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Racial and Ethnic Disparities in Atopic Dermatitis

Jonathan I. Silverberg

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Abstract Atopic dermatitis (AD) is the most common chronic inflammatory skin disorder in the USA and worldwide. There are significant differences in the epidemiology, phenotype, and genetics of AD in different racial and ethnic subgroups. In particular, patients of African descent have been found to have higher prevalence of AD in the USA and England, whereas Hispanic Americans have lower prevalence of AD. Further, African Americans have been found to have more severe disease and more comorbid allergic disorder. Patients of African descent appear to have different genetic risk factors, with less loss-of-function filaggrin 1 mutations and more filaggrin 2 mutations than patients of Northern or Eastern European origin. Finally, AD has different clinical phenotypes in African Americans, which clinicians need to recognize for the proper diagnosis and assessment of AD.

Keywords Atopic dermatitis · Eczema · Race · Ethnicity · African American/Black · Hispanic · Prevalence · Severity · Genetics · Phenotype · Morphology · Distribution · Allergic disease · Asthma · Hay fever · Food allergy

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J. I. Silverberg (✉)
Department of Dermatology, Northwestern University Feinberg School of Medicine, Suite 1600 676 N St Clair Ave, Chicago, IL 60611, USA
e-mail: JonathanISilverberg@Gmail.com

J. I. Silverberg
Department of Preventive Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL 60611, USA

J. I. Silverberg
Department of Medical Social Sciences, Northwestern University Feinberg School of Medicine, Chicago, IL 60611, USA

Abbreviations

AD	Atopic dermatitis
NSCH	National Survey of Children's Health
NHIS	National Health Interview Survey
NHANES	National Health and Nutrition Examination Survey
ISAAC	International Study of Asthma and Allergies in Childhood
FLG	Filaggrin
NMF	Natural moisturizing factor
IgE	immunoglobulin E
Th2	T helper 2

Introduction

Atopic dermatitis (AD) is a chronic, intermittent inflammatory skin disease that is characterized by intensely pruritic ill-demarcated erythematous patches and plaques. There are a number of racial and ethnic differences of the prevalence, severity, genetics, phenotype, and comorbidities of AD. This is of particular importance with the growing diversification of the population in the USA and other developed countries. It is estimated that Blacks and Hispanics will represent 13.4 and 19.1 % of the US population by the year 2020, respectively [1]. The goal of this manuscript is to review the racial and ethnic differences of AD.

Prevalence of Eczema in Children

Several US population-based studies of AD prevalence in childhood have recently been performed. Analysis of the 102,353 children from the 2003 National Survey of Children's Health (NSCH) found 10.7 % prevalence of childhood AD in the USA, with significant variation between

states and districts, ranging from 8.7 to 18.1 % [2•]. Subsequently, analysis of 91,642 children from the 2007 NSCH found 12.2 % prevalence of childhood AD [3•], suggesting that the prevalence of childhood AD increased in the interval period. Indeed, analysis of data from the National Health Interview Survey (NHIS) found that the prevalence of childhood eczema continuously increased between 1997 and 2011 [4].

The International Study of Asthma and Allergies in Childhood (ISAAC) used a standardized methodology to determine the international prevalence of AD [5]. There was a wide variation in prevalence values worldwide, from 0.9 % in India to 22.5 % in Ecuador at ages 6–7 years and from 0.2 % in China to 24.6 % in Colombia at ages 13–14 years.

Prevalence of Eczema in Adults

A recent study of a registry including 7157 children and adolescents with AD demonstrated that >80 % had persistent symptoms and were using medication to treat their AD even in adulthood [6]. This suggests that AD may be more common in adults than what was previously recognized. Indeed, studies of the 2010 and 2012 NHIS including 27,157 and 34,613 adults, respectively, found 10.2 and 7.2 % 1-year prevalence of eczema in the USA. Similarly, a study of the 2005–2006 NHIS including 4972 adults found 7.4 % lifetime prevalence of eczema [7]. International studies of AD in adults found prevalence ranging from 2.0 to 6.9 % [8–12]. The wide variation of prevalence is likely attributable to a combination of methodological and regional differences.

