# **Original Article**

# Increased Prevalence of Atopic Dermatitis in Young Children Born from 2000 to 2009 in Taiwan: A Nationwide Population-Based Study

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**Objective:** Atopic dermatitis (AD) is the most common chronic disease in young children and a major socio-economic burden worldwide. However, longitudinal prevalence data based on physician-diagnosed AD in recent years are scant. We aim to study the trend of prevalence of pediatric AD in Taiwan based on physicians' diagnosis.

**Methods:** This retrospective cohort study was conducted using the National Health Insurance Research Database (NHIRD). Infants and one-year-old children with physician-diagnosed AD were enrolled. The cases were defined according to loose criteria of one outpatient visit and strict criteria of at least three outpatient visits with the diagnosis of AD (ICD-9). We calculated the prevalence of AD in first two years of life in children born from 2000 to 2009.

**Results:** There were between 13,705 and 8,275 neonates born in each year from 2000 and 2009. From 2000 to 2009, the one-year prevalence of AD in the first year of life increased from 6.37% to 16.1% according to the loose criteria, and from 0.81% to 2.82% according to the strict criteria. In the second year of life, the prevalence increased from 3.46% to 6.9% according to the loose criteria and from 0.9% to 3.02% according to the strict criteria. The trend of one-year prevalence increased in children born from 2000 to 2009 in the first year of life with R<sup>2</sup> values of 0.9564 (p < 0.0001) and 0.9292 (p < 0.0001), and in the second year of life with R<sup>2</sup> values of 0.8339 (p = 0.0002) and 0.9201 (p < 0.0001) according to the loose and strict criteria, respectively.

**Conclusion:** The prevalence of physician-diagnosed AD continuously increased in Taiwan in the first and second year of life in children born from 2000 to 2009. This trend represents the continuously increasing burden of AD on the healthcare system in Taiwan.

Key words: atopic dermatitis, prevalence, pediatric, NHIRD

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# Introduction

Atopic dermatitis (AD) is the most common chronic disease in early childhood, and the prevalence has continued to increase in recent decades worldwide. According to the allergic march phenomenon, 50% of children who have AD in the first 2 years of life will subsequently develop asthma.<sup>1</sup> AD is a heterogeneous disease that is influenced by the interaction of genomic and environmental factors. The International Study of Asthma and Allergies in Childhood (ISAAC) in 1995 and 2005 reported continuous increases in the prevalence of AD in Africa, America and parts of Asia but not in some other areas.<sup>3</sup> Several studies have also reported the high prevalence of pediatric AD in different regions in Taiwan.<sup>4</sup> However, longitudinal prevalence data based on physician-diagnosed AD in children in nationwide studies are scant.

Several methods are used to evaluate the prevalence of diseases in children, including physician diagnosis, and questionnaires completed by patients, care-givers, family, and teachers. Questionnaire surveys can be done in a large population. For example, the ISAAC used questionnaires to study the epidemiology of allergic diseases worldwide.<sup>2</sup> However, concerns with the use of questionnaires include the relatively low reliability and validity, as well as recall bias. A cohort study using a physician's diagnosis of a disease to evaluate its prevalence is a preferred method, however such studies are usually limited by a small population due to concerns over human resources.<sup>5</sup>

We conducted this nationwide populationbased study to analyze the one-year prevalence of AD and the trend of prevalence in the first and second year of life in children in Taiwan from 2000 to 2011.

# **Materials and Methods**

## Source of data

We used the data from Department of Statistics in Ministry of the Interior and National Health Insurance Research Database (NHIRD) of Taiwan. The National Health Insurance (NHI) program was initiated in 1995 to provide a healthcare system for all residents in Taiwan. The National Health



Fig. 1 Enrollment flowchart of the first and second year of life in children with atopic dermatitis.



Fig. 2 The rate and the trend of one-year prevalence of atopic dermatitis in the first year of life by loose and strict criteria in children born from 2000 to 2009.

