REVIEW

Understanding the Burden of Atopic Dermatitis in Africa and the Middle East

Khalid Abdullah Mohammad Al-Afif · Mohamad Ali Buraik ·

Joerg Buddenkotte · Mohamed Mounir · Robert Gerber ·

Haytham Mohamed Ahmed · Anna M. Tallman · Martin Steinhoff

Abstract: Atopic dermatitis (AD) is a common inflammatory skin disease characterized by intensely pruritic lesions. The prevalence of atopic dermatitis is increasing in developing regions, including Africa and the Middle East. However, these regions are underrepresented in the dermatology literature, and a better understanding of the growing burden of atopic dermatitis in Africa and the Middle East is necessary. Herein, we summarize current knowledge on atopic dermatitis epidemiology, disease burden, and treatment options in Africa and the Middle East, highlighting the unmet needs of patients in these regions. With these needs in mind, we provide clinical recommendations for appropriate management of atopic dermatitis in Africa and the Middle East.
Funding: Pfizer Inc.
Plain Language Summary: Plain language summary available for this article.

Mohamed Mounir and Anna M. Tallman: Former Pfizer employees.

K. A. M. Al-Afif (✉)
Al Noor Specialist Hospital, Mecca, Saudi Arabia
e-mail: kh_alafif5@yahoo.com

M. A. Buraik
Department of Dermatology, King Fahd Central Hospital, Jizan, Saudi Arabia

J. Buddenkotte · M. Steinhoff
Department of Dermatology and HMC Translational Research Institute, Hamad Medical Corporation, Doha, Qatar

M. Mounir
Departments of Inflammation and Immunology and Emerging Markets, Pfizer Inc, Dubai, United Arab Emirates

R. Gerber
Departments of Outcomes and Evidence and Statistics, Pfizer Inc, Groton, CT, USA

H. M. Ahmed
Departments of Inflammation and Immunology and Emerging Markets, Pfizer Inc, Jeddah, Saudi Arabia

A. M. Tallman
Global Medical Affairs, Pfizer Inc, New York, NY, USA

M. Steinhoff
Weill Cornell Medicine-Qatar, Doha, Qatar

M. Steinhoff
Qatar University, Doha, Qatar

M. Steinhoff
Department Of Dermatology, Weill Cornell University, New York, NY, USA

PLAIN LANGUAGE SUMMARY

This article reviews the epidemiology and disease burden of atopic dermatitis, an inflammatory skin disease, in Africa and the Middle East, and outlines appropriate treatment options for patients in these regions. Defining unmet needs in atopic dermatitis (AD), analyzing current treatment options, and exploring factors that contribute to AD burden in these understudied regions are important as AD is frequently encountered and difficult to manage.

INTRODUCTION

Atopic dermatitis (AD) is a common inflammatory skin disease characterized by the development of highly pruritic eczematous lesions [1, 2]. AD often begins in infancy and follows a chronic, relapsing course [1–3]. Diagnosis is based on patient and family history, as well as clinical characteristics of the disease, and is guided by several sets of diagnostic criteria, most of which derive from the 1980 Hanifin and Rajka criteria [3]. A 2003 update of the Hanifin and Rajka criteria by the American Academy of Dermatology (AAD) established essential, important, and associated features of AD [1, 2]. Essential features include pruritus and eczematous lesions that can be acute (erythema and vesicular eruptions), subacute (ill-defined weepy crusted plaques), or chronic (well-defined, dry lichenified plaques). Skin lesions often show age-specific morphology and distribution patterns [2]. Important features include early onset, dryness, and increased immunoglobulin E (IgE) level (atopy), although about 20% of patients with AD do not have elevated IgE levels [2]. Associated features assist in diagnosis and can include numerous secondary signs such as hyperlinear palms and atypical vascular responses [2]. A diagnosis of AD requires the exclusion of numerous other dermatologic conditions (e.g., scabies, seborrheic dermatitis, contact dermatitis, ichthyoses, cutaneous T cell lymphoma, psoriasis, photosensitivity dermatoses, immunodeficiency disorders, erythroderma of other causes) [2, 4]. Evidence of neuroimmune dysregulation (e.g.,

abnormal levels of interleukin [IL]-31, IL-4, IL-13, brain-derived natriuretic peptide) may further assist in differential diagnosis [5–10].

