Atopic dermatitis not only negatively impacts the child's quality of life but also that of the whole family and is associated with a burden on health-care costs and society

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Treatment of Childhood Atopic Dermatitis and Economic Burden of Illness in Asia Pacific Countries

by B.W. Lee and P.R. Detzel

Key insights

Atopic dermatitis is the most commonly occurring inflammatory disease in childhood. Contrary to previous belief, this disease not only affects developed countries. In the Asia Pacific, the prevalence of atopic dermatitis is on the rise, affecting not only the patients but their entire families and generating a significant economic burden.

Current knowledge

The costs related to the disease may be classified according to direct costs (associated with the use of health-care resources) and indirect costs (the nonmedical costs such as missed work time and transportation). An infant suffering from atopic dermatitis generates estimated health-care costs between USD 199 and over USD 1,000 per year. In general, the costs are higher in developed countries (such as Australia, North Korea and Singapore) compared to less developed countries (such as the Philippines and Indonesia).

Practical implications

NICE guidelines recommend a stepped approach in the management of childhood atopic dermatitis, with treatment tailored to disease severity. This approach includes education, avoidance of triggering factors, use of emollients and topical corticosteroids, topical calcineurin inhibitors, bandages and systemic immunosuppressive therapy. In the Asia Pacific region, treatment of atopic dermatitis also depends on factors such as the country's health-care system and the specific climate. Bath-

Estimates of the direct and indirect costs related to atopic dermatitis in Asia Pacific countries.

ing followed by the application of a skin moisturizer are frequently used, but there is no consensus on the frequency or duration of bathing for atopic dermatitis. Bleach baths are useful for disinfecting skin lesions and provide a practical alternative to antibiotic treatment. Further data are needed to identify the most effective and cost-effective measures for treatment and prevention in different countries.

Recommended reading

Rubel D, Thirumoorthy T, Soebaryo RW, et al: Consensus guidelines for the management of atopic dermatitis: an Asia-Pacific perspective. *J Dermatol* 2013;40:160–171.

Treatment of Childhood Atopic Dermatitis and Economic Burden of Illness in Asia Pacific Countries

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Key Messages

- Atopic dermatitis (AD) is the most common chronic inflammatory disease of childhood.
- Its prevalence in the Asia Pacific region is increasing.
- This condition impacts the quality of life not only of the patients but also of the whole family and carries a cost burden on society.
- Further evaluations of AD costs and the cost-effectiveness of pediatric AD prevention strategies in Asia Pacific countries are warranted.

Key Words

Atopic dermatitis · Treatment · Health economics · Infant · Children · Asia Pacific

Abstract

Atopic dermatitis (AD) is a common chronic inflammatory skin condition in children. In Asia, the prevalence of AD is increasing, which is largely attributed to environmental and socioeconomic factors including family income, parental education, lifestyle and metropolitan living. Current clinical guidelines recommend a stepped approach in the manage-

ment of eczema in children, with treatment steps tailored to the severity of the eczema. To address the skin barrier dysfunction, skin hydration and the application of emollients is essential. There is evidence supporting the use of bleach baths as an antimicrobial therapy against *Staphylococcus aureus*. In patients in whom topical treatment fails, wet wrap therapy may be considered as a treatment option before considering systemic therapies. In the second part of this article, the economic burden of AD is addressed. AD not only negatively impacts the child's quality of life but also that of the whole family and is associated with a burden on health-care costs and society. AD in an infant will lead to frequent additional visits to the pediatrician, to additional and partially expensive treatment costs and, in rare cases, to hospitalization. It is thus of utmost importance to define efficient strategies to not only treat AD but also to decrease the risk of developing the disease.

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Introduction

Atopic dermatitis (AD) is a common chronic skin disorder and considered to be the earliest manifestation of the atopic march. It has a chronic relapsing and remitting course which deeply affects the child's quality of life as

well as that of the whole family and imposes a substantial medical burden on society. This paper reviews the current status with regard to the management and economic burden of AD in the Asia Pacific region.

Prevalence of AD

AD is one of the most common childhood skin conditions and is associated with a significant social and financial burden [1]. There is striking worldwide geographic variability in the prevalence of AD. The reasons for this variability are as yet unclear but have been attributed in part to many environmental factors, including urbanization, diet, climate, infections and aeroallergens [2].