Research Institute (NHRI) of Taiwan manages the medical benefit claims of all 22.9 million residents of the country. Since the medical records of the beneficiaries of the NHI program are de-identified as secondary data for research purposes, this study was exempted from an ethics review. We used the Longitudinal Health Insurance Database 2010 (LHID 2010), which is a subset of the NHIRD containing the complete original claims data of one million insured individuals who were randomly sampled from the NHIRD registry in 2010. All diseases were coded using International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes from 2000.

#### **Study patients**

In this retrospective cohort study, we enrolled infants and one-year-old children diagnosed with physician-diagnosed AD from the National Health Insurance Research Database (NHIRD). We set loose criteria and strict criteria: (1) the loose criteria were the diagnosis of AD (ICD code 691.8) at one outpatient visits during one- year period, and (2) the strict criteria were the diagnosis of AD (ICD code 691.8) in at least three outpatient visits during one year period. The study flowchart is shown in Figure 1.

#### Data analysis

We calculated the one-year prevalence of AD in the first year and second year of life in children according to the loose and strict criteria. We also analyzed the trend of prevalence in these two age groups from fiscal year 2000 to fiscal year 2011. We used descriptive analysis to evaluate the one-year prevalence, and linear regression analysis to calculate the trend of one-year prevalence of AD from 2000 to 2011. All data management and calculations were performed using SAS software version 9.4 (SAS Institute, Cary, NC, USA).

## Results

#### Atopic dermatitis cases

There were between 13,705 and 8,275 neonates born in each year from 2000 and 2009. The numbers of AD cases in the first and second year of life according to the loose and

strict criteria are shown in Table 1 and Table 2, respectively. The male gender is dominant in the first and second year of life.

# One-year prevalence of atopic dermatitis in the first and second year of life in children

The one-year prevalence rates of AD in the first and second year of life in children according to the loose and strict criteria were analyzed. In children from 2000 to 2009, the one-year prevalence of AD increased from 6.37% to 16.1% according to the loose criteria, and from 0.81% to 2.82% according to the strict criteria in the first year of life (Fig. 2), and from 3.46% to 6.9% according to the loose criteria and from 0.9% to 3.02% according to the strict criteria in the second year of life (Fig. 3).

#### Trend of atopic dermatitis in pediatrics

In children from 2000 to 2009, the trend of one-year prevalence increased in the first year of life with R<sup>2</sup> values of 0.9564 (p <0.0001) and 0.9292 (p < 0.0001) (Fig. 2), and in the second year of life with R<sup>2</sup> values of 0.8339 (p = 0.0002) and 0.9201 (p < 0.0001) according to the loose and strict criteria, respectively (Fig. 3).

## Discussion

We conducted this nationwide population-based study to evaluate the prevalence of pediatric AD according to physicians' diagnosis using the LHID 2010 in Taiwan. In children from 2000 to 2009, the one-year prevalence of AD in the first year of life increased from 6.37% to 16.1% according to the loose criteria and from 0.81% to 2.82% according to the strict criteria, and in the second year of life from 3.46% to 6.9% according to the loose criteria and from 0.9% to 3.02% according to the strict criteria. We also found an increasing trend in the one-year prevalence in first and second year of life in children born from 2000 to 2009. To the best of our knowledge, this is the first large-scale study to evaluate the trend of the prevalence of AD in a nationwide population. These findings emphasize the importance of dealing with this major chronic disease in children.

Atopic dermatitis is a chronic disease and usually develops since early infant stage. We analyzed the prevalence and compares to other studies. In children born in 2009, the prevalence rate of AD was 16.1% and 2.82% in the first and 6.9% and 3.02% in the second

 Table 1. Number of children diagnosed as having atopic dermatitis (AD) in first year of life by loose and strict criteria born from 2000 to 2009.

