.0 (13.8)	40.9 (15.4)	23.5 (3.5)
Age at AA onset, mean (SD)	26.9 (21.3)	21.6 (13.7)	25.7 (16.2)	25.5 (16.2)	4.6 (6.2)
SALT at screening, mean (SD)	81.4 (24.4)	65.8 (24.4)	72.4 (26.2)	74.5 (28.3)	67.9 (24.3)
Distance to clinic, mean (miles; SD)	72.8 (145.6)	44.7 (69.5)	33.4 (33.8)	38.6 (26.3)	17.7 (15.7)
Clinical trial enrollment outcomes					
Screen failed, *n* (%)	20 (38.5)	10 (35.7)	3 (15.8)	8 (57.1)	1 (50)
Enrolled, *n* (%)	32 (61.5)	18 (64.3)	16 (84.2)	6 (42.9)	1 (50)
Enrolled and withdrew, *n* (% of enrolled)	5 (15.6)	2 (11.1)	1 (6.3)	2 (33)	0 (0)
Enrolled and early termination, *n* (% of enrolled)	0 (0)	0 (0)	1 (6.3)	1 (16.7)	0 (0)
AA type at screening					
Alopecia totalis or universalis, *n* (%)	24 (46.2)	8 (28.6)	3 (15.8)	4 (28.6)	0 (0)
Alopecia ophiasis episode, *n* (%)	2 (3.8)	2 (7.1)	0 (0)	3 (21.4)	0 (0)
Patchy AA, *n* (%)*	21 (40.4)	18 (64.3)	14 (73.7)	6 (42.9)	2 (100)
Body site involvement at screening					
Scalp, *n* (%)	51 (98.1)	28 (100)	18 (94.7)	13 (92.9)	2 (100)
Eyebrow, *n* (%)	34 (65.4)	15 (53.6)	9 (47.4)	4 (28.6)	1 (50)
Eyelash, *n* (%)*	34 (65.4)	13 (46.4)	9 (47.4)	3 (21.4)	1 (50)
Nail, *n* (%)	18 (34.6)	8 (28.6)	1 (5.3)	2 (14.3)	0 (0)
Beard, *n* (%)	15 (28.8)	5 (17.9)	4 (21.1)	0 (0)	0 (0)

AA, Alopecia areata; *SALT*, severity of Alopecia Tool.
*Statistical analysis using a chi-square test with a significant *P* value ($P < .05$).

Table II. Comorbidities of AA study participants

	White (*n* = 52)	Hispanic (*n* = 28)	Asian (*n* = 19)	Black (*n* = 14)	Pacific Islander (*n* = 2)
Any comorbidity, *n* (%)	47 (90.4)	24 (85.7)	17 (89.5)	13 (92.9)	2 (100)
Atopic disease, *n* (%)	23 (44.2)	4 (14.3)	10 (52.6)	6 (42.9)	1 (50)
Thyroid disease, *n* (%)	9 (17.3)	4 (14.3)	4 (21.1)	2 (14.3)	0 (0)
Hyperlipidemia, *n* (%)	13 (25.0)	2 (7.1)	2 (10.5)	3 (21.4)	0 (0)
Hypertension, *n* (%)	8 (15.4)	2 (7.1)	0 (0)	3 (21.4)	0 (0)
Vitamin D deficiency, *n* (%)	5 (9.6)	4 (14.3)	1 (5.3)	2 (14.3)	0 (0)
Audiologic/ophthalmic abnormalities, *n* (%)	5 (9.6)	1 (3.6)	0 (0)	3 (21.4)	0 (0)
Anemia, *n* (%)	3 (5.8)	2 (7.1)	0 (0)	1 (7.1)	0 (0)
Vitiligo, *n* (%)	2 (3.8)	0 (0)	0 (0)	1 (7.1)	1 (50)
Type 1 diabetes mellitus, *n* (%)	1 (1.9)	2 (7.1)	0 (0)	1 (7.1)	0 (0)
Obesity, *n* (%)	2 (3.8)	1 (3.6)	0 (0)	0 (0)	0 (0)
Type 2 diabetes mellitus, *n* (%)	1 (1.9)	0 (0)	0 (0)	0 (0)	0 (0)
Psychiatric comorbidities					
Other psychiatric condition, *n* (%)*	18 (34.6)	1 (3.6)	4 (21.1)	1 (7.1)	0 (0)
Depression, *n* (%)	7 (13.5)	5 (17.9)	2 (10.5)	1 (7.1)	0 (0)

*Statistical analysis using a chi-square test with a significant *P* value ($P < .05$).

characteristics of AA study participants across ethnic and racial groups at the University of California, Irvine's productive AA clinical trial unit.