Background for Racial and Ethnic Disparities in AD

The varying prevalence values suggest that there are multiple environmental risk factors that occur in different regions. Such risk factors include climate [3•], residence in an urban area [2], water hardness and increased water exposure [13], early-life infectious exposures [14, 15], diet [16], obesity [17–20], and skin care practices [21]. Many of these risk factors differentially impact some sociodemographic groups. For example, previous studies found higher consumption of Western diet [22] and obesity [23] and less early-life vaccination [24, 25] in African Americans/Blacks than in Caucasians. Lower water quality is more likely in areas of greater poverty and lower socioeconomic status [26]. It is possible that racial and ethnic differences with respect to the above risk factors contribute toward disparities in AD. In addition, previous studies found that Black subjects had lower levels of skin ceramides than Asians and Caucasians [27] and higher levels of transepidermal water loss than Caucasians [28]; both of which may contribute toward AD [29, 30].

Racial and Ethnic Differences of Eczema Prevalence

Several recent US population-based studies have demonstrated differences in the prevalence of eczema in some racial and ethnic groups, suggesting that African Americans/Blacks have significantly higher prevalence of eczema compared with Whites [3•, 19, 31, 32]. In contrast, these studies also found that children of Hispanic origin had significantly lower prevalence of eczema [3•, 19, 31, 32]. A recent meta-analysis of 264,326 children and adolescents from NSCH 2003–2004 and 2005–2006, NHIS 2008–2012, and NSCH 2003–2004 and 2007–2008 found that African Americans/Blacks had higher odds of eczema (pooled odds ratio 1.574, 95 % confidence interval 1.573–1.575) and Hispanics had lower odds of eczema (0.767, 0.766–0.767) compared with Whites [33]. Several older studies in the USA and England also reported higher prevalence of childhood eczema in African Americans, Afro-Caribbeans, and Blacks [34–36].

Birthplace is another important consideration when examining the epidemiology of childhood AD and differences of AD prevalence across race/ethnicity. Given that AD starts in many patients within their first 6–12 months of life, early-life exposures likely play an important role in childhood AD. Silverberg et al. studied 91,642 children from the 2007–2008 NSCH and found that foreign-born American children had dramatically lower rates of eczema (as well as asthma, hay fever, and food allergy) than US-born American children [37•]. However, foreign-born children who resided in the USA for 10 years or more had significantly higher odds of eczema and allergic disease than those who lived in the USA for a shorter period of time [37•]. This observation was true in all racial and ethnic groups, including African Americans/Blacks and Hispanic Americans. Of note, the prevalence of eczema in US-born Hispanic Americans (10.7 %) was similar to that of US-born Whites (12.1 %), whereas US-born African Americans had considerably higher prevalence (20.2 %) [37•]. Thus, foreign birthplace and perhaps lack of acculturation might be the major protective factor against childhood AD in a subset of Hispanic Americans.

However, the role of race and ethnicity in the prevalence of adult eczema is less clear. A recent meta-analysis of 83,511 adults from the 2010 and 2012 NHIS and the 2003–2004 and 2005–2006 NHANES found that African Americans/Blacks, Hispanics, and Asians all had significantly lower odds of eczema compared with Caucasians/Whites [33]. One might speculate that there are phenotypic differences of disease, such that AD may "burn out" more in African Americans/Blacks than in Whites. However, in the abovementioned registry-based study of AD persistence in children and adolescents with AD found that Whites were more likely to have a 6-month disease-free period than other racial and ethnic groups [6]. Thus, it seems more likely that the lower prevalence of adult AD in racial and ethnic minorities is related to other

factors, such as differences with respect to adult-onset disease and under-diagnosis secondary to decreased access to primary and specialist care in minority patients.

Racial Differences of AD Severity

Several studies have also demonstrated racial and ethnic differences with respect to AD severity. A study of 79,667 children and adolescents from the NSCH found in bivariate analyses that African Americans/Blacks and Hispanics were more likely to report moderate-to-severe eczema than Whites [38•]. However, in multivariate analyses, eczema severity was significantly associated with lower household income, but not race/ethnicity [38•]. This suggests that socioeconomic status plays an important role in eczema severity and may underlie the observed racial differences of eczema severity.

This observation of racial/ethnic disparities in eczema severity is reminiscent of those observed in asthma. Studies of racial and ethnic disparities in asthma found that African Americans/Black have worse asthma outcomes and Hispanics have lower quality of life secondary to asthma [39]. African-American/Black children were also found to use preventive medications for asthma less often than White or Hispanic children [40] and were more likely to have lower health literacy [39]. Thus, racial/ethnic disparities also appear to occur in the severity of allergic disease.