AD etiology is heterogeneous and complex, involving genetic, environmental, and neuroimmune factors that contribute to skin barrier dysfunction and inflammation [1]. Family history of AD is the strongest risk factor for the condition [1]. Known genetic risk factors include null mutations in the filaggrin (*FLG*) gene that encodes an epidermal structural protein and risk genes in susceptibility loci related to immune mechanisms of AD [1, 11]. Environmental factors such as climate, urban versus rural dwelling, diet, breastfeeding, obesity, and pollution also contribute to AD risk [12]. Cutaneous inflammation, a hallmark of AD, is characterized by processes that include $CD4^+$ cell infiltration and elevated inflammatory cytokines [1]. Recently, neuroimmune risk factors including IL-4, IL-13, and IL-31 have been implicated in AD inflammation and pruritus [5, 6, 8, 13, 14]. IL-31 has also been shown to promote growth of itch-related sensory nerves [15].

Guidelines for AD treatment are similar globally (Table 1) [16–21]. Nonpharmacological treatment primarily focuses on adequate skin care, with regular moisturizer and emollient use recommended to prevent dryness and transepidermal water loss [16–21]. Other nonpharmacological treatments include behavioral interventions [18–20, 22] and stress reduction and psychological counseling [18, 19, 21, 23]. Common behavioral interventions involve identification and avoidance of triggers of itch, such as excessive sweating, wearing of wool fabrics, and food and environmental allergens [18–20, 22]. Topical corticosteroids (TCSs) remain the primary anti-inflammatory treatment option for AD [16, 18–20]. However, topical calcineurin inhibitors (TCIs) may be preferable for treatment of sensitive areas (face, neck, genitals), and they can be used in conjunction with or in place of TCSs for long-term use as steroid-sparing therapies [16, 18–20]. Other therapeutic approaches include ultraviolet therapy and systemic treatments such as antibiotics and broad immunosuppressants (e.g., cyclosporine A, azathioprine, methotrexate, mycophenolate mofetil) [17–21]. Recently

Table 1 Comparison of global guidelines for treatment of atopic dermatitis (AD)

Type of treatment	Emollients and moisturizers	Topical corticosteroids (TCSs)	Topical calcineurin inhibitors (TCIs)	Systemic therapies	Other
AAD [16, 17]	• Moisturizers are essential components of therapy [16]	• For management of AD unresponsive to emollients [16] • May be applied up to twice daily (acute) or intermittently (maintenance) [16] • Duration and location of use should inform potency [16] • Can be used with wet wraps [16]	• For short-term/immediate and long-term treatment and maintenance with or without concurrent TCS [16] • May be preferable to TCS for sensitive skin sites (face, anogenital area, skin folds), in patients unresponsive to TCS, and as steroid-sparing therapy [16]	• Systemic immunomodulatory agents (cyclosporine, azathioprine, methotrexate, mycophenolate mofetil) at minimally effective dose for refractory AD unresponsive to topical and ultraviolet phototherapy [17] • Interferon gamma for AD unresponsive to other systemic therapies and ultraviolet phototherapy [17] • Systemic antibiotics and antiviral agents for infected AD [17] • Sedating antihistamines for sleep loss [17]	• Wet wraps, bleach baths, and intranasal mupirocin (moderate to severe AD) [16] • UV phototherapy as second-line therapy after failure of emollients, TCS, TCI, or as maintenance therapy [17]
AAAAI/ ACAAI [18]	• Moisturizers are first-line therapy	• For management of AD not adequately controlled by moisturizers • Low potency TCS: maintenance therapy • Higher potency TCS: flares • Can be used with wet wraps to increase effectiveness	• For AD on the face, eyelids, and skin folds that is unresponsive to TCS • For treatment and prevention of flares	• Antihistamines for pruritus, vitamin D supplementation • Immunomodulatory agents/ biologics for severe refractory AD • Allergen immunotherapy for patients sensitive to aeroallergen • Systemic antibiotics and antiviral agents for infected AD	• Avoidance of allergens and AD triggers • Diluted bleach baths, tar preparations, and wet wraps • UV phototherapy for recalcitrant AD • Patient education and monitoring of QoL and psychological stress • Hospitalization

Table 1 continued

	Type of treatment				
	Emollients and moisturizers	Topical corticosteroids (TCSs)	Topical calcineurin inhibitors (TCIs)	Systemic therapies	Other
EADV [20, 21]	• Emollients should be used frequently and applied liberally [20]	• Important for acute treatment of AD and to control pruritus; may be used proactively or in conjunction with wet wraps [20]	• Especially recommended for the face, intertriginous sites, anogenital area [20] • May be used proactively and to control pruritus [20]	• Antihistamines for pruritus if TCS and emollients are insufficient [21] • Systemic antibiotics and antiviral agents for infected AD [21] • Cyclosporine or methotrexate for severe AD [21]; azathioprine or mycophenolate mofetil if cyclosporine is ineffective [21] • Dupilumab for moderate to severe AD uncontrolled by topical therapy and where other systemic treatments are inadvisable [21] • Mepolizumab, apremilast, or short-term use of oral glucocorticosteroids in select cases [21] • Alitretinoin for atopic hand eczema [21] • Immunoadsorption, allergen immunotherapy for select patients with severe AD [21]	• Avoidance of allergens and dietary triggers [20] • Childhood vaccination and introduction of diverse complementary foods; breastfeeding if possible for infants [20, 21] • Antiseptic baths for infected AD [20, 21]; thermal balneotherapy for mild to moderate AD [21] • UV phototherapy for chronic AD and pruritus relief [20] • Psychological counseling and educational programs [21]

