Epidemiology, Diagnosis, and Treatment of Atopic Dermatitis in the Developing Countries of Asia, Africa, Latin America, and the Middle East: A Review

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ABSTRACT

Atopic dermatitis (AD), the leading cause of skin-related burden of disease worldwide, is increasing in prevalence in developing countries of Asia, Africa, Latin America, and the Middle East. Although AD presents similarly across racial and ethnic groups as chronic and relapsing pruritic eczematous lesions, some features of the disease may be more or less prominent in patients with darker skin. Despite a similar presentation, consistent diagnostic criteria and consistent treatment guidelines are lacking. Because of these and other challenges, adherence to treatment guidelines is difficult or impossible. Previous studies have stated that many patients with AD receive ineffective or inappropriate care, such as oral antihistamines, oral corticosteroids, or traditional medicines, if they are treated at all; one study showed that approximately one-third of patients received medical care for their dermatologic condition; of those, almost three-quarters received inappropriate or ineffective treatment. In addition, other challenges endemic to developing countries include cost, access to care, and lack of specialists in AD. Furthermore, most of the available diagnostic criteria and treatment guidelines are based on European and North American populations and few clinical trials report the racial or ethnic makeup of the study population. Drug pharmacokinetics in varying ethnicities and adverse effects in different skin physiologies are areas yet to be explored. The objective of this review is to describe the diagnosis, treatment, and management of AD in developing countries in Asia, Africa, Latin America, and the Middle East; to discuss the differences among the countries; and to establish the unmet needs of patients with AD in them. The unmet medical need for treatment of AD in developing countries can be addressed by continuing to train medical specialists, improve...
access to and affordability of care, and develop new and effective treatments. **Funding** Pfizer Inc.

**Keywords:** Africa; Asia; Atopic dermatitis; Developing countries; Latin America; Middle East; Unmet medical need

**INTRODUCTION**

Atopic dermatitis (AD) is a chronic, relapsing-remitting skin disease characterized by pruritic eczematous lesions [1], and it is the leading cause of skin-related burden of disease globally [2]. The pathogenesis of AD is multifactorial and includes genetic factors, which have been shown to vary across racial groups [3–5]. The pathogenesis of AD also depends on environmental factors; as a result, there are wide variations in epidemiology from country to country [5, 6]. Although it seems to have leveled off in developed countries, AD prevalence appears to be increasing in developing countries [7], likely because of increasing urbanization, pollution, Western diet consumption, and obesity [6]. Among 13- to 14-year-old adolescents in the International Study of Asthma and Allergies in Childhood (ISAAC) Phase 3, AD prevalence for Africa and Latin America was high at 12–14% and 6–10%, respectively, whereas for Asian-Pacific countries, the Eastern Mediterranean region, and the Indian subcontinent values were lower at 3–6%; among 6- to 7-year-old children, AD prevalence for Asian-Pacific countries, Africa, and Latin America was high at approximately 10%, whereas values for the Eastern Mediterranean region and Indian subcontinent were lower at 3–5% [8]. Likewise, prevalence in the first 2 years of life was also high at 7–27% in Asian-Pacific countries, including South Korea [9], China [10], Singapore [11], Malaysia [12], and Taiwan [13–15]. This review presents the diagnosis, treatment, and management of AD in developing countries in Asia, Africa, Latin America, and the Middle East. We discuss the differences in epidemiology, diagnosis, and treatment among the countries to establish the unmet needs of patients with AD living in these countries. This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

**CLINICAL PRESENTATION**

Overall, AD presents similarly across racial and ethnic groups as chronic or relapsing pruritic eczematous skin lesions; however, some features may be more or less prominent in patients with darker skin. Erythema is often less obvious in patients with darker skin and may appear reddish-blue or purple (violaceous) rather than red [5, 16]. Perifollicular accentuation, papulation, scaling, lichenification, and pigmentary changes may also be more prominent in patients with darker skin [5, 16, 17]. In addition, Asian populations demonstrate greater helper T cell (Th) 17/Th22 polarization than other populations, leading to a phenotype that combines features of AD and psoriasis [5, 18]. The pattern of lesions may also vary, with patients who have darker skin tones being more likely to present with lesions on extensor surfaces rather than the typical pattern of predominantly flexural lesions [5, 16, 17, 19, 20].

