Race and Alopecia Areata amongst US Women

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Few studies have examined the clinical epidemiology of alopecia areata (AA) in regard to patient race, and therefore, any disparities in incidence or prevalence of disease are largely unexplored. We sought to investigate potential racial disparities amongst two large cohorts of women. We conducted a cross-sectional analysis from the Nurses' Health Study (NHS) and Nurses' Health Study II (NHSII), wherein participants self-reported a diagnosis of AA. We determined odds ratios for AA by race in a multivariate analysis. Among 63,960 women from NHS and 88,368 women from NHSII with information on race and diagnosis of AA, we identified 418 and 738 cases of AA, respectively. In NHS, the multivariate-adjusted odds ratio for AA was 2.72 (95% confidence interval 1.61–4.61) amongst black women as compared with white women. In NHSII, the multivariate-adjusted odds ratio was 5.48 (95% confidence interval 4.10–7.32) amongst black as compared with white women. In a secondary analysis designating participants by Hispanic ethnicity, in NHSII the multivariate odds ratio was 1.94 (95% CI 1.24–3.02) in Hispanic compared with non-Hispanic white women. In this study, we found increased odds of AA based on self-reported race in black and Hispanic women as compared with white women. Further studies are needed to explore the mechanism of this racial disparity related to AA.

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INTRODUCTION

Alopecia areata (AA) is a nonscarring form of immune-mediated hair loss. To date, there have been relatively few epidemiologic studies of AA, and thus, certain aspects of burden of disease have yet to be described. Current understanding is largely attributed to two population-based studies in Olmstead County, Minnesota, wherein the lifetime incidence rate was 1.7% in years 1975–1989 (Safavi et al., 1995), and 2.1% from 1990 to 2009 (Mirzoyev et al., 2014), with no significant gender difference. However, detailed assessment of incidence based on patient race was not described, and to our knowledge this important epidemiologic aspect of disease is previously unreported. Therefore, the purpose of the current study was to determine potential disparities of AA based on race in two cohorts of female nurses.

RESULTS

A total of 63,960 women from the Nurses' Health Study (NHS) and 88,368 women from the Nurses' Health Study II (NHSII) were included in this study. We identified 418 and 738 cases of AA, respectively. Age-standardized baseline characteristics of participants at the time of collection of information on diagnosis of AA by race are shown in Table 1. Participants from NHS were older than those in NHSII (mean age approximately 77 vs. 57). Alcohol intake was greatest amongst white women, and the history of hypertension and type 2 diabetes was greatest amongst black women. Otherwise, there were no compelling differences in standard lifestyle characteristics between races. Lifetime incidence and odds ratios (ORs) of AA by participant race are shown in Table 2. In age-adjusted analyses, black as compared with white women had greater lifetime incidence of AA in NHS (OR: 2.63; 95% confidence interval [CI] 1.56–4.42) and in NHSII (OR: 5.23; 95% CI 3.95–6.93). The results were similar in multivariate analyses. Compared with white women, there was no difference in AA incidence in a composite "other" race group in NHS (multivariate OR: 0.95; 95% CI 0.35–2.57) or NHSII (multivariate OR: 1.10; 95% CI 0.67–1.83). When characterizing women by Hispanic ethnicity (Supplementary Table S1 online), there was a greater lifetime incidence of AA in Hispanic women compared with non-Hispanic white women in NHSII (multivariate OR: 1.94; 95% CI 1.24–3.02). There was no significant difference in incidence by Hispanic ethnicity in the NHS cohort (multivariate OR: 1.14; 95% CI 0.42–3.09).

