

# Factors Associated With Atopic Dermatitis In Elementary School Children In Suburban Area In Indonesia: Original Research

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## Abstract

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**Background:** There was limited data of Atopic Dermatitis (AD) prevalence and its associated factors in Indonesia. Therefore, the aim of this study was to identify and evaluate the AD prevalence and factors associated with AD in elementary school children in suburban area in Banten.

**Methods:** A cross-sectional study was conducted in 3 elementary schools children age 6–7 years old who were randomly selected. Information was obtained through an Indonesian version of the International Study of Asthma and Allergies in Childhood questionnaire (ISAAC).

**Results:** From 304 school children in semi-urban area, AD was reported as ever had an itchy rash which was recurrent for at least 6 months in 17.4% of the children, 19.5% of the children had this itchy rash at any time in the past 12 months, and 11.4 % reported doctor-diagnosed AD. The factors found to be associated with an increased risk of AD were allergic rhinitis (OR 2.151 CI: 1.086-4.261), history of premature birth (<37 weeks) (OR 5.306, CI:1.577-17.858), exclusive breastfeeding (OR 3.126 CI:1.314-7.439), and food allergy (OR 2.912 CI:1.386-6.119).

**Conclusion:** The results of this study showed that allergic rhinitis, history of premature birth (<37 weeks), exclusive breastfeeding, and food allergy were factors associated with AD in Indonesian schoolchildren.

## Introduction

Atopic dermatitis (AD) is a chronic inflammatory skin disorder, characterized by cutaneous dryness, intense itching, scratching, skin damage, and secondary infections. Atopic dermatitis (AD) is one of the most common skin diseases in the world, particularly in neonates, children, and adolescents.<sup>1</sup> AD is caused by a combination of genetic and environmental factors. The disease is closely associated

with asthma and allergic rhinitis. Although this disorder is not fatal, it can lead to skin damages, secondary infections, sleep disorders in children and parents, reduced quality of life, high costs, loss of confidence, and reduced functional capacity that can interfere athletic activities and social relationships.<sup>2,3</sup>

As a result of previous studies based on ISAAC, the incidence of AD in the infant population was estimated to be 15–20%, showing an increase in prevalence.

It has also compared the prevalence among the different countries and showed differences in each region.<sup>4</sup> The prevalence of AD is reported to be 17.2% in American children, 15.6% in European Children, 24% in Japanese children aged 5-6 years old, 19.1% in Korea, and 20% in other countries. The prevalence of allergic diseases has increased not only in high income but also in low-to-middle income countries (LMIC), such as Indonesia.<sup>1</sup>

There is a wide spectrum of presentations of atopic eczema, from minimal flexural eczema to erythroderma. The skin of a child with eczema is generally dry. The eczema can occur anywhere, but there are particular patterns that are more common at certain ages. The face is usually the first to be affected. In crawling infants the forearms, extensor aspects of the knees, and the ankle flexures are often the most affected. In older children the flexor aspects of the elbows and the knees are mostly affected. The eczema may be moist and weeping or may be thickened (lichenified) and dry. In children with darker skin the rash may have a papular nature. Scratch marks are always seen.<sup>1</sup>

For primary, secondary and tertiary prevention of childhood AD, it is crucial to determine the factors which are associated with the development or exacerbation of AD. Known associated factors linked to the incidence of AD from previous studies were the presence of asthma or rhinitis symptoms, positive family history for allergic diseases<sup>5</sup>, indoor allergens such as dust mite, animal dander and fur<sup>6</sup>, environmental tobacco smoke (ETS)<sup>7</sup>, exclusive breastfeeding history<sup>8</sup>, low birth weight, prematurity, house mould, higher exposure to air pollution, smaller families with less exposure to infections, animal contact in first year of life and within the last year, higher maternal age, consumption of paracetamol in first year of life and within the last year<sup>9</sup>, and a wider range of foods.<sup>2,3,10</sup> The association between atopic eczema and food allergy is complex, though it is usually children with severe atopic eczema have food allergy.<sup>2</sup>

There was limited data of AD prevalence and its associated factors in Indonesia. Therefore, the aim of this study was to identify and evaluate the AD prevalence and factors associated with AD in elementary school children in suburban area in Indonesia.

## **Material And Methods**

### ***Study design and subjects***

This cross-sectional study was performed in January 2018. A total of 304 children, chosen from a random sample of 3 elementary schools in Tangerang, Indonesia, were included in this study. After coordination with the schools under study, researchers presented letters referred to schools according to ISAAC protocol, and obtain informed consent. Based on ISSAC protocol, after distributing the questionnaires, each question was explained by a trained interviewer. The questionnaires were completed preferably by the parents and by the students themselves if the parents were absent. The data collected were entered into Microsoft Excel.

### ***Questionnaires***

Allergic disorders were assessed with a validated questionnaire for age 6-7 years old developed by International Study of Asthma and Allergy in Childhood (ISAAC) which had been translated into Bahasa Indonesia to accommodate local study requirements. AD ever was defined as a positive response to the question "Have you ever had an itchy rash which was coming and going for at least 6 months?" The prevalence of asthma symptoms were obtained from the questions: "Has your child and family member ever had wheeze?" The prevalence of rhinitis symptoms were obtained from the following questions: "Has your child and family member ever had a problem with sneezing or a runny or blocked nose when you (he/she) did not have a cold or the flu?"