Differences in age of onset, disease severity, and genetic susceptibility may occur across racial and ethnic groups. The prevalence of AD in adults appears to be greater among some Asian populations, potentially because of higher rates of disease onset in adulthood [16, 20–23]. Although their prevalence of the two most common filaggrin (FLG) mutations leading to AD (R501X and 2282del4) is lower, patients of African descent appear to be at greater risk for severe AD [16, 17]. Other studies have reported the prevalence of different FLG mutations in Asian patients (S1695X, Q1701X, Q1745X, Y1767X, Q1790X, S2554X, S2889X, S3296X, 3222del4, S1515X, Q2417X, and K4022X) and Middle Eastern patients (S417S and D1921N, among others) [24, 25]. Pruritus may be more severe in patients with darker skin [17, 19, 26, 27]. It must be noted, however, that many of the available data on differences in clinical presentations are based on data from...
patients of African descent living in the US or Europe, not in developing countries.

**DIAGNOSTIC CRITERIA**

Hanifin and Rajka diagnostic criteria [28] and the UK Working Party’s diagnostic criteria [29] have both been used to diagnose AD in Chinese [30, 31], Taiwanese [32], Indian [33], and South African [34] patients (Table 1). However, in a survey of Southeast Asian dermatologists, all Indonesian respondents (100%) were familiar with the UK Working Party’s diagnostic criteria, whereas respondents from Malaysia (73%), Singapore (75%), or Thailand (90%) were more familiar with the Hanifin and Rajka criteria, but less than half of the Filipino and Vietnamese respondents (5–39%) were familiar with either set of criteria [35].

Some population-specific diagnostic criteria have been proposed (Table 1). Liu et al. [22] proposed criteria for the diagnosis of AD in Chinese adults and adolescents that are based on only two features—persistent or recurrent symmetrical AD for > 6 months with one or both of the following: (1) personal or familial history of atopy and/or (2) elevated total serum immunoglobulin (Ig) E level, positive allergen-specific IgE, and/or eosinophilia. In an earlier iteration, Kang and Tian [36] proposed criteria for diagnosis in Chinese patients (regardless of age) based on the presence of two basic features (chronic or chronically relapsing pruritic dermatitis and personal or family history of atopy) or the first basic feature plus ≥ 3 minor features (onset before 12 years of age; xerosis, ichthyosis, or palmar hyperlinearity; allergic conjunctivitis, food intolerance, immediate skin reactivity, eosinophilia, or elevated serum IgE level; tendency to cutaneous infections or impaired cell-mediated immunity; facial pallor, white dermatographism, or delayed bland; periorbital darkening, perifollicular accentuation, or tendency to nonspecific hand and foot dermatitis). Wisuthsarewong and Viravan [37] proposed and Wanitphakdeedecha et al. [38] validated criteria for the diagnosis of AD in Thai patients older than 13 years based on a history of flexural dermatitis plus ≥ 2 of the following: duration > 6 months, visible flexural dermatitis, and visible dry skin. The Korean Atopic Dermatitis Association [39] proposed the Reliable Estimation of Atopic Dermatitis of ChildHood (REACH) diagnostic criteria for South Korean children 4–12 years of age based on the presence of 2 major features (remitting-relapsing itchy rash in the past 12 months; itchy rash on antecubital/popliteal fossae in the past 12 months) or 1 major feature and ≥ 4 minor features (personal/family history of atopy; itchy rash around/on the eyes, ears, lips, neck, infra-gluteal folds, wrist/ankle joints; or itch when sweating in the past 12 months; unusually dry skin in past 12 months). Last, the South African Childhood Atopic Eczema Working Group [40] proposed criteria for South African children based on the presence of pruritus plus ≥ 3 of the following: flexural dermatitis, previous flexural dermatitis, dry skin, other atopic disease, and/or onset before 2 years of age.