Table 1 continued

Type of treatment				
	Emollients and moisturizers	Topical corticosteroids (TCSs)	Topical calcineurin inhibitors (TCIs)	Systemic therapies	Other
South Africa [19]	• Moisturizers should be applied frequently	• Short-term application of mild/moderate (face and genital area) or moderate/potent (other areas of the body, flares) strength as monotherapy or in conjunction with other therapies • Can be used with wet wraps to increase effectiveness	• Intermittent application to affected areas as second-line therapy/when TCS is contraindicated (mild AD) or as maintenance therapy (moderate AD)	• Cyclosporine, azathioprine plus systemic corticosteroids, or mycophenolate mofetil for severe, refractory AD • Systemic antibiotics and antiviral agents for infected AD • Sedating antihistamines for moderate AD and acute flares	• Avoidance of inhaled and ingested allergens • Avoidance of irritating clothing and laundry practices • Wet wrap dressings, salt baths, antiseptics • Complementary/ alternative therapies • Short-term UV phototherapy as second-line treatment • Patient education and psychological intervention

AAAAI American Academy of Allergy, Asthma, and Immunology, *AAD* American Academy of Dermatology, *ACAAI* American College of Allergy, Asthma, and Immunology, *EADV* European Academy of Dermatology and Venerology, *QoL* quality of life, *UV* ultraviolet

developed anti-inflammatory medications such as dupilumab injection and crisaborole ointment are thus far approved for treatment of AD in the USA (dupilumab, crisaborole) [24, 25], the European Union (dupilumab) [25], Canada (dupilumab) [26], and Japan (dupilumab) [27]. Crisaborole ointment is a nonsteroidal phosphodiesterase 4 inhibitor for the treatment of mild to moderate AD [28]. Dupilumab is a biologic that targets the IL-4 receptor [24]. While recommendations for crisaborole are not yet included in clinical guidelines documents, dupilumab was recommended in the 2018 European Academy of Dermatology and Venerology (EADV) guidelines update for treatment of moderate to severe AD in patients whose AD is inadequately controlled by topical therapies and for whom other systemic therapy is inadvisable [21].

AD is highly prevalent in developed countries, where prevalence rates seem to have plateaued at 10–20% [1]. However, AD prevalence is increasing in developing countries, including Africa and the Middle East [29, 30]. Although AD is becoming a pressing public health concern in Africa and the Middle East, these regions are underrepresented in the AD literature [31]. Treatment has been hindered by a lack of regionally appropriate diagnostic and research tools and by gaps in knowledge and reporting of AD [31]. An investigation of the nature and underlying causes of growing burden of AD in Africa and the Middle East can help address challenges to medical care in these regions and inform our understanding of AD. In this review, we will explore the epidemiology, etiology, and treatment of AD in the Middle East and Africa and provide recommendations for addressing unmet therapeutic needs in these regions.

OBJECTIVE

We aim to (1) provide an overview of the burden of AD in Africa and the Middle East, (2) outline the unmet need for novel therapeutic options for AD in this part of the world, and (3) offer clinical recommendations for improving the management of atopic disease in Africa and the Middle East.

METHODS

A literature search was conducted using PubMed and Web of Science for articles published in English within the previous 10 years. Search terms included "atopic dermatitis," "Middle East," "Africa," "prevalence," and "treatment." Articles were manually reviewed for relevance, and additional searches were conducted to supplement the narrative where appropriate. Articles referenced throughout the current review include primary articles, clinical guidelines documents, and reviews, with primary articles preferentially referenced where possible. 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.

PREVALENCE

The prevalence of AD varies significantly throughout the world [29]. Historically, the prevalence of AD in Africa and Middle Eastern countries has generally been lower than in Europe and North America, but recent time trends show increasing AD prevalence in the developing world [1, 31]. The most comprehensive global epidemiological data can be sourced from the International Study of Asthma and Allergies in Childhood (ISAAC) [32, 33]. Investigators from ISAAC phase 3, which surveyed more than 1 million schoolchildren throughout the world between 1999 and 2004, estimated the lifetime prevalence of AD in 6- to 7-year-old children to be relatively low in the eastern Mediterranean (7.2%) and high in Africa (23.3%) [32, 33]. The global prevalence for 6- to 7-year-old children was 14.2%. The investigators from ISAAC phase 3 estimated the lifetime prevalence of AD in 13- to 14-year-old children to be moderate in the eastern Mediterranean (10.8%) and in Africa (15.2%). The global prevalence for 13- to 14-year-old children was 12.8%. Prevalence differed between and within countries in the Middle East and Africa.