We conducted a cross-sectional study of 115 subjects screened for enrollment in AA therapeutic, randomized clinical trials (2017-2022). Trial subjects were recruited by the following means in order of frequency: university dermatologists, outside dermatologists, and direct marketing efforts. Statistical analyses of differences between racial/ethnic groups were assessed using one-way analysis of variance and chi-square tests.

In total, 115 patients with AA were identified as follows: (1) 45.2% ($n = 52$) White, (2) 24.3% ($n = 28$) Hispanic, (3) 16.5% ($n = 19$) Asian, (4) 12.2% ($n = 14$) Black, and (5) 1.7% ($n = 2$) Pacific Islanders (Table I). There were significant differences between racial/ethnic groups in "study completion status" (completed, ongoing, or withdrawn/discontinued; $P = .0131$). Asian patients had the highest enrollment rates (84.2%) and the lowest screen failure rates (15.8%). In contrast, Black patients had the lowest enrollment rates (42.9%) and the highest screen failure rates (57.1%). Withdrawal and early termination rates were also the highest in Black patients (33% and 16.7%, respectively), but these rates were the lowest in Pacific Islanders (0%).

There were significant differences in AA type of scalp involvement in screened patients, with patchy alopecia ($P = .0346$) being the most common among Asian and Pacific Islander patients and least common among White patients. The most significant differences in body site involvement were observed at screening, with eyelash hair loss ($P = .0499$) being common in White patients (65.4%) but rare in Black patients (21.4%). Comorbidities were similar across racial groups, with atopic diseases, thyroid diseases, and hyperlipidemia being the most common (Table II). The only observed differences were among comorbid psychiatric diseases, excluding depression ($P = .0382$), and these differences were the highest in White patients.

Patients of color have been shown to have decreased access to dermatologic care and higher rates of undiagnosed disease[3]; ensuring accessibility of clinical trials is crucial for understanding the ethnic/racial variations in AA. Although our study is limited by small size and retrospective nature, the subjects recruited are reflective of the general ethnic and racial breakdown in our county.[4]

Low enrollment rates of Black patients were due to high screen failure ($n = 8$) as a result of incorrect alopecia diagnosis, low Severity of Alopecia Tool score, pregnancy, malignancy, abnormal thyroid levels, hepatitis B, anemia, and inability to attend visits. Particularly, incorrect diagnosis highlights the need for improved evaluation of hair loss conditions among patients of color. Also, our Black patients experienced higher rates of study noncompletion in comparison to Asian patients, which is attributable to the following reasons: (1) early termination due to a serious adverse effect (rash; $n = 1$), (2) loss to follow-up ($n = 1$), and (3) limited ability to attend appointments ($n = 1$). Although we did not identify any socioeconomic factors that affected study recruitment and enrollment, we cannot exclude the possibility of these elements influencing patient retention. Identifying and alleviating these factors can potentially improve retention and lead to more representative results in AA clinical trials.[5]

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Funding sources: None.

IRB approval status: Reviewed and approved by the University of California, Irvine IRB (#2016-3076).

Patient consent: Not applicable.

Previous presentation: Information contained in this letter was previously presented at the 17th and 19th Annual Skin of Color Society Scientific Symposium.

Key words: alopecia areata; clinical trial enrollment; clinical trial retention; race; racial disparities; skin of color.

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Conflicts of interest

Dr Mesinkovska has served as an adviser and speaker for Lilly, Pfizer, and Concert as well as a board member of the American Hair Research Society and former Chief Scientific Officer for the National Alopecia Areata Foundation. The other authors have no potential conflict of interest to disclose.

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Association of vitiligo and inflammatory arthropathy in hospitalized US adults

To the Editor: Vitiligo is an autoimmune depigmenting disease affecting 0.05% to 2.0% of the population.[1] Numerous studies show bidirectional relationships of vitiligo with autoimmune diseases.[2] Previous studies found conflicting results regarding associations of vitiligo with autoimmune arthritis.[3,4] Our study utilizes a large inpatient database to investigate associations of vitiligo with autoimmune arthropathies.