The American Academy of Dermatology has published diagnostic criteria as well [41]. These are largely based on the Hanifin and Rajka criteria [28].

**TREATMENT GUIDELINES**

Treatment guidelines are available for Asian-Pacific countries overall [42, 43] and Taiwan [44], Singapore [45], South Korea [46–48], and India [49–51], specifically; Latin America overall [52] and Mexico [53, 54] and Argentina [55] specifically; South Africa [40, 56, 57]; and the Middle East [58] (Table 2). Unfortunately, no treatment guidelines could be identified for other countries in Africa or the Middle East. It is not clear whether emerging market-specific criteria are preferred by physicians. One survey of South Korean physicians found that 97% of pediatric allergists preferred the South Korea-specific allergy guidelines, whereas dermatologists preferred the South Korean, European, and American dermatology guidelines about equally [59].

All of these treatment guidelines largely reflect the American Academy of Dermatology (AAD) [41, 60–62], the American Academy of Allergy, Asthma, and Immunology (AAAAI)/
| Source                      | Developing country population                                      | Criteria                                | Major features                                                                 | Minor features                    |
|-----------------------------|---------------------------------------------------------------------|-----------------------------------------|---------------------------------------------------------------------------------|-----------------------------------|
| Hanifin and Rajka [28]      | Indian hospitalized, pediatric patients [33]                        | ≥ 3 major PLUS ≥ 3 minor                | Pruritus                                                                        | Xerosis                           |
|                             |                                                                     |                                         | Typical morphology (flexural lichenification or linearity in adults, facial and extensor involvement in infants and children) | Anterior subcapsular cataracts     |
|                             |                                                                     |                                         | Chronic or chronically relapsing dermatitis                                     | Orbital darkening                 |
|                             |                                                                     |                                         | Personal or family history of atopy                                             |                                   |
| UK Working Party [29]       | Chinese patients of all ages [30, 31]; Taiwanese adults [32]; hospitalized Indian pediatric patients [33]; Xhosa-speaking South African children aged 3–11 years [34] | Major PLUS ≥ 3 minor                   | Itchy skin condition (or parental report of scratching or rubbing in a child)  | History of flexural involvement (including cheeks in children < 10 years) |
|                             |                                                                     |                                         |                                                                                | Personal history of asthma or hay fever (or history of atopy in first-degree relative in children < 4 years) |
|                             |                                                                     |                                         |                                                                                | History of a general dry skin in last year                                      |
|                             |                                                                     |                                         |                                                                                | Visible flexural eczema (or eczema involving the cheeks/forehead and extensor surfaces in children aged < 4 years) |
|                             |                                                                     |                                         |                                                                                | Onset < 2 years of age (not used for child aged < 4 years)                        |
| Source | Developing country population | Criteria | Major features | Minor features |
|--------|-----------------------------|----------|---------------|---------------|
| Liu et al. [22] | Chinese adults and adolescents | Major PLUS ≥ 1 minor | Persistent or recurrent symmetrical dermatitis for > 6 months | Personal or family (first-, second-, or third-degree relative) history of atopy | Elevates total serum IgE level, positive allergen-specific IgE, or eosinophilia |
| Kang and Tian [31, 36] | Chinese patients of all ages | Both major ~ OR ~ First major PLUS ≥ 3 minor | Chronic or chronically relapsing pruritic dermatitis (inflammatory eczematous lesions on face and extensor surfaces in infants/children, lichenification of flexural and extensor surfaces in adolescents/adults) | Onset < 12 years of age | Xerosis, ichthyosis, or palmar hyperlinearity |
| Wisuthsarewong and Viravan [37] and Wanitphakdeedecha et al. [38] | Thai adolescents and adults aged ≥ 13 years | Major PLUS ≥ 2 minor | History of flexural dermatitis | Duration > 6 months | Visible flexural dermatitis |
| Korean Atopic Dermatitis Association [39] | Korean children aged 4–12 years | Both major ~ OR ~ 1 major PLUS ≥ 4 minor | Relapsing–remitting itchy rash in past 12 months | Personal or family (father, mother, brothers, or sisters) history of atopy | Intermittent itch, wrinkles, or darkening around the eyes in past 12 months |
| | | | Itchy rash on antecubital/popliteal fossae in past 12 months | Intermittent itch or oozing around the ears in past 12 months | Intermittent chapping or oozing around the lips in past 12 months |
| | | | | Intermittent itch, thickening, or darkening around the neck in past 12 months | Intermittent itch, oozing, or thickening in infragluteal folds in past 12 months |
| | | | | Intermittent itch or oozing around wrist/ankle joints in past 12 months | Unusually dry skin in past 12 months |
| | | | | Itch when sweating in past 12 months | |
American College of Allergy, Asthma, and Immunology (ACAAI) [63], and European guidelines [64, 65], with skin care and hydration, trigger avoidance, topical anti-inflammatory drugs [topical corticosteroids (TCSs) or topical calcineurin inhibitors (TCIs)] as first-line treatment for mild-to-moderate AD; short courses of systemic corticosteroids and phototherapy as second-line treatment for moderate-to-severe AD; and systemic immunosuppressive therapies or biologics if further treatment is necessary for severe AD. However, some do differ in their recommendations regarding TCI use—the Middle Eastern [58] and Latin American guidelines [52], and one of the Mexican [54] (but not the other Mexican [53] or Argentinian [55] guidelines) recommend TCIs as first-line treatment, whereas one of the South African guidelines [57] is silent on this, and the rest recommend TCIs as second-line treatment. Regarding oral antihistamine use, one of the Mexican [54], one of the South Korean [47], and one of the South African [57] guidelines recommend them for pruritus relief; however, the rest only suggest the use of oral antihistamines in the context of other atopic comorbidities or for their sedating effects. Some guidelines also specifically address issues with AD management in tropical and subtropical regions, including the occlusiveness of ointments/emollients and the practicality of wet wrap therapy in hotter, more humid climates [42, 52, 66].

