The Clinical Diversity of Atopic Dermatitis

Karishma Daftary, MD; Raj Chovatiya, MD, PhD, MSci

PRACTICE POINTS
- Social determinants of health play a central role in observed racial and ethnic differences in studies of atopic dermatitis (AD) in patients with skin of color.
- Prurigo nodules, lichenoid papules, perifollicular papules, nummular lesions, and psoriasiform lesions are among the diverse lesion morphologies seen with AD.
- Key signs of cutaneous inflammation and lesional severity, including erythema, may present differently in darker skin tones and contribute to underestimation of severity.
- Postinflammatory dyspigmentation is common among patients with skin of color, and treatment can substantially improve quality of life.

Atopic dermatitis (AD) is a common chronic inflammatory skin condition associated with diverse cutaneous presentations. Differences in clinical phenotypes in skin of color (SOC) patients with AD have been previously noted in race-based analyses. We conducted a narrative review to better characterize the clinical diversity of AD and understand these differences in the context of race, ethnicity, and SOC. Notable racial and ethnic differences in clinical phenotypes have been observed; however, these analyses often are limited by deeper understanding of the true causative factors driving observed differences. Dermatologists should be familiar with the heterogeneity of AD lesional morphology and inflammation severity across all skin types.

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heterogeneity of the US population. Overgeneralization of racial and ethnic categories may dull or obscure true differences among populations.\(^7\)

From an evolutionary perspective, skin pigmentation represents the product of 2 opposing clines produced by natural selection in response to both need for and protection from UV radiation across latitudes.\(^8\) Defining SOC is not quite as simple. Skin of color often is equated with certain racial/ethnic groups, or even binary categories of Black vs non-Black or White vs non-White. Others may use the Fitzpatrick scale to discuss SOC, though this scale was originally created to measure the response of skin to UVA radiation exposure.\(^9\) The reality is that SOC is a complex term that cannot simply be defined by a certain group of skin tones, races, ethnicities, and/or Fitzpatrick skin types. With this in mind, SOC in the context of this article will often refer to non-White individuals based on the investigators’ terminology, but this definition is not all-encompassing.

Historically in medicine, racial/ethnic differences in outcomes have been equated to differences in biology/genetics without consideration of many external factors.\(^10\) The effects of racism, economic stability, health care access, environment, and education quality rarely are discussed, though they have a major impact on health and may better define associations with race or an SOC population. A discussion of the structural and social determinants of health contributing to disease outcomes should accompany any race-based guidelines to prevent inaccurately pathologizing race or SOC.\(^10\)

Within the scope of AD, social determinants of health play an important role in contributing to disease morbidity. Environmental factors, including tobacco smoke, climate, pollutants, water hardness, and urban living, are related to AD prevalence and severity.\(^11\) Higher socioeconomic status is associated with increased AD rates,\(^12\) yet lower socioeconomic status is associated with more severe disease.\(^13\) Barriers to health care access and suboptimal care drive worse AD outcomes.\(^14\) Underrepresentation in clinical trials prevents the generalizability and safety of AD treatments.\(^15\) Disparities in these health determinants associated with AD likely are among the most important drivers of observed differences in disease presentation, severity, burden, and even prevalence—more so than genetics or ancestry alone—yet this relationship is poorly understood and often presented as a consequence of race. It is critical to redefine the narrative when considering the heterogeneous presentations of AD in patients with SOC and acknowledge the limitations of current terminology when attempting to capture clinical diversity in AD, including in this review, where published findings often are limited by race-based analysis.

Epidemiology
The prevalence of AD has been increasing over the last few decades, and rates vary by region. In the United States, the prevalence of childhood and adult AD is 13% and 7%, respectively.\(^16,18\) Globally, higher rates of pediatric AD are seen in Africa, Oceania, Southeast Asia (SEA), and Latin America compared to South Asia, Northern Europe, and Eastern Europe.\(^19\) The prevalence of AD varies widely within the same continent and country; for example, throughout Africa, prevalence was found to be anywhere between 4.7% and 23.3%.\(^20\)

Lesion Morphology
Although AD lesions often are described as pruritic erythematous papules and plaques, other common morphologies in SOC populations include prurigo nodules, lichenoid papules, perifollicular papules, nummular lesions, and psoriasiform lesions (Table). Instead of applying normative terms such as classic vs atypical to AD morphology, we urge clinicians to be familiar with the full spectrum of AD skin signs.

