

The burden of atopic dermatitis

Brian Reed, M.D. and Michael S. Blaiss, M.D.

ABSTRACT

Background: Atopic dermatitis (AD) is a dermatologic condition that affects a large percentage of children and adults in the United States. The disease process is not fully understood, and, currently, there is no cure, so today's treatment methodologies focus on the rash and the symptoms, e.g., pruritus. Even though there is no mortality with this condition, there is significant morbidity and burden.

Objective: This review concentrated on several areas in which AD influences quality of life. The areas include sleep, interference with daily activities (e.g., school and/or work), psychological stressors, and the impact on parents and caregivers. The direct and indirect costs of AD are also examined.

Methods: A medical literature search was conducted that focused on quality of life (QOL), health-related quality of life, and costs in patients with AD.

Results: AD caused poor QOL as assessed in both generic and specific QOL questionnaires. Skin pain was frequently experienced in this condition, which worsens QOL. A significant effect on sleep was found in multiple studies. A large amount of school and/or work absenteeism and psychological stressors was seen in patients with AD. Multiple burdens of the caregivers and parents of patients with AD were documented. Medical costs were also significantly higher compared with patients without AD.

Conclusion: The impact of AD is likely more significant than previously acknowledged. AD results in significant morbidity as seen through generic and specific QOL questionnaires, sleep studies, and other questionnaires that measure psychological effects. Physicians should consider evaluating patients with AD beyond their rash and symptoms to achieve the best care possible.

(Allergy Asthma Proc 39:406–410, 2018; doi: 10.2500/aap.2018.39.4175)

Atopic dermatitis (AD) is an inflammatory, dermatologic condition, without a fully understood etiology. It is a relapsing disease, with frequent exacerbations of pruritic and eczematous lesions. The lesions appear erythematous and often occur with excoriations and lichenification, although presentation is very heterogeneous.¹ Excoriations and lichenification occur due to skin damage from skin scratching, which results in skin barrier disruption and potential secondary infection. Skin pain is a frequent symptom in AD in addition to pruritus.² AD may lead to sleep disturbances, impacted social functioning and choice of occupation, which result in a worsening of the patient's quality of life (QOL) and in high costs.³ With genetically determined pathophysiology,⁴ there is no current cure for AD, and treatment focuses on prevention and control.⁵ The National Eczema Association funded a review that investigated the burden of AD, and multiple gaps were identified.⁶ Some of these gaps include

the need for updated direct and indirect financial burdens of AD, evaluation of QOL in the primary care setting, and the impact on families of adults with AD.⁶ Just recently Drucker⁷ published an analysis of the burden of AD and the effect on QOL; this review examines several factors that lead to the high affliction that AD places on the patient and his or her parents or caregivers.

METHODS

The medical literature was searched by using PubMed and focused on clinical studies and reviews in all age groups with the search words of "quality of life," "health-related quality of life," and "costs" with "atopic dermatitis" in English language journals over the past 15 years. Articles were selected at our discretion.

Prevalence of AD in Children and Adolescents

Children from all over the world experience AD, as documented in The International Study of Asthma and Allergies in Childhood,⁸ and the prevalence is increasing. Studies limited to the United States revealed that the peak incidence of AD occurred in children <5 years of age.⁹ A cross-sectional study published in 2014 presented the prevalence of eczema in 3556 adolescents ages 18–19 years as 9.7%, with 11.9% in girls and 7.0%

From the Medical College of Georgia, Augusta University, Augusta, Georgia
Presented at the Eastern Allergy Conference, June 2, 2018, Palm Beach, Florida
No external funding sources reported
The authors have no conflicts of interest to declare pertaining to this article
Address correspondence to Michael S. Blaiss, M.D., 1090 Windfaire Place, Roswell, GA 30076
E-mail address: michael.blaiss@gmail.com
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in boys.¹⁰ In 2017, latent class analysis was used to identify four phenotypes of AD with a point prevalence of 11.4–16.9%.¹¹ A more recent study, published in 2018, identified six phenotypes of AD in children among two population-based cohorts, with a prevalence of 13–15%.¹²