GUIDELINE ADHERENCE/PHARMACOLOGIC TREATMENT UTILIZATION

Adherence to treatment guidelines was quite good regarding topical treatment of AD in surveys of physicians in Southeast Asia; however, adherence to systemic treatments was not as high. The use of emollients for clearance and maintenance was high (98–100% and 86–100%, respectively) among dermatologists surveyed from the Philippines, Thailand, Malaysia, and Singapore but was significantly less likely among dermatologists from Vietnam or Indonesia [35]. The use of topical anti-inflammatory therapies was also quite high, with
| Source       | Step-up therapy                                      | First line          | Second line                  | Third line                                                                 |
|--------------|------------------------------------------------------|---------------------|------------------------------|----------------------------------------------------------------------------|
| Asia–Pacific | Emollients                                           | TCI                 | TCS                          | Rescue therapy (TCS, wraps/soaks, antibiotics)                             |
| [42]         | Trigger avoidance                                    | Proactive/intermittent TCS | TCI                         |                                                                             |
|              | Patient education                                    | NB-UVB phototherapy  | NB-UVB/UVAI phototherapy     |                                                                             |
|              | Rescue therapy (TCS, antihistamines)                 |                     | Infection control            |                                                                             |
| Taiwan [44]  | Emollients                                           | TCI                 | Short-term oral corticosteroid| Systemic immunosuppressant                                                 |
|              | Trigger avoidance                                    | Proactive/intermittent TCS |                      |                                                                             |
|              | Patient education                                    | NB-UVB phototherapy  | NB-UVB/UVAI phototherapy     |                                                                             |
|              | Rescue therapy (TCS, antihistamines)                 |                     | Infection control            |                                                                             |
| Singapore [45]| Gentle skin care                                     | Mild TCS            | Moderate TCS                 | Potent TCS                                                                |
|              | Emollients                                           | TCI                 | Antimicrobials for secondary skin infections |                                                                             |
|              |                                                     |                     | Antimicrobials               |                                                                             |
|              |                                                     |                     | Phototherapy                 |                                                                             |
|              |                                                     |                     | Systemic immunosuppressant   |                                                                             |
| South Korea [46, 47]| Emollients                                        | TCI                 | Wet dressings                | Systemic immunosuppressant                                                 |
|              | Trigger avoidance                                    | TCS                 |                             |                                                                             |
|              | Patient education                                    | Antihistamines       |                             |                                                                             |
|              | Proactive treatment for patients with persistent/frequent flares (intermittent TCI/TCS, psychologic support) | |                             |                                                                             |
| Source          | Step-up therapy                          | Basic treatment                                                                 | First line                           | Second line                         | Third line                             |
|-----------------|------------------------------------------|---------------------------------------------------------------------------------|--------------------------------------|--------------------------------------|----------------------------------------|
| Latin America   | Skin care                                |-emollients                                                                      | TCS                                  | Antihistamines                        | Other oral immunosuppressants          |
| [52]            | Irritant avoidance                       |                                                                                  | TCI                                  | Oral corticosteroid                   |                                        |
|                 | Proactive treatment as needed            |                                                                                  | If patient has allergic sensitization | Phototherapy                          |                                        |
|                 | If patient is sensitized (trigger avoidance, exclusion diet) |                                                                                  | (allergen-specific immunotherapy)    | Cyclosporin                           |                                        |
| South Africa    | Emollients                               |                                                                                  | Potent TCS                           | Oral corticosteroid                   |                                        |
| [56]            | Appropriate general measures            |                                                                                  | Proactive/long-term TCI              | Phototherapy                          |                                        |
|                 | Patient education                        |                                                                                  | Sedating antihistamines              | Systemic immunosuppressant            |                                        |
|                 |                                          |                                                                                  | Rescue therapy (potent TCS)          | Psychotherapeutic intervention        |                                        |
| Middle East     | Emollients                               |                                                                                  | Proactive TCI                        |                                      |                                        |
| [58]            | Patient education                        |                                                                                  | TCS for flares                       |                                      |                                        |
|                 | Trigger avoidance                        |                                                                                  |                                      |                                      |                                        |

*NB-UVB* narrow band ultraviolet B, *TCI* topical calcineurin inhibitor, *TCS* topical corticosteroid, *UVA1* ultraviolet A1
91–100% of respondents prescribing TCSs [35, 59]. The majority (86–90%) of respondents from Singapore, Thailand, and South Korea had used TCIs; however, few (9–24%) of the respondents from Indonesia, Malaysia, or Vietnam had used them, mostly because of a lack of access to these medications (55–67%) [35, 59].

The use of oral antihistamines (86–100%) and oral corticosteroids (67–100%) was quite high [35, 59], despite the lack of recommendations for their use or against it. Single-center studies conducted in India and Pakistan showed that most patients are treated with emollients (95%) and topical anti-inflammatory therapies (75%, nearly all TCSs) [20, 67, 68] in accordance with guidelines. However, 75% of patients received antihistamines [20] and 25–78% received oral corticosteroids, although they were prescribed on a short-term basis [20, 67]. Although treatment guidelines caution against chronic use of systemic corticosteroids, they are used this way quite frequently in Latin America [52].