The International Study of Asthma and Allergies in Childhood (ISAAC), an international multi-country cross-sectional survey of school children, was conducted to investigate the epidemiology and geographic variability and trends in prevalence of asthma, rhinitis and AD [3]. The ISAAC Phase One study was conducted in the early to mid-1990s. To monitor the evolution in the prevalence of these disorders, ISAAC Phase Three was carried out about 7 years later using the same methodology and survey questionnaire. This follow-up study involved 193,404 children aged 6–7 years from 66 centers in 37 countries and 304,679 children aged 13–14 years from 106 centers in 56 countries.

Data from the ISAAC Phase Three study revealed that the prevalence of AD symptoms in the 6- to 7-year and the 13- to 14-year age groups ranged from 1.8 to 23.4 and 0.9 to 21.1%, respectively [4]. In the Asia Pacific region, the 12-month prevalence of AD in children aged 13–14 years was reported to be as high as 9% in Malaysia and Singapore and as low as 0.9% in China. Notably, China had the lowest prevalence in the world. The reasons for these differences in AD prevalence are poorly understood, but industrialization and socioeconomic factors have been implicated [5–10].

The 12-month prevalence of AD in children aged 13–14 years was reported to be as high as 9% in Malaysia and Singapore.

Compared to the ISAAC Phase One results [11], 44 of the 52 centers recorded an increase in the prevalence of AD, whereas only 8 centers reported a decrease in ISAAC Phase Three. ISAAC Phase Three also highlighted the

Asia Pacific as an area of increasing AD prevalence. Of the 44 centers with an increase in prevalence, 10 were from the Asia Pacific, hence putting this region second to Western Europe (17 centers) for centers with an increase in AD prevalence.

Data for Singapore, derived from the ISAAC surveys, indicated a modest increase in prevalence in both age groups, but an increased severity of symptoms in the 12- to 15-year age group [12]. The latter is in agreement with a cross-sectional epidemiological study involving 12,323 students in Singapore (7-, 12- and 16-year age groups) reporting a prevalence of AD of 20.8% [13], an incidence markedly higher than that reported in younger age groups [14, 15]. The increasing prevalence and severity of AD is concerning and further highlights the need for improved management of this condition.

Pathogenesis of AD

AD is a chronic inflammatory disease often exhibiting marked xerosis, pruritus and skin lesions. Although it is incompletely understood, the pathogenesis of AD is thought to result from the complex interaction between defects in skin barrier function, immune abnormalities involving IgE-mediated and a non-IgE-mediated hypersensitivity and environmental as well as infectious agents [16, 17].

AD is mediated by Th1/Th2 immune responses. In the initial acute phase, AD skin lesions predominantly secrete the Th2 cytokines, whereas in the chronic phase, Th1 cells secrete IFN- γ [18]. The shift from Th2- to Th1-predominant immune responses plays an important role in the development of AD [19]. It has also been suggested that the hyperreactive immune response may be a consequence of defects in the epidermal barrier [20]. The defective epidermal barrier may allow the allergens to enter through the skin, facilitating the interaction of these allergens with the local antigen-presenting cells and immune effector cells. This may trigger the transition from a nonallergic to an allergic state associated with a rise in IgE [21–23].

Early sensitization has been shown to influence the onset, duration and severity of AD. In a population-based, noninterventional study of a cohort of 562 newborns conducted at the Danish Allergy Research Centre (DARC), early onset and persistence of allergen sensitization beyond the age of 2 years were associated with more persistent AD [24]. In contrast, children with early, non-IgE-mediated (intrinsic) AD were more likely to outgrow their eczema than sensitized children.

Management of AD

There are a number of evidence-based international guidelines on the management of AD. Of interest is 'Management of Atopic Eczema in Children Aged up to 12 Years' [25], published by the National Institute for Health and Clinical Excellence (NICE), which provides specific recommendations for children from birth to 12 years.

The NICE guidelines adopt a holistic approach in assessing AD, taking into account the physical severity of the atopic skin disorder and its impact on the quality of life. A grading system was outlined: clear = normal skin; mild = dry skin with infrequent scratching; moderate = areas of dry skin and frequent itching and redness; severe = widespread areas of dry skin, incessant scratching, redness, oozing and crusting, lichenification and pigment changes. Whereas scoring of AD severity is not required in clinical practice, documentation of symptoms, including descriptions of the extent and nature of lesions, skin dryness and intensity of itchiness, can help better manage the condition.

Patient education is paramount for successful therapy.