According to a 2012 systematic review, the prevalence of AD in Africa was increasing [29]. The lifetime prevalence of AD symptoms in 13-

to 14-year-old children approximately doubled in Morocco, South Africa, and Kenya over an approximate 7-year period (1995–2001/2002). In contrast, the prevalence of AD symptoms in 13- to 14-year-old Nigerian children decreased during this period, although this trend may have been impacted by extremely high baseline prevalence. The same review did not find a clear time trend of change in Middle Eastern prevalence, citing studies that indicated increasing (Israel) and decreasing (Kuwait) lifetime prevalence. A 2008 comparison of ISAAC phases 1 (1992–1997) and 3 (1999–2004) found large increases in prevalence (at least two standard errors [SE]) in 13- to 14-year-old children in Kenya and Algeria [30]. Of nine African regions/countries surveyed in both phases, seven had higher lifetime prevalence in phase 3 than in phase 1 among 13–14 year olds. Of the six eastern Mediterranean regions/countries surveyed in both phases, four had higher phase 3 than phase 1 lifetime prevalence in this age group. All four eastern Mediterranean regions/countries surveyed for 6–7 year olds reported higher phase 3 than phase 1 lifetime prevalence.

Regional and ethnic diversity may play a significant role in variable rates of prevalence in the Middle East. For instance, prevalence differs between countries of Semitic (Qatar, Oman, Saudi Arabia) and Persian (Iran) origin, and between urban and rural or desert regions in Iran [34].

IMPACT OF SOCIAL, ENVIRONMENTAL, AND ECONOMIC FACTORS ON THE BURDEN OF ATOPIC DERMATITIS

Many environmental, social, and economic factors relevant to Africa and the Middle East contribute to increasing prevalence and burden of AD (Table 2) [12, 19, 35–49]. Dwelling in urban environments compared with rural environments has been linked to AD in both the Middle East and Africa [34, 37]. In Iran, prevalence of AD is higher in Tehran (17.6%) and

Kerman (9.1%) than in Shahr-e-Kord (2.1%), a western city where a greater proportion of citizens have rural lifestyles [34]. A similar pattern has been observed in Africa, with higher income and more urban countries such as South Africa showing large recent increases in AD prevalence [50]. Within individual African countries, AD risk often follows an urban–rural gradient, with a higher rate of AD in city dwellers than in rural dwellers [37]. Effects of increased socioeconomic status and urbanization on prevalence of AD are thought to stem from factors that include increased air pollution, sedentary lifestyle and diet, and smaller family size [12, 31, 50].

Findings in Africa support the "hygiene hypothesis," which argues that increased prevalence of AD stems, at least in part, from decreased exposure to infection and microorganisms in early childhood [12]. In rural Ethiopia, higher rates of AD have been reported in children with access to piped drinking water than in children who drink river water, an effect attributed to reduced exposure to enteric infections [51]. Helminth (parasitic) infections, which are highly prevalent in Africa, have been shown to promote protection from atopic illness [31]. Results of an analysis of more than 2000 children in Uganda showed that maternal hookworm infection during pregnancy and early childhood infection with *Trichuris trichiura* or hookworm both were negatively associated with AD [37]. Protection may be mediated by regulatory T and B cells, parasite-induced expression of the anti-inflammatory cytokine IL-10, and reduced expression of atopy-associated genes in infected individuals [31]. However, a study in Ethiopian children showed a positive association between intestinal infection with the *Trichuris* parasite and risk for AD [51]. This study also showed a history of malaria to be a predictor of risk for AD [51]. Taken together, this underscores the need for additional research. Other hygiene-related factors associated with increased AD prevalence and burden include reduced pre- and postnatal exposure to farm animals and to dogs, antibiotic exposure, and reduced diversity of gut flora [12].

Table 2 Environmental risk factors for atopic dermatitis (AD)