UTILIZATION OF TRADITIONAL/HERBAL REMEDIES

The Asian-Pacific, Taiwanese, and South Korean guidelines recommend that patients be advised about the lack of high-quality evidence to support the use of traditional/herbal remedies [42–44, 47]. Accordingly, a majority of Southeast Asian dermatologists surveyed do not recommend the use of these alternative treatments [35]. However, in many developing countries, traditional medicine continues to play an important role in meeting healthcare needs [69]. In surveys of South Korean patients with AD, approximately 70% reported using complementary alternative medicine (i.e., bath therapy, dietary therapy, health supplements, massage, traditional Chinese medicine, topical applicants) [70, 71]. In Brazilian AD and Nigerian dermatology populations, the prevalence of use was only slightly less at 64% and 65%, respectively [72, 73].

In areas of limited resources, these remedies are often more accessible and less expensive than pharmacologic treatments; however, their efficacy may be limited and is largely unproven. In fact, only 32% of South Korean users believed that their AD had improved with complementary alternative medicine [71]. A recent Cochrane review failed to find sufficient high-quality evidence to support the use of Chinese herbal medicine [74], and 76% of allergists and dermatologists surveyed in South Korea believe that the lack of evidence for complementary alternative medicine was a barrier to proper AD management. Although traditional/herbal remedies are often perceived as being safer than pharmacologic treatments, they are not without some concerning potential side effects, including liver and kidney toxicity, and are more often subject to contamination [5, 75]. However, the greater use of these alternative treatments observed in older children with long-standing disease [72, 76, 77] and children with more atopic comorbidities/higher IgE levels—although this difference was not significant [76, 77]—may reflect frustration with pharmacologic treatments or fear of using higher doses of pharmacologic treatments for more severe/recalcitrant disease. In fact, approximately one-third of traditional Chinese medicine users (31–36%) use it in combination with corticosteroids or other “Western medicine” [76, 77], possibly in an effort to reduce the need for TCSs [78] (see the Challenges in AD Management section for more information on TCS misuse).

CHALLENGES IN AD MANAGEMENT

Some challenges in AD management are universal. Thus far, no cure exists for AD, and treatment is targeted at symptom management. Currently available treatments for severe AD are costly and require subcutaneous injection (e.g., dupilumab [79]) or associated with significant adverse effects (e.g., systemic corticosteroids [80]). Topical corticosteroids, the mainstay of treatment for mild-to-moderate AD, require complex dosing regimens (i.e., low potency for the face and neck, higher potency for other body areas) [81], are associated with significant adverse effects when used chronically [82], and can lead to hypopigmentation in darker skin
| TCS                  | Hydrocortisone | Desonide furoate | Mometasone furoate | Fluticasone propionate | Triamcinolone acetonide | Betamethasone valerate | Betamethasone dipropionate | Clobetasol propionate |
|---------------------|----------------|------------------|--------------------|------------------------|--------------------------|------------------------|----------------------------|-------------------------|
| **East Asia**       |                |                  |                    |                        |                          |                        |                            |                         |
| China [89]          | ✓              | ✓                | ✓                  | ✓                      |                          |                        |                            | ✓                       |
| Hong Kong [90]      | ✓              | ✓                | ✓                  | ✓                      | ✓                        | ✓                      |                            | ✓                       |
| Indonesia [91]      | ✓              |                  | ✓                  | ✓                      | ✓                        | ✓                      |                            | ✓                       |