Racial Differences of the Genetics of AD

Filaggrin (FLG) is broken down into natural moisturizing factor (NMF) in the stratum corneum and plays an integral role in skin barrier function [41]. FLG loss-of-function gene mutations lead to a deficiency of NMF [42] and xerosis in AD [43]. Multiple FLG mutations have been identified and shown to be a risk factor for AD [44, 45]. A study found that FLG mutations are detected in 27.5 % of White and only 5.8 % of African-American children with AD [46••]. A follow-up study from the same group demonstrated common loss-of-function mutations of the filaggrin 2 gene in African Americans, which were not present in patients of Northern and Western European ancestry; children with FLG2 loss-of-function mutations were less likely to be symptom free over time [47•]. A study of 18 African-American children with AD and ichthyosis vulgaris and 17 African-American non-atopic controls found that only 22.2 % of those with AD and 5.9 % of controls were heterozygous for FLG null mutations [48]. Together, these studies suggest that FLG2 may play an important role in AD in African Americans, but that one or more factors other than FLG mutations are responsible for AD in African Americans/Blacks and other patient subsets. Very little is known about the genetics of AD in Hispanics/Latinos in general and Hispanic Americans in particular.

Racial Differences of AD Phenotype

The classical presentations of AD are essentially the same across all racial and ethnic groups. However, there are a number of distinguishing features that occur more commonly in some racial and ethnic groups than others. Erythema in skin of color often appears hyperpigmented or violaceous. A previous study of Nigerian patients with AD found that 54.1 % had lichenoid lesions and 70.3 % had a perifollicular, micropapular rash, on the extensor aspects of the joints [49]. These phenotypic differences may delay the diagnosis and treatment of AD and allow for more severe disease to develop [30, 50]. When the lesions of AD resolve, they can cause persistent dyschromia or pigmentary alterations. These are almost always more pronounced in patients of racial and ethnic groups with darker skin [30].

Racial Differences of Allergic Disease in AD Patients

AD is associated with higher rates of allergic disorders, including asthma, hay fever, and food allergies [51]. These allergic disorders are mediated largely by T helper 2 (Th2)-mediated immune responses and increased levels of immunoglobulin E (IgE) [52]. While the inflammation in AD is also caused largely by Th2, there are similar Th2 responses in AD patients whether they have high IgE levels or not [53]. Thus, IgE does not appear to play a major role in the pathomechanism of AD. Rather, impaired skin barrier function in AD may allow for transcutaneous sensitization to allergens, thereby facilitating the development of systemic allergic disease. A recent study of 619 3-month-old infants who were exclusively breastfed elegantly demonstrated that AD predisposed to higher rates of food sensitization, including egg, cow's milk, and peanuts [54]. Moreover, moderate-to-severe AD was associated with an even higher risk of food sensitization than mild AD [54]. Some authors have proposed the "atopic march," where AD appears first in early life, followed by asthma and hay fever at later stages of life [55]. Given the abovementioned studies demonstrating increased prevalence and severity of AD in African Americans, it is logical that African-American/Black children with AD have greater risk for allergic disease.

Indeed, a birth cohort follow-up study in the Detroit metropolitan area found that African-American children at age 2 years were significantly more likely to have multiple positive IgE-specific tests; this group was also the most likely to have a diagnosis of AD [56]. Otherwise, little is known about the differential effects of AD on the development of allergic

disease in African Americans/Blacks or other racial/ethnic subsets of patients.

Future Research

There is a growing body of epidemiological, clinical, and genetic evidence demonstrating racial and ethnic differences of AD. Yet, little is known about the clinical course and response to therapy in racial and ethnic minorities. A recent systematic review found that very few studies of systemic therapy in AD examined treatment efficacy in African Americans, most did not even document the racial/ethnic breakdown of their cohorts, and *none* of them were designed to identify the most effective therapies in African and Hispanic Americans [57]. Future clinical and therapeutic studies must include adequate representation of African Americans and other racial/ethnic subgroups in their cohorts. More well-designed prospective studies are needed to establish evidence-based guidelines for the evaluation and management of AD in all racial and ethnic subgroups.

Compliance with Ethics Guidelines

Conflict of Interest JI Silverberg declares no conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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