Factor	Associated effect on AD risk
Urban versus rural dwelling	Increased risk for AD with urban dwelling [12, 19]
Socioeconomic status	Increased risk for allergic sensitization in children with increasing parental socioeconomic status/goods ownership [38]
Education level of parents	Increased risk for allergic sensitization and AD in children with increasing parental education level [38, 51]
Climate	Increased risk for AD in colder climates; decreased risk for AD with UV light exposure [12, 19]
Pollution	Increased risk for AD with exposure to pollution [12] and with maternal exposure to active or passive cigarette smoking during prenatal period [39]
Family size	Increased risk for AD with smaller family size [19]
Personal hygiene, sanitation	Increased risk for AD with better personal hygiene in early childhood [40]; increased risk for allergic sensitization/AD in children with access to sanitation (modern toilets, piped drinking water) [38, 51]
Antibiotic use	Increased risk for AD with antibiotic exposure in prenatal period [39] and during the first year of life [41]; decreased risk with antibiotic exposure after the first year of life [39]
Breastfeeding	Decreased risk for AD in infants with familial history of AD [19]
Farm and animal exposure	Decreased risk for AD with frequent prenatal exposure to farm animals; most protective when compounded with direct exposure [42]; potential decreased risk with postnatal exposure to furry pets, particularly dogs [39, 43, 44]
Intestinal microflora	Decreased risk for AD with greater diversity of gut microflora in infancy [45]; decreased risk for allergic sensitization/AD with colonization favoring lactobacilli and bifidobacteria in infancy or childhood [46–49]

Climate conditions in Africa and the Middle East are also likely contributors to the burden of AD. In Iran and Saudi Arabia, desert conditions are associated with higher burden of AD because high temperatures and low humidity exacerbate dry skin [34, 52]. In Africa, high humidity and temperature promote growth of allergens, including mold [31].

QUALITY OF LIFE

Most available data regarding the impact of AD on patient quality of life (QoL) in the Middle East is from Saudi Arabia. Numerous studies have reported that QoL is significantly affected in Saudi Arabian patients with dermatologic diseases, including AD [53–56]. Abolfotouh et al. reported data from 283 adult Saudi Arabian patients with skin disease who completed the Skindex-16 scale, which assesses QoL across symptom, emotional, and functional domains [53]. They used an Arabic version of Skindex-16 adapted for and validated in Saudi Arabian individuals. The authors found that, of the eight diagnoses represented among patients, eczematous dermatitis was associated with the highest mean symptom domain score, indicating a high physical burden of disease in patients with AD [53]. Another study by Ibrahim Al-Hoqail [54] of adult patients in outpatient dermatology treatment in Saudi Arabia used an Arabic version of the Dermatology Life Quality Index (DLQI), which has shown adequate

validity and reliability in Moroccan patients with psoriasis but has not yet been validated for AD [57, 58]. The DLQI measures the effect of dermatologic disease on numerous aspects of daily life, including physical symptoms, feelings such as embarrassment, activities (social, recreational, work), and personal relationships. Higher scores are associated with poorer QoL. The author found that patients with eczematous dermatitis had the third highest mean DLQI score of eight skin diseases, with only patients who have papulosquamous disorders (not otherwise specified by the authors) and connective tissue/immunological disorders showing poorer QoL [54]. In another study of Saudi Arabian adult and teenaged dermatology outpatients, Ahmed et al. found that most patients with dermatologic disease (79%) experienced low QoL, as measured by the DLQI [56]. The most common dermatologic diagnoses among study patients were acne vulgaris (29.5%), AD (22.3%), vitiligo (20.7%), and psoriasis (6.4%).

Additional data indicate that family QoL is significantly affected when an infant or child has AD in Saudi Arabia [55, 59, 60]. A study of the families of 447 Saudi Arabian infants and children with AD found that only 15 families (3.4%) had normal QoL; most families (66.4%) experienced a moderate impact on QoL [60]. The authors measured QoL with an Arabic version of the Dermatitis Family Impact Questionnaire, which they tested for clarity and feasibility. Results of numerous studies have shown that degree of impairment in QoL of Saudi Arabian families is directly proportional to severity of child disease [55, 59, 60].

QoL data from the remainder of the Middle East are limited. A study conducted in the Sanandaj, Kurdistan province of Iran found that 1- to 6-year-old children with severe AD had significantly lower QoL than the same-age children with moderate AD [61]. The authors reported itching/scratching and sleep problems as the greatest contributors to poor QoL in patients with severe AD.

QoL data from Africa are limited but have been reported for South Africa and Uganda. A 2015 South African qualitative study involving interviews with ten parents of children aged 0–12 years who have AD helped identify detrimental physical, emotional, and social effects of AD to children and families [62]. Consistently reported factors with prominent impact on child QoL included physical discomfort from persistent itching and scratching, low self-esteem, and social isolation. Parents reported fatigue owing to care-related loss of sleep and change in daily routine, as well as emotional burden, including feelings of frustration, stress, and confusion. In another study, 81 Ugandan patients 1.5–75 years of age with pruritus owing to dermatoses, including AD, were surveyed, and the QoL of Ugandan patients was compared with that of German dermatology patients [63]. QoL was measured using a study-specific questionnaire translated by a physician. Ugandan patients were more likely than German patients to experience normal emotional reactions and were less likely to experience adverse emotional reactions in the form of aggressive behavior and loss of drive. The authors reported a trend toward higher frequency of pruritus affecting QoL and self-assessment in German patients than in Ugandan patients. Although this study did not account for disease severity, results suggest that the burden of AD on QoL may be lower in African patients than in European patients. However, additional research is necessary to make informed comparisons between African and European or North American patients.