DISCUSSION

In this study, we found a higher lifetime incidence of AA in black as compared with white women in two large cohorts of US nurses. Increased incidence of AA was also found in Hispanic women in NHSII. The current understanding of AA epidemiology is primarily based on population studies in Olmsted County, Minnesota, a location with a predominately white racial demographic (United States Census Bureau, 2015). In the most recent assessment, only 18 black patients were identified amongst the 530 total patients with AA (Mirzoyev et al., 2014). One study has alluded to a disparity in incidence between black and white patients. Using International Classification of Disease, Ninth Revision codes,

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Abbreviations: AA, alopecia areata; CI, confidence interval; NHS, Nurses' Health Study; OR, odds ratio; SLE, systemic lupus erythematosus

Table 1. Age-standardized characteristics of study participants by race in the Nurses' Health Study (in 2012) and Nurses' Health Study II (in 2011)

	Nurses' Health Study			Nurses' Health Study II		
	Race			Race		
	White (n = 62,376)	Black (n = 905)	Others[1] (n = 679)	White (n = 85,062)	Black (n = 1,352)	Others[1] (n = 1,954)
Age, mean (SD)	76.3 (6.6)	76.6 (6.0)	76.9 (6.0)	56.6 (4.6)	57.7 (4.5)	57.0 (4.5)
Body mass index (kg/m^2), mean (SD)	26.2 (5.4)	27.7 (5.4)	24.8 (4.9)	27.7 (6.4)	30.9 (7.0)	25.7 (5.3)
Current smoking (%)	4.5	2.2	2.7	5.9	5.3	3.7
Physical activity level (metabolic equivalents hours/wk), mean (SD)	19.0 (23.9)	16.1 (18.2)	24.0 (29.7)	23.8 (29.4)	18.3 (30.0)	24.8 (44.0)
Alcohol intake (g/d), mean (SD)	6.1 (10.6)	2.8 (7.9)	2.8 (7.6)	6.6 (10.8)	3.0 (7.8)	3.7 (9.0)
History of comorbid disease						
Atopy (%)	–	–	–	8.3	8.8	11.2
Cardiovascular disease (%)	5.6	4.6	4.1	1.2	1.3	0.9
Hypertension (%)	50.6	62.5	50.5	37.1	59.5	42.2
Hypercholesterolemia (%)	44.1	46.7	44.2	35.2	34.8	36.8
Other immune-mediated disease[2] (%)	10.0	8.1	9.9	7.7	8.4	5.9
Type 2 diabetes (%)	11.4	20.4	15.9	6.4	14.6	8.9
Menopausal status and hormone use						
Pre (%)	0	0	0	16.6	15.7	17.4
Post—never use (%)	21.2	27.9	16.2	37.3	43.6	44.1
Post—current (%)	10.4	7.0	10.6	16.7	10.8	11.6
Post—past (%)	68.4	65.0	73.2	29.4	29.9	26.8
Annual UV flux[3], RB	125.2 (26.7)	131.0 (29.2)	141.8 (26.8)	125.7 (24.8)	133.1 (27.6)	140.8 (26.1)

Values are means (SD) or percentages and are standardized to the age distribution of the study population.
Values of polytomous variables may not sum to 100% because of rounding.
Abbreviations: AA, alopecia areata; RB, Robertson-Berger; SD, standard deviation.
[1]Other races include American Indian, Asian, and Native Hawaiian or Pacific Islander.
[2]Includes Crohn disease or ulcerative colitis, multiple sclerosis, psoriasis, polymyositis, rheumatoid arthritis, Sjögrens syndrome, scleroderma, and vitiligo.
[3]Value is ($\times 10^{-4}$ RB units); an estimate of amount of UVR reaching Earth's surface of residence within 1 y.

McMichael et al. (2007) characterized outpatient visits for AA from 1990 to 2000, from the North American Medical Care Survey. They identified a relatively greater number of black versus white patients presenting with AA (108 vs. 91 patients per 10,000 population).

In the current study, we identified a significantly greater lifetime incidence of AA in black and Hispanic females, compared with white females. Other immune-mediated diseases are known to disproportionately affect certain racial or ethnic groups, and previous studies might provide clues toward the underlying cause of the disparity we have identified with AA. For example, systemic lupus erythematosus (SLE), like AA, is an immune-mediated disease that disproportionately affects women with African or Hispanic ethnic backgrounds (Fernández et al., 2007). In a multiethnic, multicenter cohort of patients with SLE, Fernández et al. (2007) found that African American and Texan Hispanic patients had more severe disease, including greater frequency