| Malaysia [92]       | ✓              | ✓                | ✓                  | ✓                      | ✓                        | ✓                      |                            | ✓                       |
| Philippines [93]    | ✓              |                  | ✓                  | ✓                      | ✓                        | ✓                      |                            | ✓                       |
| Singapore [94]      | ✓              | ✓                | ✓                  | ✓                      | ✓                        | ✓                      |                            | ✓                       |
| South Korea [95]    | ✓              |                  | ✓                  | ✓                      | ✓                        | ✓                      |                            | ✓                       |
| Taiwan [96]         | ✓              | ✓                | ✓                  | ✓                      | ✓                        | ✓                      |                            | ✓                       |
| Thailand [97]       | ✓              | ✓                | ✓                  | ✓                      | ✓                        | ✓                      |                            | ✓                       |
| Vietnam [98]        | ✓              | ✓                | ✓                  | ✓                      | ✓                        | ✓                      |                            | ✓                       |
| **South Asia**      |                |                  |                    |                        |                          |                        |                            |                         |
| Bangladesh [99]     | ✓              |                  | ✓                  |                        |                          |                        |                            | ✓                       |
| India [100]         |                | ✓                | ✓                  |                        |                          |                        |                            | ✓                       |
| Pakistan [101]      | ✓              |                  | ✓                  |                        |                          |                        |                            | ✓                       |
| **Latin America**   |                |                  |                    |                        |                          |                        |                            |                         |
| Argentina [102]     | ✓              |                  | ✓                  |                        |                          |                        |                            | ✓                       |
| Brazil [103]        | ✓              |                  | ✓                  |                        |                          |                        |                            | ✓                       |
| Chile [104]         | ✓              |                  | ✓                  |                        |                          |                        |                            | ✓                       |
| Colombia [105]      | ✓              |                  | ✓                  |                        |                          |                        |                            | ✓                       |
| Mexico [106]        | ✓              |                  | ✓                  |                        |                          |                        |                            | ✓                       |
| Peru [107]          | ✓              |                  | ✓                  |                        |                          |                        |                            | ✓                       |
| TC | Hydrocortisone | Desonide | Mometasone | Fluticasone | Triamcinolone | Betamethasone | Clobetasol | Pimecrolimus | Tacrolimus | Methotrexate | Dupilumab |
|----|----------------|----------|------------|-------------|---------------|---------------|------------|--------------|------------|--------------|----------------|
| TCS | TCS | TCS | TCS | TCS | TCS | TCS | TCS | TCS | TCS | TCS | TCS |
| TCS | Venezuela [108] | Egypt [109] | Morocco [110] | Nigeria [111] | South Africa [112] | Tunisia [113] | Middle East | Jordan [114] | Lebanon [115] | Oman [116] | Qatar [117] | Saudi Arabia [118] | Turkey [119] | United Arab Emirates [120] |
| TCS | East Asia [89] | Hong Kong [90] |