COMORBIDITIES

In the study measuring QoL of Saudi Arabian patients with skin diseases, Abolfotouh et al. found that 31.4% of patients had comorbidities, the most common being diabetes (43.8%) and hypertension (47.2%) [53]. About 20% of patients reported a comorbid psychiatric condition. Numerous additional studies support a relationship between dermatologic and psychiatric conditions in the Middle East. A 2016 study of 254 teenage and adult Saudi Arabian outpatients with dermatologic conditions, including AD, reported overall prevalence rates for depression, anxiety, and stress of 12.6%, 22.1%, and 7.5%, respectively [56]. The

prevalence rates among the 56 patients with AD were similar: 10.7% (depression), 21.4% (anxiety), and 7.1% (stress). Dermatology patients with poor QoL were 3.5 times more likely to report depression, anxiety, or stress. Women were nearly three times more likely to report at least one negative emotional condition than men, although this was not statistically significant. Another study of 875 Saudi Arabian dermatology patients estimated high overall prevalence of anxiety (29%) and depression (14%) [64]. A cross-sectional study of Iranian dermatology patients reported psychiatric comorbidities in more than 50% of patients and showed higher rates of psychiatric comorbidities in patients with recurrent disease [65]. Collectively, these statistics suggest a potentially alarming pattern of psychological distress in Middle Eastern patients with dermatological conditions, including AD.

Although data are limited, comorbidities have also been noted in African patients. In the study in which QoL of Ugandan and German patients with pruritic conditions owing to dermatoses was compared, depressed mood was reported in 41% of Ugandan patients (vs 49% of German patients) [63]. Results of a survey of Senegalese infants and children with AD showed that AD significantly increased the risk for malarial infection in children older than 3.5 years of age and delayed development of clinical immunity [66].

CURRENT TREATMENT OPTIONS AND UNMET NEEDS

Although AD treatment guidelines are similar globally, in managing AD, Africa and the Middle East face challenges that contribute to disease burden. In Saudi Arabia, numerous AD medications are available over the counter, and medical consultation and treatment are free for citizens at government hospitals [67]. However, patients often prefer to see a specialist rather than a general practitioner, resulting in long wait lists and potentially delayed diagnosis. A case report from Saudi Arabia cites use of traditional medicine, general practitioner nonadherence to clinical guidelines, and lack of

access to systemic therapies as contributing factors to disease severity and burden in a pediatric patient [52]. The author recommended numerous steps to improve local care for AD in Saudi Arabia, including adequate refresher training in dermatology for general practitioners; use of specialized nurses in dermatology; and enhanced coordination of primary, secondary, and tertiary care. The report also emphasized the need for further research into traditional Middle Eastern medicine and enhanced regulation of long-term prescription of potent topical steroids.

A qualitative report of parent impressions of AD management in the Gauteng district of South Africa identified dispensation of inappropriate medication or insufficient amounts of medication, inadequate primary care, financial obstacles, and lack of disease education for parents and health care providers as unmet needs in AD treatment [68]. The authors describe barriers of care general to South Africa. These include inadequate knowledge of allergic conditions among primary care providers and unavailability of treatment. Issues are amplified in rural settings, where lack of drugs and equipment, ill-informed health care providers, and financial obstacles add to the burden of AD. As in Saudi Arabia, a high proportion of South African patients report using alternative and traditional medicine.

AD research and care in Africa might also be affected by underreporting of the disease, stemming from limited access to health care and prioritization of infectious, highly virulent diseases such as malaria and tuberculosis [31]. Furthermore, many diagnostic tests were developed for use in European and North American individuals, and allergens inherent to tools such as the skin prick test for IgE immunoreactivity may not be relevant to African local environments. In regions with severe shortages of physicians such as sub-Saharan Africa, innovative tools to promote access to AD care such as the African Teledermatology Project, which connects sub-Saharan medical facilities to dermatologists in the USA, Europe, and Australia, are emerging [69]. However, the effectiveness of such tools in alleviating AD burden in Africa requires further research.

Taking into consideration the unmet needs of AD patients in Africa and the Middle East, we outlined treatment recommendations for management of AD in these patient populations in Table 3 based on literature [16, 20, 70–93] and our clinical experience. The goal of treatment should be threefold: to break the itch–rash cycle by controlling pruritus, to suppress inflammation, and to restore skin barrier function. When colonization or infection occurs, antiseptics, antibiotics, or antivirals are necessary [16–18, 20, 21]. The merits and drawbacks of therapeutic options should be weighed when developing a treatment plan. Furthermore, regional differences with respect to affordability and availability of AD therapies should be considered as these obstacles have been reported in Africa [68] and the Middle East [52].