Table 2. Race and AA in the NHS and NHSII

Cohort	Race	Total participants	No. of AA cases	Lifetime incidence (%)	Age-adjusted OR (95% CI)	Multivariate-adjusted OR[1] (95% CI)
NHS	White	62,376	399	0.64	1 (referent)	1 (referent)
	Black	905	15	1.66	2.63 (1.56–4.42)	2.72 (1.61–4.61)
	Other[2]	679	4	0.59	0.93 (0.35–2.49)	0.95 (0.35–2.57)
NHSII	White	85,062	667	0.78	1 (referent)	1 (referent)
	Black	1,352	55	4.07	5.23 (3.95–6.93)	5.48 (4.10–7.32)
	Other[2]	1,954	16	0.82	1.03 (0.63–1.70)	1.10 (0.67–1.83)

Abbreviations: AA, alopecia areata; CI, confidence interval; NHS, Nurses' Health Study; NHSII, Nurses' Health Study II; OR, odds ratio.
[1]Multivariate model adjusts for age (continuous), body mass index (<22, 22–24.9, 25–29.9, 30–34.9, >35 kg/m^2), alcohol intake (0, 0.1–4.9, 5–9.9, >10 g/d), UV flux (quintiles), and post-menopausal hormone use (premenopausal, postmenopausal never, past, or current use), smoking history (never, past, current), history of type 2 diabetes, cardiovascular disease, and history of any of the following immune-mediated diseases: Crohn disease or ulcerative colitis, multiple sclerosis, psoriasis, polymyositis, rheumatoid arthritis, Sjögren syndrome, scleroderma, and vitiligo. Atopic dermatitis (eczema) was an additional covariate in NHSII analysis
[2]Other races include American Indian, Asian, Native Hawaiian or Pacific Islander.

of acute disease onset and renal involvement. In that cohort and in others (Sánchez et al., 2011), investigators have identified specific genetic susceptibility loci that differ by racial or ethnic background. Additionally, studies have identified higher IFN-α activity amongst black patients with SLE (Weckerle et al., 2011). These pathophysiological factors in SLE could play a role in the mechanism of racial disparity we have found in AA. Interestingly, AA has been reported in association with IFN-α therapy for hepatitis C (Goh, 2013), and type 1 IFN-related protein expression has been described in inflammatory AA lesions (Ghoreishi et al., 2010).

Other mechanisms could contribute to our findings. Race and ethnicity are not only biologic but also social constructs. Socioeconomic disparities can contribute significantly to health disparities, a consideration emphasized by Fernández et al. (2007) in their work on SLE. In the present study, socioeconomic risk factors for AA might differ by racial or ethnic group. The common occupational background of nursing does standardize this aspect to some degree, but nevertheless, socioeconomic factors might still predispose black and Hispanic women to AA, an important topic of inquiry for future studies. Another consideration is that AA patches might be more apparent to black and Hispanic women or their physicians. For example, hair styles and hair attributes amongst these women might make AA patches more obvious, leading to a diagnostic bias. Additionally, black women reporting AA might instead have a history of a different form of hair loss, itself more common in this group. For example, central centrifugal cicatricial alopecia is a form of scarring alopecia common in women of African descent (Callender and Onwudiwe, 2011). However, given the health care background of these nurses, their report of AA is presumably more reliable than in the general population (Colditz et al., 1986).

The effect estimates for AA in black women were significantly higher in the NHSII cohort versus NHS (multivariate OR: 5.48 vs. 2.72). Furthermore, a lifetime incidence of AA was significantly higher in Hispanic versus non-Hispanic white women only in NHSII. This difference could arise from the larger sample size under study in NHSII. Additionally, because NHSII participants were younger at the time of survey, it is possible that their recall would be more reliable, considering that AA predominantly affects younger individuals (Villasante Fricke and Miteva, 2015).

Our study is strengthened by a well-powered analysis of two large cohorts of women. Additionally, multivariate analysis helped to control for potential confounders. Our study has important limitations for consideration in future study designs. As previously mentioned, black or Hispanic women may have a history of hair loss that is not AA specifically. This is compounded by the fact that an exact hair loss diagnosis without skin biopsy can be challenging, even for dermatologists. Furthermore, the large-scale questionnaire in this study did not allow for more granular inquires on hair loss. For example, ideally participants could be presented with the opportunity to choose amongst different types of hair loss (e.g., central centrifugal cicatricial alopecia vs. frontal fibrosing alopecia), or to choose amongst photos to aid in selection of the correct diagnosis. These are valuable considerations for the design of future epidemiologic questionnaires for the study of AA. Additionally, our cohorts are female-only and AA cases are self-reported. However, as previously mentioned, the health care background of participants should improve specificity of AA diagnosis. Finally, although there was greater racial diversity in our study than in previous AA epidemiologic studies, our cohorts still included primarily white participants.