Prevalence of AD in Adults

AD occurs most often in childhood and enters remission in many cases. However, AD is also seen to persist into adulthood or even start in adults.¹ A nationwide registry of 7157 patients diagnosed with AD revealed that symptoms may persist well into the second decade of life.¹³ In addition, a study that used the 2010 National Health Interview Survey revealed that the yearly prevalence of AD in adulthood of 10.2% does not differ much from that in childhood.¹⁴ A more recent study,¹⁵ in 2013, presented different subgroups of AD in adolescents and adults. The most frequent subgroup was early onset in children that persisted to adulthood.¹⁵ AD continued to adulthood in 60% of children in another study.¹⁶ This is in contrast to previous reports that stated that the majority of subjects achieve resolution of AD by age 12 years.¹⁷ In addition, this condition is not limited to the United States. An international survey of multiple countries, which consisted of Canada, France, Germany, Italy, Spain, United Kingdom, and Japan, and including the United States was published in 2018.¹⁸ The adult AD prevalence in these countries ranged from 2.1 to 4.9%.¹⁸ The International Study of Life with Atopic Eczema (ISOLATE) reported that 24% of the patients evaluated received the diagnosis after 18 years of age.¹⁹

QOL and Health-Related QOL

QOL is the general well-being of individuals, including the physical, mental, and social domains of life. Evaluating QOL assists in understanding the patient's well-being or lack thereof. Health-related QOL (HRQOL) refers to QOL in the context of health and disease, which allows distinction from other aspects of QOL. HRQOL encompasses multiple aspects, including the physical, emotional, mental, and social areas. This allows an overall gauge of a disease's impact on QOL. In recent years, the importance of QOL in chronic conditions has been documented because medical literature on this subject has increased dramatically.²⁰

Multiple tools exist on measuring HRQOL in patients with AD. Some of these tools are generic and assess QOL in any disease state or condition, *e.g.*, the 36-Item Short Form Health Survey.²¹ The Children's Dermatology Life Quality Index (CDLQI) comprises 10 questions specifically for children.²² It is based on the Dermatology Life Quality Index (DLQI) for adults, which also has 10 questions. The DLQI score ranges

from 0 to 30; the lower the score, the more profound effect on a person's QOL.²³ A review article²⁴ examined 10 years of publications that used the DLQI scoring tool in 36 dermatologic conditions. The most common condition for which it was used was psoriasis and the next condition was AD. When examining the mean of means AD was the second highest, at 12.2, and the highest score was hirsutism, at 12.8. Common dermatologic conditions seen in an allergy setting include chronic urticaria at 9.9, latex allergy at 11, occupational contact dermatitis at 7.5, and pruritus at 10.3. For comparison, the mean score for a normal population ranges from 0 to 0.5.²⁴ Evaluation of patients with moderate-to-severe AD in a clinical trial had a mean DLQI score of 14.3.²⁵ Analysis of these data clearly demonstrates the poor QOL in patients with AD.

Some studies correlate disease severity with tools such as Scoring Atopic Dermatitis (SCORAD)²⁶ and the impact on QOL. A recent study in 50 children and 50 adults with AD found a significant correlation between SCORAD and CDLQI as well as between SCORAD and DLQI.²⁷ Sleep disturbances in adults with AD were evaluated by using The Pittsburgh Sleep Quality Index,²⁸ and it correlated significantly with the DLQI but not with SCORAD scores.²⁷ This study indicated that, even in patients with mild AD, they can experience poor sleep quality and overall decreased QOL.²⁷ Patient perception was found to correlate with QOL when using survey data from 2014 by Wei *et al.*²⁹ A poorer QOL and worse symptoms were found in those with inadequately controlled AD. DLQI was found to suggest a large impact on patient's lives, more than other dermatologic conditions, such as psoriasis, chronic urticaria, and pruritus. Multiple studies note that QOL worsens as the severity of AD increases.^{30–32}

The impact of AD on QOL includes the psychological realm as well. HRQOL was significantly reduced in physical and mental aspects for patients with AD compared with non-AD controls in the National Health and Wellness Survey.³³ A review published in 2017 presents nine instruments to also evaluate the impact of skin disease on family members and caregivers.³⁴ Warschburger *et al.*³⁴ noted that the mental health scores from the 12-Item Short Form Survey (SF-12), a generic QOL instrument, in mothers of patients with AD was significantly worse compared with reference standards.