Despite some deviations, our recommendations largely align with established international guidelines and comprise a multifaceted approach to treatment [16–21]. Emollients and moisturizers should be treatment mainstays. Topical corticosteroids are first-line therapies, but strength and treatment duration should be considered to avoid adverse events. Calcineurin inhibitors for AD are an important option, especially in children and for certain areas such as the face, neck, and intertriginous areas. Systemic therapies and phototherapy are useful for moderate to severe cases that remain uncontrolled by topical treatments. Behavioral interventions and disease state education should also be provided because these interventions can improve self-management and QoL, promote optimal sleep and dietary habits, and reduce physician visits and costs [21, 23].

As new treatments such as topical crisaborole and the biologic dupilumab become available in Africa and the Middle East, they should be added to AD management plans where indicated. However, there is a need for real-world efficacy, safety, and tolerability data for novel therapies in Africa and the Middle East because racial and ethnic differences in genetic and immune profiles relevant to AD pathophysiology have been documented [94, 95] and may impact treatment response. Furthermore, studies of the cost-effectiveness of these therapies

will be especially important for regions of low socioeconomic status.

TREATMENT EFFECT ON QOL

Available information is very limited regarding the effect of treatment on QoL of patients with AD in the Middle East and Africa. Results of an Iranian study showed that 6 weeks of dermatologic treatment with ultraviolet light, TCSs, and topical ointments produced a statistically significant improvement in QoL (57% change) as measured by a Persian version of the DLQI in patients with chronic dermatitis [96]. Statistically significant improvement after treatment was observed for all DLQI subdomains, but the greatest improvement was seen in the symptoms and feelings domain. Results of a study in Pretoria, South Africa, of 20 infants and children with severe AD showed a 33% improvement in mean Parent Index QoL (PIQoL) score following treatment with pimecrolimus [97]. The PIQoL questionnaire was translated from English as needed.

CONCLUSIONS

AD is a common, chronic inflammatory skin disease that is becoming increasingly prevalent in the developing world. Time trends in Africa and the Middle East suggest a growing regional burden of AD. Although data from Africa and the Middle East are limited, available information suggests relatively consistent increases in prevalence, with particularly large increases in Africa, and significant impact on QoL. Growing AD prevalence and burden is a serious public health problem in Africa and the Middle East because these regions face unique challenges in delivering care to patients with AD. Environmental factors contributing to AD prevalence that are specific to Africa and the Middle East should be considered for therapeutic strategies, education, and prevention.

Meaningful understanding of the burden and treatment of AD in the Middle East and Africa is impeded by significant gaps in data; therefore, it requires further investigation. Most

Table 3 Clinical recommendations for treatment of atopic dermatitis (AD) in Africa and the Middle East

Type of treatment	Recommendation	Merits	Drawbacks
Emollients and moisturizers	• Emollients should be the mainstay of treatment • Should be applied at least 5 times/day (acute) or 3 times/day (maintenance)	• Improve skin barrier function and symptoms [16, 70] • Reduce need for prescription anti-inflammatory therapies [16, 71] • Generally affordable treatment option [16, 72]	• Insufficient for moderate to severe cases [16, 18] • Greasiness/smell of moisturizer, frequent application, and adverse reactions may lead to poor adherence [72] • Specialized emollients and prescription emollient devices can be costly [16, 20]
Topical corticosteroids (TCSs)	• Should be applied 2 times/day for 7 days (acute); then 1 time/day for 7 days or twice weekly (maintenance)	• Recommended first-line anti-inflammatory therapy [16, 18–20] • Effective with satisfactory safety profile when used as directed [16, 73, 74] • Low cost for prescription therapy with several generic options [74, 75]	• Potential for long-term local side effects such as skin atrophy and systemic side effects such as HPA axis suppression merits routine monitoring [74] • Limited use in children [74] • Potential for hypopigmentation in patients with skin of color [74]
Topical calcineurin inhibitors (TCIs)	• Should be applied 2 times/day for 1 month (acute); then 2 times/week (maintenance)	• Effective for short- and long-term treatment of mild to severe AD in adults and children [16, 76–79] • Steroid sparing; reduces need for TCS when used for long-term, proactive prevention of flares [80] • Useful for sensitive areas (face, genitals, skin folds) [16, 20]	• Higher cost prescription therapy [75] • Local tolerability issues (stinging/burning) may require patient counseling to prevent nonadherence [16, 18] • Limited in combination with phototherapy as sun exposure should be avoided during TCI treatment [81, 82] • FDA boxed warning for cancerogenesis [81, 82]