Birth Year	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Total children(n)#	13,705	11,620	10,991	10,045	9,538	9,040	8,938	8,904	8,627	8,275
AD case(n) by loose criteria	873	824	1,034	1,060	1,213	1,104	1,219	1,254	1,302	1,332
Male (%)	55.3	56.7	56.2	58.3	57.1	55.0	56.0	55.0	57.1	55.1
AD case(n) by strict criteria	111	114	142	155	222	188	200	214	238	233

#Retrieved from Department of Statistics in Ministry of the Interior, Taiwan

*Table 2. Number of children diagnosed as having atopic dermatitis(AD) in the second year of life by loose and strict criteria born from 2000 to 2009.* 

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Birth Year	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Total children(n)#	13,705	11,620	10,991	10,045	9,538	9,040	8,938	8,904	8,627	8,275
AD case(n) by loose criteria	474	512	516	527	573	570	617	669	550	571
Male (%)	50.6	53.5	51.4	52.2	51.0	52.8	53.0	51.1	51.8	51.8
AD case(n) by strict criteria	124	124	166	203	224	215	218	241	231	250

#Retrieved from Department of Statistics in Ministry of the Interior, Taiwan



Fig. 3 The rate and the trend of one-year prevalence of atopic dermatitis in the second year of life by loose and strict criteria in children born from 2000 to 2009.

year of life by loose and strict criteria, respectively. In other studies, the prevalence was 6.7% in infants at 6 months of age in 2005 and 7.9% in children at 18 months in 2007 according to Taiwan national birth cohort. In another overall 8-year prevalence study from 2000 to 2007, the mean one-year prevalence was 22.4% in the age group less than one-year old in another NHIRD study by Hwang et al. In general, the prevalence of AD was high, and the absolute prevalence were different according to different criteria and different study methods. In addition, the present study revealed that the prevalence in boys was 54.9% - 58.3% in the first year and 50.6% - 53.5% in the second year of life between 2000 to 2011. This male dominant tendency was the same as previous study.

Some studies have evaluated the trend of the prevalence of AD, including the ISSAC study. According to the ISSAC questionnaire, the prevalence of AD increased from 23.9% in 1994 to 29.8% in 2007 in 6- to 7-year-old children in Taipei.<sup>8</sup> However, it was unclear whether the trend of AD in early children had increased, was stable or had decreased in the last decade. AD can result in school absences, caregiver stress, and increased use of healthcare resources. It usually attacks in early life, and especially before 2 years of age. Therefore, in this study we focused on the first two years of life in children. Mohn et al. reported an increase in the incidence of AD from 0.052 (95% CI, 0.050 – 0.053) in 2009 to 0.073 (95% CI, 0.071 - 0.075) in 2014 for children younger than one year in Norway. Of these cases, 45% were found to occur within the first 6 months of life, and 60% during the first year of life. According to the allergic march phenomenon, 50% of children with AD in the first 2 years of life will subsequently develop asthma later in life. Our study revealed an increasing trend of AD in children born from 2000 to 2009 in Taiwan. Since AD is the initial presentation in allergic march, early prevention strategies for AD should be emphasized to prevent the development of subsequent allergic diseases such as asthma and allergic rhinitis.<sup>1</sup>

The absolute prevalence depended on the different diagnostic criteria of AD used by different studies and methods.<sup>11</sup> In addition to investigating the one-year prevalence rate, the aim of this study was to examine the trend of the prevalence of AD. Accordingly, we set loose and strict criteria for the case definition of AD, and found the same result that the trend of the prevalence of AD increased with both case definitions. According to the literature, using health administrative and survey data to examine the trend of AD is both consistent and reliable.

Atopic dermatitis is a heterogeneous chronic disease caused by the interaction of genomic and environmental factors. There is currently no consensus on the biomedical and environmental factors that contribute to the increased prevalence of AD, however, under the consideration of genetic stability, environmental factors are thought to be responsible for the increased trend. Although many scientific and epidemic studies have been published, the etiology of the increasing prevalence is still unclear. Many factors are thought to contribute to the increasing trend, including genetic factors, obesity, allergens, air pollution and viral infections, and these factors have also been reported in studies conducted in Taiwan. Food allergens and environmental aeroallergens are known to contribute to both AD and respiratory sensitization in individuals of different ages. Prevention strategies include good skin care, dietary management, avoiding allergens, and environmental management. Primary prevention is aimed at preventing and inhibiting sensitization, which can subsequently lead to the development of allergic presentations. Secondary prevention is recommended to avoid sensitized individuals from exposure to environmental triggers. Multiple intervention strategies are necessary to decrease the prevalence of AD, and decrease the healthcare and psych-social burden caused by AD. Since the one-year prevalence is still increasing in the early children in Taiwan, further studies are needed to elucidate the major corresponding etiologies, and the government should establish policies to prevent and control pediatric AD.