\(\Delta\) Adis
| Country       | TCIs | Topical PDE4 inhibitors | Systemic immunosuppressants | Biologics |
|--------------|------|-------------------------|-------------------------------|-----------|
| Indonesia    | ✓    | ✓                       | ✓                             | ✓         |
| Malaysia     | ✓    | ✓                       | ✓                             | ✓         |
| Philippines  | ✓    | ✓                       | ✓                             | ✓         |
| Singapore    | ✓    | ✓                       | ✓                             | ✓         |
| South Korea  | ✓    | ✓                       | ✓                             | ✓         |
| Taiwan       | ✓    | ✓                       | ✓                             | ✓         |
| Thailand     | ✓    | ✓                       | ✓                             | ✓         |
| Vietnam      | ✓    | ✓                       | ✓                             | ✓         |
| Bangladesh   | ✓    | ✓                       | ✓                             | ✓         |
| India        | ✓    | ✓                       | ✓                             | ✓         |
| Pakistan     | ✓    | ✓                       | ✓                             | ✓         |
| Argentina    | ✓    | ✓                       | ✓                             | ✓         |
| Brazil       | ✓    | ✓                       | ✓                             | ✓         |
| Chile        | ✓    | ✓                       | ✓                             | ✓         |
| Colombia     | ✓    | ✓                       | ✓                             | ✓         |
| Mexico       | ✓    | ✓                       | ✓                             | ✓         |
| Peru         | ✓    | ✓                       | ✓                             | ✓         |
| Venezuela    | ✓    | ✓                       | ✓                             | ✓         |
| Egypt        | ✓    | ✓                       | ✓                             | ✓         |