Table 3 continued

Type of treatment	Recommendation	Merits	Drawbacks
Topical PDE4 inhibitors	• Crisaborole ointment, 2%, should be applied 2 times/day • Maintenance algorithm is not yet defined	• Effective treatment for mild to moderate AD in children and adults ≥ 2 years of age [83] with satisfactory short- and long-term safety profile [83, 84]	• Cost-effectiveness unestablished [85] • Limited real-word effectiveness, head-to-head comparative efficacy, and safety data available [20] • Local tolerability events including application site pain among most common treatment-related adverse events in pivotal [83] and long-term safety trials [84] • Currently approved only in USA [24]
Systemic therapies	• Sedating antihistamines at bedtime; nonsedating antihistamines during the day if necessary • Systemic immunosuppressants (methotrexate, cyclosporine, azathioprine) or biologics as second- or third-line therapies	• Antihistamines: widely available with low side effect profile (second-generation H$_1$ antagonists) [86] • Systemic immunosuppressants: effective in moderate to severe cases [73, 87, 88] • Biologics: dupilumab effective in moderate to severe cases [89]	• Antihistamines: efficacy in AD unproven [90], recently associated with ADHD symptoms in children with AD [91] • Systemic immunosuppressants: limited long-term use [17, 73]; pronounced side effect profile necessitates close monitoring [17, 73] • Biologics: very cost intensive [92]; some are investigational and lack long-term safety and efficacy data in AD [17, 18, 21]; dupilumab approved only in USA [25], Europe [25], Canada [26], and Japan [27]

Table 3 continued

Type of treatment	Recommendation	Merits	Drawbacks
Other	• UV phototherapy if unresponsive to topical therapies • Education regarding appropriate skin care • Avoidance of triggers (e.g., scented soaps)	• Behavioral modifications and patient education: cost effective with good efficacy [21, 23] • UV phototherapy: effective with good side effect profile [93]	• UV therapy: high costs (machine and maintenance) [20, 93]; requires patient access to a phototherapy center and frequent visits [20, 93]; limited long-term use and use in hairy/intertriginous areas [93]

ADHD attention deficit hyperactivity disorder, *FDA* US Food and Drug Administration, *HPA* hypothalamic-pituitary-adrenal, *PDE4* phosphodiesterase 4

region-specific data regarding AD in Africa and the Middle East are concentrated on epidemiology and risk factors associated with AD. Although many studies have been conducted to investigate the QoL of dermatology patients in the Middle East, most are from Saudi Arabia. Very limited information is available regarding QoL of patients with AD in Africa and regarding the effect of treatment on QoL in the Middle East and Africa. Furthermore, tools to effectively measure QoL are limited. An Arabic version of the Skindex-16 has been validated in patients with inflammatory dermatoses (psoriasis, vitiligo, eczematous dermatitis) [98]. Arabic and Persian versions of the DLQI have been validated in Moroccan and Iranian dermatology patients [57, 58, 99]. However, these versions of the DLQI were not specifically validated in AD patients, and no information is available regarding the validity of QoL instruments in other Middle Eastern ethnicities/cultures or in Africa. Available data do not adequately address the economic and academic/occupational impact of AD in Africa and the Middle East. There is also a lack of data regarding the region-specific symptom burden of AD (e.g., pruritus as a disease burden), which would necessitate tools such as a standardized itch questionnaire.

Data on treatment options and unmet needs are limited and are derived primarily from qualitative case studies and interviews, underscoring the need for further research on treatment options and effectiveness in Africa and the Middle East. These types of data are especially important because the primary diagnostic tools and treatments for AD were developed in European and North American patients. Additional studies are necessary to better understand differences in disease presentation in Africa and the Middle East compared with other regions and the potential implications of regional phenotypic differences on treatment effectiveness. Our clinical recommendations for improving management of AD in Africa and the Middle East outline a multifaceted approach of pharmacological and nonpharmacological topical treatments, systemic therapies, phototherapy, and behavioral interventions.

ACKNOWLEDGEMENTS

with Good Publication Practice (GPP3) guidelines (*Ann Intern Med.* 2015;163:461–464).

Authorship. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this manuscript, take responsibility for the integrity of the work as a whole, and have given final approval to the version to be published.

Disclosures. Khalid Abdullah Mohammad Al-Afif, Mohamad Ali Buraik, Joerg Buddenkotte, and Martin Steinhoff have nothing to disclose. Mohamed Mounir was an employee of Pfizer at the time of the study. Haytham Mohamed Ahmed is an employee of Pfizer. Robert Gerber is an employee and shareholder of Pfizer. Anna M. Tallman was an employee of Pfizer at the time of the study. Anna M. Tallman is now an employee of Dermavant.

Compliance with Ethics Guidelines. 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.

Data Availability. Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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