**Prurigo Nodules**—Prurigo nodules are hyperkeratotic or erosive nodules with severe pruritus, often grouped symmetrically on the extensor surfaces of the arms, legs, and trunk (Figure 1).\(^14,21\) The skin between lesions usually is unaffected but can be dry or lichenified or display postinflammatory pigmented changes.\(^14\) Prurigo nodules are common. In a study of a cohort of patients with prurigo nodularis (N=108), nearly half (46.3%) were determined to have either an atopic predisposition or underlying AD as a contributing cause of the lesions.\(^21\)

Prurigo nodules as a phenotype of AD may be more common in certain SOC populations. Studies from SEA have reported a higher prevalence of prurigo nodules among patients with AD.\(^28\) Although there are limited formal studies assessing the true prevalence of this lesion type in African American AD patients in the United States, clinical evidence supports more frequent appearance of prurigo nodules in non-White patients.\(^29\) Contributing factors include suboptimal care for AD in SOC populations and/or barriers to health care access, resulting in more severe disease that increases the risk for this lesion type.\(^14\)

**Lichenoid Papules**—Papular lichenoid lesions often present on the extensor surfaces of the arms and legs in AD (Figure 2).\(^22\) In a study of Nigerian patients with AD (N=1019), 54.1% had lichenoid papules.\(^24\) A systematic review of AD characteristics by region similarly reported an increased prevalence of this lesion type in African studies.\(^28\) Lichenoid variants of AD have been well described in SOC patients in the United States.\(^25\) In contrast to the lesions of lichen planus, the lichenoid papules of AD usually are round, rarely display koebnerization, do not have Wickham striae, and predominantly are located on extensor surfaces.

**Perifollicular Papules**—Perifollicular accentuation—dermatitis enhanced around hair follicles—is a well-described lesional morphology of AD that is noted in all racial/ethnic groups (Figure 3).\(^22\) In fact, perifollicular accentuation is included as one of the Hanifin and Rajka...
minor criteria for AD. Studies performed in Nigeria and India showed perifollicular accentuation in up to 70% of AD patients. In a study of adult Thai patients (N=56), follicular lesions were found more frequently in intrinsic AD (29%) compared with extrinsic AD (12%).

**Nummular and Psoriasiform Lesions**—Nummular lesions may be red, oozing, excoriated, studded with pustules and/or present on the extensor extremities (Figure 4). In SOC patients, these lesions often occur in areas where hyperpigmentation is noted. Studies in the United States and Mexico demonstrated that 15% to 17% of AD patients displayed nummular lesions. Similar to follicular papules, nummular lesions were linked to intrinsic AD in a study of adult Thai patients.

Psoriasiform lesions show prominent scaling, lichenification, and clear demarcation. It has been reported that the psoriasiform phenotype of AD is more common in Asian patients, though this is likely an oversimplification. The participants in these studies were of Japanese and Korean ancestry, which covers a broad geographic region, and the grouping of individuals under a heterogeneous Asian category is unlikely to convey generalizable biologic or clinical information. Unsurprisingly, a systematic review of AD characteristics by region noted considerable phenotypical differences among patients in SEA, East Asia, Iran, and India.