The NICE guidance recommends a stepped approach in the management of AD in children, with treatment steps tailored to the severity of the eczema [25]. In this regard, patient education is paramount for successful therapy. Mild AD should be managed with emollients, avoidance of triggering factors and mild-potency topical corticosteroids. Moderately severe AD should be managed with emollients, topical corticosteroids with mild potency, topical calcineurin inhibitors and bandages in a stepwise approach. In addition to emollients, moderate and severe AD requires a stepwise treatment which may include potent topical corticosteroids, topical calcineurin inhibitors, bandages and systemic immunosuppressive therapy. A recent review proposes an updated treatment algorithm for AD which includes recommendations for the treatment of refractory cases [18]. Treatment of complications such as skin infections, particularly due to *Staphylococcus aureus* and Herpes simplex virus, is also an important aspect of the management of eczema flares. In a small proportion of infants and young children with severe eczema, food allergy may also contribute to failure to respond to standard therapy [26].

Dermatologists in the Asia Pacific region have also published consensus guidelines of AD and highlighted

the various treatment practices in this region, which are influenced by differences in health-care systems, access to medical care as well as by cultural and environmental factors including climate [27].

Bathing

Bathing, followed by moisturizer application, is thought to help hydrate the skin and reduce itchiness; however, there is little consensus regarding the frequency or duration of bathing appropriate for patients with AD. Of particular interest is bleach bathing to disinfect the skin lesions. During AD disease flares, the diversity of the skin microbiome is greatly reduced, *S. aureus* tends to predominate and AD symptoms tend to worsen [28].

Antibiotic therapy against *S. aureus* is an important component of AD management as it reduces both the severity of AD and the likelihood of secondary infections. However, with the growing concern regarding the emergence of antibiotic resistance, bleach baths are sometimes recommended for patients with AD to reduce *S. aureus* skin colonization or infection [29]. A randomized, placebo-controlled study has demonstrated that compared to placebo, coadministration of intranasal mupirocin ointment and bleach baths (0.005%) for 5–10 min twice weekly decreased the clinical severity of AD in patients with clinical signs of secondary bacterial infections [30].

Wet Wraps

In recent years, wet wrapping, i.e. the application of wet bandages wrapped over emollients and/or topical steroid creams, has been used as a treatment option for AD.

A cohort study of 50 children (aged 4–27 months) with moderate to severe eczema was conducted to evaluate the effectiveness of wet wrap therapy to improve disease severity [31]. A comparison of disease severity at admission and at discharge showed an average of 70% reduction in SCORAD scores (49.68 ± 17.72 vs. 14.83 ± 7.45 , respectively) in patients who received the in-patient wet wrap therapy [31]. The investigators suggest that wet wrap therapy may be considered as a treatment option before considering systemic therapies in patients for whom topical therapy has failed.

Economic Burden of Pediatric AD in the Asia Pacific Region

To estimate the economic burden of pediatric AD in the Asia Pacific region, an electronic literature search was conducted in PubMed, Google scholar and Asian elec-

Table 1. Studies regarding the economic burden of pediatric AD

Study	Country	Study design	Population type/sample	Mean age (range), years	n	Year of cost data	Cost included		Case distribution (%)		
							direct	indirect	mild	moderate	severe
Su et al. [32], 1997	Australia	cross-sectional survey	presenting at dermatologic clinic	4.5 (0.3–15)	48	1997	yes	yes	38	42	21
Su et al. [33], 2012	Australia	model and expert opinion	with atopic heredity	n.a. (0–1)	n.a.	2009	yes	yes	60	35	5
Kang et al. [34], 2012	South Korea	cross-sectional survey	attending allergy clinic	5.49 (1–12)	196	n.r.	yes	yes	42	31	27
Ngamphaiboon et al. [35], 2012	Thailand	model and retrospective analysis	attending pediatric hospital department	n.a. (0–5)	n.a.	2010	yes	no	79 ^a	18 ^a	3 ^a
Bhanegaonkar et al. [37], 2014	Indonesia	model-based/expert opinion	urban, affluent, with atopic heredity	n.a. (1–6)	n.a.	2013	yes	yes	50/60 ^b	40/30 ^b	10/10 ^b
Bhanegaonkar et al. [37], 2014	Malaysia	model and expert opinion	urban, affluent, with atopic heredity	n.a. (1–6)	n.a.	2013	yes	yes	43/50 ^b	37/28 ^b	20/22 ^b
Bhanegaonkar et al. [37], 2014	Singapore	model and expert opinion	urban, affluent, with atopic heredity	n.a. (1–6)	n.a.	2013	yes	yes	58/80 ^b	38/17 ^b	5/4 ^b
Bhanegaonkar et al. [36], 2014	Philippines	model and expert opinion	urban, affluent, with atopic heredity	n.a. (1–6)	n.a.	2013	yes	yes	60/85 ^c	25/10 ^c	15/5 ^c

n.r. = Not reported; n.a. = not applicable. ^a Calculated based on the data in Matsuoka et al. [6]. ^b The first value is for age <1 year, the second value is for age >1 year. ^c The first value is for age <2 years, the second value is for age >2 years.