Because AD is a common dermatologic condition that affects people worldwide and is not limited to children but continues into adulthood for some, the burden and subsequent QOL are a major concern.²⁰ Treatment of AD must take into account other aspects of the disease and not just the clinical manifestations. There is a burden of disease even if AD is well controlled by avoiding triggers and by applying topical treatments.³⁵ When developing a treatment regimen,

physicians should consider multiple aspects, including educational and psychological, because the alleviation of skin symptoms alone may not completely improve QOL.³⁶

Burden of AD in Children and Adolescents

AD causes a burden to children and adolescents in multiple ways. One of these is impairment of sleep. A recent study³⁷ that evaluated sleep in children with AD revealed that wake after sleep onset was higher and that sleep efficiency was worse. In addition, the children with AD were noted to have more daytime sleepiness and restless sleep.³⁷ As the severity of AD lesions increases, the number of nights affected during an AD flare increases as well.¹⁹ The Children's Sleep Habits Questionnaire³⁸ was used to measure sleep disturbances in children with AD and was found to correlate significantly with SCORAD and also with the CDLQI scores for children.²⁷ Treatment of AD lesions and the accompanying itch result in improved sleep.³⁹

Children are affected in other ways besides sleep. AD resulted in avoidance of everyday activities in 68% of children 2–13 years old and in 83% of adolescents 14–17 years old.¹⁹ Thirty percent of these children and 46% of these adolescents experienced disruption of school and work life, which led to 2 and 3.5 days absent from school and work, respectively. Home and social life were also impacted. Flares resulted in 29% of the children and 50% of the adolescents, who experienced concern about being seen in public.¹⁹ A cross-sectional study¹⁰ of adolescents 18–19 years old revealed that those with AD were significantly more likely to consider suicide than those who had never experienced AD. The Strength and Difficulties Questionnaire revealed¹⁰ a significant increase in mental health problems for those with AD. In addition, those with AD experience significantly more mental distress, as measured by the Hopkins Symptom Checklist 10.¹⁰

Burden of AD in Parents and Caregivers

Those who care for patients with AD experience burden from the disease as well. ISOLATE pointed out that 37% of caregivers of children 2–13 years old believe that a child's AD affects other members of the household.¹⁹ There is an association between the severity of a child's AD and the QOL of a parent. When children experience symptoms and sequelae of AD, *e.g.*, scratching, parents or caregivers may have difficulty caring for the child.^{20,30} There also is an effect on the length of sleep and emotions that stem from their child's illness. Chamlin *et al.*⁴⁰ showed that 61% of parents experienced disturbed sleep in a series of 270 pediatric patients with AD. Another study revealed⁴¹ parents of patients with AD spent a significantly longer time per night attending to their child compared with

another chronic disease, asthma. Although parents of children with asthma spent minimal time nightly, mothers and fathers of patients with AD spent 39 minutes and 45 minutes a night, respectively.⁴¹ Another study reported that families spent 63 minutes a day caring for a child with AD, which includes the time applying topical treatments, cleaning the skin, and visits to physicians.³⁵ Devoting this much time to care for a child with AD is burdensome on parents and caregivers⁴² with multiple instruments available to measure that burden.⁴³ More research is needed because most of these studies tended to contain limitations, such as a small sample size, lack of validation, or single institution setting. However, the overall trend points toward a significant burden to parents and caregivers.

