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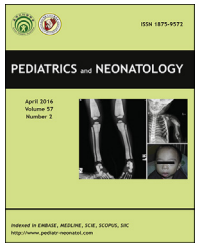

REVIEW ARTICLE

Childhood Atopic Dermatitis in Taiwan

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The prevalence of atopic dermatitis (AD) appears to have increased dramatically over the past decades. It is generally believed that such rapid increase in prevalence cannot be explained fully by genetic factors. Environmental factors might play a role in such an increment. Children with AD are most likely to suffer considerable school absences, family stress, and health care expenditures. Because the onset of AD occurs relatively early in life, identification of early life risk factors and early management for AD to prevent the development of atopic march are of critical importance. However, there is still no consensus on coordinated prevention and management for AD in Taiwan. In this review, we discuss the specific risk factors of AD and important results of recent articles on AD from Taiwan. The management and prevention strategies of AD for Asian skin are also discussed.

1. Introduction

Atopic dermatitis (AD) is a chronic inflammatory pruritic skin disease that affects a large number of children in industrialized countries. In Taiwan, the prevalence of AD appears to have increased dramatically over the past decades.[1] According to Taiwan national birth cohort, AD was noted in 118 of 1760 (6.7%) infants at 6 months of age in 2005 and in 1584 (7.9%) out of 19,968 children at 18 months in 2007.[2,3] In 6- to7-year-old schoolchildren in Taipei, the prevalence of AD significantly increased in 2007 (29.8%) compared to 1994 (23.9%) and 2002 (26.3%).[4] Because population genetic variability does not change with such rapidity, changing environmental factors are likely to be responsible for the rise in the number of AD. The quality of life of children with AD and their families is obviously affected.[5] It leads to considerable

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financial and psychosocial burden to individuals and society. The rising prevalence in the pattern of skin diseases and psychosocial burden makes AD one of the most important groups of chronic childhood diseases.

Because the onset of AD occurs relatively early in life, identification of early life risk factors among genetically susceptible children and early management for AD to prevent the development of atopic march are of critical importance. However, we still lack a consensus on prevention and management of AD in Taiwan. In this review, we discuss the specific risk factors and important results from recent primary literature articles in Taiwan. Then, we discuss how to take care of the AD skin in our humid climate and how to manage children who do not respond to conventional treatment.

2. Risk factors

The development and phenotypic expression of AD depends on a complex interaction among genetic factors, perinatal environmental exposure to allergens, and nonspecific adjuvant factors, such as pollution, infections, and climates.[1,6] Food allergens may be the major trigger of AD in early life, after which the role of environmental aeroallergens becomes more important and may be associated with respiratory sensitization.[6]

2.1. Hereditary factors

AD may be inherited preferentially through the maternal line.[2] It was reported that maternal history of AD, maternal grandparents' history of AD, higher family income, and higher maternal education level increased the risk of pediatric AD.[2] The mode of inheritance and genes involved are not clear. Genes associated with adaptive immunity and skin-barrier formation have been involved in the development of AD. For example, single nucleotide polymorphisms in Toll-like receptors, ST2, interleukin (IL)-3, IL-4, IL-5, IL12RB1, and IL-13 have been shown to be associated with the pathogenesis of AD.[7] Genetic mutations in filaggrin (FLG), which is essential for the maintenance of the skin-barrier function, are significantly associated with the risk of AD and disease severity in different ethnic populations.[8] Among Chinese individuals, the FLG P478S polymorphism may confer susceptibility to the development of AD and may be modified by immunoglobulin E (IgE) levels.[9] Another recent study indicated that genetic polymorphisms of ORAI1 are involved in the susceptibility to AD in Japanese and Taiwanese populations.[10] Genome-wide association study also identified two new susceptibility loci at 5q22.1 and 20q13.33 for AD in the Chinese Han population.[11] Determining the candidate susceptibility genes for AD will not only help us understand the pathophysiology but will also affect the response to therapy, which is important in pharmacogenetics.

2.2. Allergens

Allergens play an essential role in AD, either intrinsic or extrinsic.[12] They provoke cutaneous inflammation via IgE-dependent and cell-mediated immune reactions.[12] Sensitization to food allergens (egg, milk, wheat, soy, and peanut) is associated with AD and related to disease severity and persistence.[13] Only in a minority of those with food sensitization (about 33% with moderate to severe AD) are food allergens of clinical relevance, as demonstrated by food challenge tests.[13] It is well established that food can exacerbate AD both through allergic and nonallergic hypersensitivity reactions. Furthermore, direct food contact with the skin might be an important factor for the aggravation of AD.[14] Beyond the age of 5 years, food allergy is frequently outgrown, but sensitization to inhalant allergens is common.[6] Exposure to aeroallergens (mites, animal danders, cockroach, molds, and pollen) has been clearly shown to increase the risk factors for AD and AD severity.[1] In humid climate such as that found in Taiwan, fungi are especially important and their impacts might start at the early infant stage.[15] Skin lesions can develop after inhalation challenge with aeroallergens in patients with AD. Moreover, epicutaneous application of aeroallergens on uninvolved skin of patients with AD elicits eczematoid reactions in patients with AD.[14] Therefore, identification of individualized allergen sensitization by skin prick tests or allergen-specific IgE may provide a strategy for better control of AD and avoidance of atopic march.[12]

2.3. Infection

The hygiene hypothesis offers an explanation of why certain environmental exposures early in life may suppress or activate clinical disease. There is evidence to support an inverse relationship between AD and endotoxin, early day care, and farm animal and dog exposure in early life.[16] Helminth infection at least partially protects against AD. This is not the case for viral and bacterial infections.[16] The effect of routine childhood vaccinations on AD risk is controversial. There is a potential risk for AD after receiving Hib combination vaccines. However, the vaccination is important to public health, and therefore the observation requires further investigations.[3]

2.4. Pollutants and chemicals

During the same period that modern pollutants and chemicals have increased, there has been a remarkable increase of allergy in children. Smoke exposure during pregnancy has been demonstrated to increase the risk of AD in children.[17] Exposure to environmental tobacco smoke in childhood is associated with the development of adult-onset AD.[18] Moreover, air pollutants, such as hydrogen sulfide, nitrogen dioxide, carbon monoxide, and formaldehyde, may increase the prevalence and severity of AD.[1,19] Exposures to perfluorinated chemicals, a kind of endocrine-disrupting chemicals, were reported to be positively correlated with blood IgE levels and AD.[20] Early phthalate exposure may also increase the risk of allergic sensitization and AD.[21] The biological effects of these pollutants are different depending on the presence or absence of an antigen, which is called an adjuvant effect.[22]

2.5. Gene and environment interaction

AD is a complex genetic disorder influenced by environmental factors. Based on hereditary and environmental