tronic reference databases to identify studies reporting on pediatric AD cost estimates. These searches were complemented by manual reviews of bibliographies of the articles reporting cost estimates, discussions with AD experts and economic models (Singapore, Malaysia and Indonesia) presented at the International Conference of Health Economics – ISPOR 6th Asia-Pacific Conference (Beijing, China, 2014). All costs were inflated and converted to 2013 USD for comparison purposes.

A total of 5 published studies were identified (table 1): 2 for Australia [32, 33], 1 for South Korea [34], 1 for Thailand [35] and 1 for the Philippines [36], which required reanalyses to generate some of the outcomes presented herein. These studies were further complemented with unpublished analyses conducted by some of the coauthors in Indonesia, Malaysia and Singapore [37]. The analyses varied in terms of country considered, study design, target populations and setting of care, average age and range, sample size, the type of cost included and the case mix of AD severity (table 1).

Patients included in one of the Australian studies were attending a dermatology clinic [32], whereas patients in the South Korean study were recruited in an allergy department [34]. Patients from these 2 studies had the low-

est proportion of mild cases. This led to a selection bias and to an overestimate of AD costs as mild cases were not well reflected in the estimates. Patients in the other studies were treated in a general/pediatric setting.

Most countries reported both direct and indirect costs (fig. 1), except for the study in Thailand, which assessed direct costs only. By direct costs, all costs are meant which are associated with the use of health-care resources. Indirect costs reflect nonmedical costs, such as time losses for parents, etc.

The direct costs of AD per patient per year ranged from USD 199 in Thailand to USD 4,842 in Australia. Discarding the Australian estimates (reflecting severe cases), a significant high economic burden of illness of AD in the region can still be observed (fig. 2). An infant suffering from AD will generate health-care costs between USD 199 and over USD 1,000 per year. This represents substantial medical costs for a disease characterized by a high and increasing prevalence.

The indirect costs of AD per patient per year ranged from USD 8 in the Philippines to USD 2,268 in South Korea. These costs will be covered exclusively by the parents/relatives of the infant suffering from AD as these costs are not related with the medical treatment of the child but are

Fig. 1. Annual total (direct and indirect) costs for AD in different countries.

Fig. 2. Annual direct costs for AD in different countries.

Fig. 3. Components of direct costs for AD in different countries. Data from South Korea [34] are not included as insufficient details were provided for analysis.

linked with the time losses and transportation costs of the parents.

The estimation of total AD costs varies significantly across countries and across severity levels (table 1). The lowest costs were observed in Thailand [35] (USD 199 across all severities, ranging from USD 124 among mild cases to USD 968 among severe cases), in part because only direct costs were reported.

Costs were higher in more developed countries (Australia, North Korea and Singapore), with overall costs

ranging from approximately USD 1,000 to 6,000, than in less developed countries (Philippines, Indonesia and Malaysia), where costs ranged from USD 199 to 743.

The components of direct costs for AD are generally consistent across countries, with medical visits and creams, dressing, ointments and medications reported in all studies (fig. 3). This illustrates that infants suffering from AD are treated following consistent and coherent guidelines across the region.

Conclusions

Allergic conditions are among the most common medical conditions affecting children, and the incidence of allergies, especially AD, is increasing. These conditions impact the quality of life not only of the patients but also of the whole family and carry a cost burden on society. Guidelines for treatment of AD are available; the NICE guidelines recommend a stepped approach in the management of AD in children, with treatment steps tailored to the severity of the eczema. The approach includes education, use of emollients, avoidance of triggering factors and topical corticosteroids, topical calcineurin inhibitors, bandages and systemic immunosuppressive therapy. Various bathing procedures and wet wraps have been reported to be effective.

The economics of pediatric AD in the Asia Pacific region have not been extensively studied. Based on available

evidence, annual pediatric AD costs are generally high but vary widely across studies/countries. Variations in cost estimates make comparisons difficult and may be due to differences between studies in countries considered, population/sample studied, types of costs included, severity of AD and costing methodology.

Further evaluations of the AD costs and the cost-effectiveness of pediatric AD prevention strategies in Asia Pacific countries are warranted.

Disclosure Statement

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