Burden of AD in Adults

Adults with AD also experience widespread burdens that affect QOL. AD skin lesions frequently result in pain, in addition to pruritus. In a study of 305 patients,² 144 (42.7%) reported having skin pain within that week; this was labeled as severe or very severe in 42 (13.8%). Those with excoriations were more likely to experience skin pain.² A recent study⁴⁴ that evaluated >5500 subjects in the 2005–2006 National Health and Nutrition Examination Survey revealed that sleep disturbances are more common in adults with AD than in adults without AD; these disturbances include shorter sleep duration and early morning awakenings. In addition, an impairment in instrumental activity of daily living was discovered.⁴⁴ Findings from the 2012 National Health Interview Survey⁴⁵ revealed a similar picture of a significantly higher prevalence of fatigue, daytime sleepiness, and insomnia in subjects with AD. AD was also associated with having fair or poor overall health compared with those without AD.⁴⁵ Data from the National Health and Wellness Survey revealed a significantly greater percentage of anxiety, depression, and sleep disorders in subjects with AD.³³ ISOLATE provided data that adults with AD experienced 8.4 nights of disrupted sleep during a flare.¹⁹

Pruritus is a common concern, rated as severe in 46% and unbearable in 14% of the patients over a 2-week period in a phase IIb clinical trial²⁵ of 380 adults with moderate-to-severe AD. Nearly all (86%) reported pruritus every day of the week.²⁵ There were substantial reports of embarrassment, self-consciousness, interference with personal life, and prevention of work or study in patients with AD.²⁵ A common concern is of being seen in public during a flare, which affects confidence and possibly results in bullying.¹⁹ Patients with AD are more frequently diagnosed with depression and anxiety.^{33,46} An area of social burden unique to adults involves an impact on sexuality and libido, as described in a French study⁴⁷ in 2017. More than 1000

subjects with AD responded to a questionnaire; nearly 82% experienced an impact on their sexuality.⁴⁷ There also is a higher rate of work absenteeism seen in adults but not in adolescents.^{33,48} Adults frequently avoid everyday activities during flares.¹⁹ Because the prevalence of AD in adults is higher than previously suspected, there is likely a more significant amount of burden than previously recognized.¹⁷

Cost

There is a large financial impact of AD. This includes the price of over-the-counter medications, prescription medications, physician visits, emergency department (ED) visits, and hospitalization. The indirect costs, such as loss of work days or decreased productivity at work, must also be included.⁶ An estimated cost of AD in the United States in 2004 was \$4.228 billion. Given there is a higher prevalence of AD now than in 2004 and with inflation in health-care costs, the cost of AD may be significantly higher.⁴⁹ Also this study did not include over-the-counter medications.⁴⁹ A more recent study, by Drucker *et al.*,⁵⁰ that used 2013 data from Truven Health Marketscan Commercial Claims and Encounters data base (Truven Health Analytics Inc., Ann Arbor, MI) separated patients with AD and with or without treatment regimens of phototherapy or systemic immunomodulatory agents to classify as more severe or less severe. The adjusted total annual costs ranged from \$3302 per patient for less-severe cases to \$4463 for more-severe cases.⁵⁰

Another study estimated that the mean annual indirect cost burden was \$2400 more per patient for those with AD compared with propensity-matched controls.³³ Also, the total annual mean direct cost was nearly \$10,000 more for those with AD, also compared with propensity-matched controls.⁵¹ A study that used data from the 2010 and 2012 National Health Interview Survey revealed that AD was associated with higher costs, more lost work days, physician visits, ED visits, hospitalizations, and home health-care usage, along with more difficulty in obtaining medications and care than those without AD.⁵² The National Health and Wellness Survey also reported an increased rate of work absenteeism, work impairment, and presenteeism compared with those without AD.³³ Analysis of the same data⁵¹ revealed a significantly higher use of health-care resources, including health-care provider visits, ED visits, and hospitalizations. AD was also associated with significantly higher ED visits, with nearly twice the annual ED visit costs compared with psoriasis.⁵¹ The mean monthly personal cost of AD in children 6 months to 12 years of age was noted by Filanovsky *et al.*⁵³ as \$274; however, literature about the cost in children is limited. As treatment for AD evolves, use of newer therapies, *e.g.*, biologics, sublin-

gual immunotherapy, may raise the overall cost burden of AD.⁵⁴

CONCLUSION

AD affects patients in many ways, well beyond skin pruritus and rash. Patients experience skin pain, disrupted sleep, psychological factors, and many other burdens that lead to a poor QOL. Parents and caregivers experience many challenges in caring for the child with AD. Because of the issues seen in patients with AD, physicians must consider a holistic approach in the management and control of this condition as well as in the education of the disease process for patients and caregivers.

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