Table 3 continued
### Table 3 continued

| Country                  | Pimecrolimus | Tacrolimus | Crisaborole | Methotrexate | Cyclosporine | Dupilumab |
|--------------------------|--------------|------------|-------------|--------------|--------------|-----------|
| Morocco [110]            | ✓            |            |             | ✓            | ✓            |           |
| Nigeria [111]            | ✓            |            |             | ✓            | ✓            |           |
| South Africa [112]       |             | ✓          |             | ✓            | ✓            |           |
| Tunisia [113]            | ✓            |            |             | ✓            | ✓            |           |
| Middle East              |              |            |             | ✓            | ✓            |           |
| Jordan [114]             | ✓            |            |             | ✓            | ✓            |           |
| Lebanon [115]            | ✓            |            |             | ✓            | ✓            |           |
| Oman [116]               | ✓            |            |             | ✓            | ✓            |           |
| Qatar [117]              | ✓            |            |             | ✓            | ✓            |           |
| Saudi Arabia [118]       | ✓            |            |             | ✓            | ✓            |           |
| Turkey [119]             | ✓            |            |             | ✓            | ✓            |           |
| United Arab Emirates [120]| ✓            |            |             | ✓            | ✓            |           |

All information accessed in 2019

*PDE4* phosphodiesterase 4, *TCIs* topical calcineurin inhibitors, *TCS* topical corticosteroids
These problems have led to corticosteroid phobia among many patients with AD and underuse and/or nonuse of prescribed TCSs [40, 59, 70, 83]. However, in India, most TCSs are available over the counter, which has led to misuse [84, 85]; efforts are underway to curtail this practice by making TCSs available by prescription only [86].

Other challenges are more specific to developing countries. Limited/ineffective healthcare systems [59, 87] and a lack of specialists with training in the management of AD [59, 88] are among the major challenges. In addition, regional differences in availability (Table 3) [89–120] present a challenge, as does the cost of AD treatment [121, 122], especially for newer, more effective treatments [123–125]. Lower socioeconomic status can also have a negative impact on access to care and adherence to treatment [17, 121], and the differences in clinical presentation and symptoms for patients with darker skin tones and different ethnic origins mentioned above may lead to delayed diagnosis and, in turn, more severe disease at diagnosis.

Other challenges arise from the fact that most diagnostic criteria and guidelines have been developed for European and North American populations, and very few clinical studies of dermatologic treatments (11%) conducted outside/not exclusively within the US even report the racial or ethnic makeup of the study population [126]. Although approximately 60% of US-based studies do include such information [126, 127], the applicability to developing countries is, of course, limited because of differences in environment, etc.

The efficacy and safety of several treatments have been assessed in patients living in developing countries (including tacrolimus for patients in China [128], South Korea [129], Thailand [130], and Bangladesh [131]; TCSs for patients in Singapore [132], India [133], and Bangladesh [131]; and methotrexate for patients in Egypt [134]). In one analysis, results from clinical studies of tacrolimus conducted in eight Asian countries (China, Indonesia, South Korea, Malaysia, Philippines, Singapore, Taiwan, and Thailand) were pooled and found to be similar to those observed for studies conducted in the US and Europe [135]. However, differences between racial groups in drug pharmacokinetics and skin physiology may affect treatment response (although to a lesser degree than other factors, such as age and skin barrier function), and the potential for these differences to affect outcomes remains largely unexplored [5].

CONCLUSIONS

Globally, a substantial unmet medical need exists in AD management. This need is magnified in developing countries by many of the factors discussed above and may lead to inadequate or inappropriate treatment. In fact, 15% of patients in one community-based study in Singapore reported receiving no treatment [136]. In another study, only 36% of patients in an area of North India with limited resources sought medical care for their dermatologic condition, and 69% received inappropriate or ineffective treatment according to the authors [137].

Increased training of primary care physicians and specialists, changes in healthcare systems to improve access and affordability of care, and the development of new and more effective treatments will help reduce this unmet need. In addition, innovations in healthcare delivery such as teledermatology [138, 139] and task sharing/shifting [140] may also improve patient care. Patient and caregiver education may also improve AD treatment adherence and clinical outcomes as well as patient and family quality of life in developing countries [141–145].

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