### Diverse Features of Atopic Dermatitis

<table>
<thead>
<tr>
<th>Type</th>
<th>Characteristics</th>
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<tr>
<td><strong>Morphology</strong></td>
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<tr>
<td>Prurigo nodules</td>
<td>Hyperkeratotic or erosive nodules associated with severe underlying pruritus; often found on the extensor surfaces of arms, legs, and trunk</td>
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<tr>
<td>Lichenoid papules</td>
<td>Flat-topped, nonviolaceous but often erythematous papules; usually found on the extensor surfaces of arms and legs</td>
</tr>
<tr>
<td>Perifollicular papules</td>
<td>Dermatitis enhanced around hair follicles</td>
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<tr>
<td>Nummular lesions</td>
<td>Red, oozing, excoriated, coin-shaped plaques often studded with pustules; may occur in areas where hyperpigmentation is noted</td>
</tr>
<tr>
<td>Psoriasiform lesions</td>
<td>Scaling, lichenified, and clearly demarcated elevated plaques</td>
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<tr>
<td><strong>Markers of severity</strong></td>
<td></td>
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<tr>
<td>Erythema</td>
<td>May appear red, maroon, violaceous, or brown</td>
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<tr>
<td>Erythroderma</td>
<td>Erythema on at least 90% of the total body surface area; often spares the palms and soles</td>
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<tr>
<td>Excoriation</td>
<td>Often a predominant finding on physical examination occurring secondary to itch</td>
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<tr>
<td>Lichenification</td>
<td>Leathery, elevated appearance with exaggerated skin lines</td>
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<tr>
<td>Xerosis</td>
<td>Dry skin, often with scaling</td>
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<tr>
<td>Postinflammatory dyspigmentation</td>
<td>Hyperpigmented and hypopigmented macules and patches</td>
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Dermatological training must adequately teach physicians to recognize erythema across all skin tones.37

Erythroderma (also known as exfoliative dermatitis) is rapidly spreading erythema on at least 90% of the total body surface area, often sparing the palms and soles.32 Erythroderma is a potentially life-threatening manifestation of severe AD. Although erythroderma may have many underlying causes, AD has been reported to be the cause in 5% to 24% of cases,38 and compared to studies in Europe, the prevalence of erythroderma was higher in East Asian studies of AD.28

Excoriation and Pruritus—Pruritus is a defining characteristic of AD, and the resulting excoriations often are predominant on physical examination, which is a key part of severity scores. Itch is the most prevalent symptom among patients with AD, and a greater itch severity has been linked to decreased health-related quality of life, increased mental health symptoms, impaired sleep, and decreased daily function.39,40 The burden of itch may be greater in SOC populations. The impact of itch on quality of life among US military veterans was significantly higher in those who identified as non-White ($P$=.05).41 In another study of US military veterans, African American individuals reported a significantly higher emotional impact from itch ($P$<.05).42

Lichenification—Lichenification is thickening of the skin due to chronic rubbing and scratching that causes a leathery elevated appearance with exaggerated skin lines.27 Lichenification is included as a factor in common clinical scoring tools, with greater lichenification indicating greater disease severity. Studies from SEA and Africa suggested a higher prevalence of lichenification in AD patients.28 A greater itch burden and thus increased rubbing/scratching in these populations may contribute to some of these findings.42,43

Xerosis—Xerosis (or dry skin) is a common finding in AD that results from increased transepidermal water loss due to a dysfunctional epidermal barrier.44 In a systematic review of AD characteristics by region, xerosis was among the top 5 most reported AD features globally in all regions except SEA.28 Xerosis may be more stigmatizing in SOC populations.
populations because of the greater visibility of scaling and dryness on darker skin tones.1

Postinflammatory Dyspigmentation—Postinflammatory pigment alteration may be a consequence of AD lesions, resulting in hyperpigmented and hypopigmented macules and patches. Patients with AD with darker skin tones are more likely to develop postinflammatory dyspigmentation.26 A study of AD patients in Nigeria found that 63% displayed postinflammatory dyspigmentation.35 Dyschromia, including postinflammatory hypopigmentation, is one of the most common reasons for SOC patients to seek dermatologic care.46 Postinflammatory pigment alteration can cause severe distress in patients, even more so than the cutaneous findings of AD. Although altered skin pigmentation usually returns to normal over weeks to months, skin depigmentation from chronic excoriation may be permanent.25 Appropriately treating hyperpigmentation and hypopigmentation in SOC populations can greatly improve quality of life.47

Conclusion

Atopic dermatitis is a cutaneous inflammatory disease that presents with many clinical phenotypes. Dermatologists should be trained to recognize the heterogeneous signs of AD present across the diverse skin types in SOC patients. Future research should move away from race-based analyses and focus on the complex interplay of environmental factors, social determinants of health, and skin pigmentation, as well as how these factors drive variations in AD lesional morphology and inflammation.

REFERENCES