There are some limitations to the present study. First, the NHIRD is derived from claims

data of all physicians in the NHI program. The diagnostic criteria may be some difference between physicians. A prospective cohort study can make the diagnosis more consistent. Second, the NHIRD lacks the allergy tests, the severity of AD, or environmental factors, Therefore, we were unable to analyze the correlations between AD and atopy, and other environmental factors in NHIRD database.

In conclusion, this nationwide study in the first and second year of life in children revealed an increasing trend in the one-year prevalence of AD in children born from 2000 to 2009 in Taiwan based on physicians' diagnosis of AD. These findings indicate that the healthcare and socio-economic burden of pediatric AD continues to increase in Taiwan. Further studies are warranted to elucidate the etiology of the increased prevalence so that strategies to prevent and control pediatric AD can be established.

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## References

- 1. Warner JO: Early treatment of the atopic child. Pediatr Allergy Immunol 1997:8(10 Suppl):46-8.
- 2. Kauffmann F, Demenais F: Gene-environment interactions in asthma and allergic diseases: challenges and perspectives. J Allergy Clin Immunol 2012; 130:1229-40; quiz 1241-2.
- 3. Pearce N, Aït-Khaled N, Beasley R, et al: Worldwide trends in the prevalence of asthma symptoms: phase III of the International Study of Asthma and Allergies in Childhood (ISAAC). Thorax 2007:62:758-66.
- Ho CL, Chang LI, Wu WF: The prevalence and risk factors of atopic dermatitis in 6-8 year-old first graders in Taipei. Pediatr Neonatol 2019:60:166-71.
- 5. McKenzie C, Silverberg JI: The prevalence and

persistence of atopic dermatitis in urban United States children. Ann Allergy Asthma Immunol 2019; 123:173-178.e1.

- Wang IJ, Wang JY, Yeh KW: Childhood atopic dermatitis in Taiwan. Pediatr Neonatol 2016;57: 89-96.
- 7. Hwang CY, Chen YJ, Lin MW, et al: Prevalence of atopic dermatitis, allergic rhinitis and asthma in Taiwan: a national study 2000 to 2007. Acta Derm Venereol 2010:90:589-94.
- 8. Wu WF, Wan KS, Wang SJ, et al: Prevalence, severity, and time trends of allergic conditions in 6-to-7-year-old schoolchildren in Taipei. J Investig Allergol Clin Immunol 2011:21:556-62.
- 9. Mohn CH, Blix HS, Halvorsen JA, et al: Incidence trends of atopic dermatitis in infancy and early childhood in a nationwide prescription registry study in Norway. JAMA Netw Open 2018:1:e184145.
- 10. Lin YT, Wang CT, Chiang BL: Role of bacterial pathogens in atopic dermatitis. Clin Rev Allergy Immunol 2007:33:167-77.

- 11. Liao MF, Huang JL, Chiang LC, et al: Prevalence of asthma, rhinitis, and eczema from ISAAC survey of schoolchildren in Central Taiwan. J Asthma 2005:42:833-7.
- 12. Huzel L, Roos LL, Anthonisen NR, et al: Diagnosing asthma: the fit between survey and administrative database. Can Respir J 2002:9:407-12.
- 13. David Boothe W, Tarbox JA, Tarbox MB: Atopic dermatitis: pathophysiology. Adv Exp Med Biol 2017:1027: 21-37.
- 14. Kim J, Kim H, Lim D, et al: Effects of indoor air pollutants on atopic dermatitis. Int J Environ Res Public Health 2016;13:pii: E1220.
- 15. Wang IJ, Lin YT, Yang YH, etal: Correlation between age and allergens in pediatric atopic dermatitis. Ann Allergy Asthma Immunol 2004;93:334-8.
- 16. Sublett JL: The environment and risk factors for atopy. Curr Allergy Asthma Rep 2005:5:445-50.