We analyzed data from the 2002-2016 Nationwide Inpatient Sample (NIS) according to Healthcare Cost and Utilization Project (HCUP) policies (Supplementary Methods, available via Mendeley at https://doi.org/10.17632/gjvyh2gmpm.1). Vitiligo and autoimmune arthritides were identified by International Classification of Disease (ICD) codes (Supplementary Table 1, available via Mendeley at https://doi.org/10.17632/gjvyh2gmpm.1). Statistical models used survey weighted procedures in SAS 9.4 (SAS Institute) that incorporated discharge trend weights, clustering by individual hospitals, and sample strata provided by the NIS. The study did not require approval by the University of Texas at Austin Institutional Review Board (IRB).

Between 2002 and 2016, 96,970,768 admissions were captured, including 18,231 (0.02%) with vitiligo. Vitiligo patients were 44.3% female, 45.6% White, 93.4% insured, and mean ± std. dev. 55.05 ± 20.23 years old (Supplementary Table 2, available via Mendeley at https://doi.org/10.17632/gjvyh2gmpm.1).

In survey weighted logistic regression models, vitiligo was significantly associated with higher odds of any inflammatory arthritis (OR [95% CI]: 2.23 [1.96-2.54]), psoriatic arthritis (4.74 [2.97-7.56]), rheumatoid arthritis (RA; 2.09 [1.82-2.41]), and other inflammatory arthritis (4.14 [2.16-7.96]) ($P < .001$ for all), with a trend toward significance with reactive arthritis (5.67 [0.80-40.30], $P = .083$) and ankylosing spondylitis (AS; 1.96 [0.99-3.85], $P = .052$). Significant associations remained significant after controlling for age, sex, race/ethnicity, and insurance (Fig 1).

Sheth et al found high prevalence of rheumatoid arthritis (RA) (2.9%) and psoriasis (7.6%) among vitiligo patients.[5] A cross-sectional study found that vitiligo probands and siblings had greater likelihood of psoriasis and RA, but similar likelihood of ankylosing spondylitis (AS) compared to the general population.[3] We similarly found that vitiligo was associated with higher odds of RA, and with a trend toward higher odds of AS. Study strengths include use of a large, nationally representative sample of US hospitalizations, with a large number of vitiligo cases. Limitations include lack of data on severity, age-of-onset, and treatments. Vitiligo and arthritis may not always be coded during hospitalization, introducing a possible source of error and underestimation of associations.

These results demonstrate clinically significant systemic autoimmunity in vitiligo patients, with higher prevalence of inflammatory arthritides. Vitiligo patients may benefit from increased screening with appropriate referral for rheumatologic care. Systemic anti-inflammatory therapy may be needed in vitiligo patients with comorbid arthritides. Further studies are needed to confirm this relationship, underlying mechanisms, and strategies for treatment and prevention.

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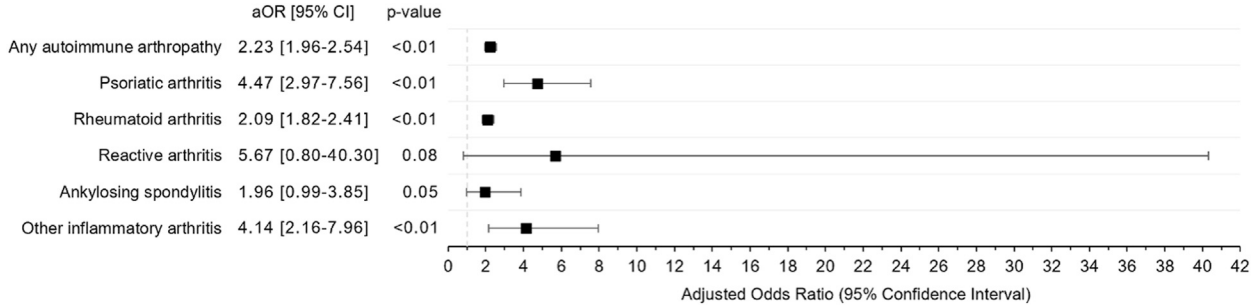

Fig 1. Odds of arthropathy given prior diagnosis of vitiligo, adjusted for age, sex, race/ethnicity, and insurance type.