In conclusion, we found a significantly greater lifetime incidence of AA in black and Hispanic as compared with white females in the USA. Further studies are needed to replicate our findings and better understand the underlying mechanisms of these disparities. Although precise diagnosis of AA in our study population is difficult, our findings provide an important suggestion of a potential disparity in AA prevalence, and more broadly, they indicate a true disparity in hair loss prevalence in general amongst these racial subsets of women. Our findings bring attention to the need for better understanding and sensitivity toward racial and ethnic disparities of disease. A greater burden of disease amongst black and Hispanic women should also encourage increased resource allocation toward diagnosis and treatment for these patients. Finally, as pharmaceutical trials for AA become more common (Kennedy Crispin et al., 2016), our study emphasizes the need for racial diversity in patient recruitment, thus allowing for treatment response and risk profiles that are well characterized in a diverse population.

MATERIALS AND METHODS

This study included participants from the ongoing NHS and NHSII cohorts (Li et al., 2016; Thompson et al., 2016). NHS was established in 1976 when 121,700 female nurses aged 30 to 55 years responded to a baseline questionnaire inquiring about lifestyle factors and medical history. NHSII was established in 1989 when 116,430 participants aged 25 to 42 years completed a similar baseline questionnaire. Follow-up questionnaires have been sent every 2 years. This study was approved by the Institutional Review Board of Brigham and Women's Hospital. Patient race was assessed in 1992 and 2004 in NHS, and 1989 and 2005 in NHSII. In the primary analysis, respondent race was separated into categories including white, black, and "other," which comprised a composite category including American Indian, Asian, and Native Hawaiian or Pacific Islander. These races were considered together, given the relatively lower number of these participants. In a secondary analysis, participants were further separated by Hispanic ethnicity into the following categories: non-Hispanic white, non-Hispanic black, Hispanic, Asian, or other (American Indian, Native Hawaiian or Pacific Islander). Diagnosis of AA was asked in 2012 in NHS and 2011 in NHSII. Participants were first asked if they had ever been previously diagnosed with AA by a physician, and if so in which time period. Participants in NHS could choose 2001 or before, 2002–2005, 2006–2009, 2010–2011, 2012 and later; those in NHSII could choose before 1 June 2009, June 2009–May 2011, or after 1 June 2011. Those women who did not respond to questions inquiring about race or history of AA were excluded from the study.

We conducted a logistic regression analysis, with ORs and 95% CIs for AA calculated from age-adjusted and multivariate models. Multivariate models were adjusted for age (continuous), body mass index (<22, 22–24.9, 25–29.9, 30–34.9, >35 kg/m^2), alcohol intake (0, 0.1–4.9, 5–9.9, >10 g/d), UV flux (quintiles), postmenopausal hormone use (premenopausal, postmenopausal

never, past, or current use), smoking history (never, past, current), history of type 2 diabetes, cardiovascular disease, and history of any of the following immune-mediated diseases: Crohn disease or ulcerative colitis, multiple sclerosis, psoriasis, polymyositis, rheumatoid arthritis, Sjögren syndrome, scleroderma, and vitiligo.

The history of atopic dermatitis (eczema) was available only in the NHSII cohort, and was included as an additional covariate in that analysis. All statistical analyses were conducted using SAS (version 9.4; SAS Institute, Cary, NC).

CONFLICT OF INTEREST

AAQ serves as a consultant for Abbvie, Amgen, Centers for Disease Control, Janssen, Merck, Novartis, and Pfizer, and is an investigator for Amgen, Regeneron, and Sanofi. JMT, MKP, and EC state no conflict of interest.

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SUPPLEMENTARY MATERIAL

Supplementary material is linked to the online version of the paper at www.jidonline.org, and at https://doi.org/10.1016/j.jisp.2017.10.007.

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