An additional questionnaire was administered to obtain demographic data, socioeconomic status, parental education, parental occupation, and other potential associated factors for the development of allergies. The potential associated factors that were investigated included the following: gender, birth weight, delivery time, number of siblings, exclusive breastfeeding history, parental asthma or allergic rhinitis or atopic dermatitis, exposure to animals in the first year of life and within the last year, exposure to tobacco smoke in at home, dampness and mold in the house, food allergy, cooking method in the house, and paracetamol consumption in the first year of life and within the last year.

Written informed consent was obtained from parent or guardian of each child. The study was approved by the Ethical Committee of the Medical Faculty, University of Pelita Harapan (ethical clearance ref: 006/K-LKJ/ETIK/VIII/2017)

### Statistical analysis

The collected data were analyzed using SPSS ver.22 (IBM, 2018). To investigate the relationship between associated factors and AD, the analysis was carried out using the *Chi-square* test, and its odds ratio (OR) and confidence interval of 95% were calculated. Statistical significance was set at  $P < 0.05$ .

### Result

Data were collected from 304 school children in semi-urban area. AD was reported as ever had recurrent itchy rash for at least 6 months in 17.4% of the children, 19.5% of the children had this itchy rash at any time in the past 12 months, and 11.4 % reported doctor-diagnosed AD. The associated factors for AD were described in table 1. In this study, the Odd ratio of asthma in patients with AD was 1.08, CI: 0.388-3.006, p value 0.884 and Odd ratio of allergic rhinitis patients with AD was 2.151 CI: 1.086-4.261, p value 0.026. Of the children with AD, 4.8% were born prematurely (<37

weeks), OR 5.306, CI:1.577-17.858, p value 0.003, 61.3% had exclusive breastfeeding (breastfed for 6 months or more), OR 3.126 CI:1.314-7.439, p value 0.007, and 17.2% had food allergy, OR 2.912, CI:1.386-6.119, p value 0.004. Household pets during infancy (in the first year of child's life) was present in 79.9% of the children, OR 0.639, CI: 0.305-1.339, p value 0.233, household pets at present (in the last 1 year) was present in 94.2% of the children, OR 0.432, CI: 0.143-1.306, p value 0.127. The Odd ratio of exposure to cigarette smoke (at present) in children with AD was 1.679, CI:0.894-3.153, p value 0.105. The family income were described in table 2.

The factors found to be associated with an increased risk of AD were allergic rhinitis, history of premature birth (<37 weeks), exclusive breastfeeding, and food allergy. However, gender, asthma, household pets (during infancy), household pets (at present), exposure to cigarette smoke (at present), and family income showed no statistical significance as a associated factor for AD.

**Table 1.** Factors associated with atopic dermatitis in children

Risk factors	%	OR (95% CI)	P value
gender (female)	47.6 %	1.36 (0.74-2.52)	0.315
asthma	9.6 %	1.08 (0.388-3.006)	0.884
allergic rhinitis	60 %	2.151 (1.086-4.261)	<b>0.026</b>
prematurity	4.8 %	5.306 (1.577-17.858)	<b>0.003</b>
exclusive breastfeeding	61.3 %	3.126 (1.314-7.439)	<b>0.007</b>
food allergy	17.2 %	2.912 (1.386-6.119)	<b>0.004</b>
household pets (during infancy)	79.9 %	0.639 (0.305-1.339)	0.233
household pets (at present)	94.2 %	0.432 (0.143-1.306)	0.127
exposure to cigarette smoke (at present)	50.7 %	1.679 (0.894-3.153)	0.105
family income			0.374

**Table 2.** Family income

Family income	%
< Rp 1,000,000	19.1%
Rp 1,000,000 – 3,000,000	38.1%
Rp 3,000,000 – 5,000,000	28.9%
>Rp 5,000,000	13.9%

## Discussion

In our study, factors found to be associated with an increased risk of AD were allergic rhinitis, history of premature birth (<37 weeks), exclusive breastfeeding, and food allergy. However, we did not find any relation between AD and other risk factors including gender, asthma, household pets (during infancy), household pets (at present), exposure to cigarette smoke (at present), and family income. Our findings were consistent with the previous studies which showed that presence of allergic rhinitis, history of premature birth (<37 weeks), and food allergy were associated with increased risk of AD.<sup>10</sup>

Patients with AD have higher rates of allergic diseases than the general population. 80% of children with AD develop asthma and/or allergic rhinitis later in life and referred to as the "allergic march" or "atopic march". The cutaneous manifestations of atopy often represent the beginning of the atopic march. Approximately half of AD patients will develop asthma, particularly with severe AD, and two thirds will develop allergic rhinitis. Epicutaneous sensitization with subsequent migration of sensitized T cells into the nose and airways, causing upper and lower airway disease.<sup>11</sup>

Ten to twenty percent of patients with AD have food-induced urticaria/anaphylaxis compared with 1-3% of the general population.<sup>12</sup> The current hypothesis is that cutaneous sensitization through disrupted skin barrier leads to food sensitization and food allergies. Defects in serine peptidase inhibitor, Kazal type 5 (SPINK5) are associated with food challenge-proven food allergy.<sup>13,14</sup> In addition, skin barrier impairment at birth which is measured by

higher transepidermal water loss (TEWL) predicts food allergy at two years of age.<sup>15</sup> Earlier onset (<3 months of age) and more severe AD is associated with high egg, milk, and/or peanut-specific IgE.<sup>16</sup> Patients with AD and concomitant egg, peanut, or dust mite allergy are more likely to have AD that persists beyond five years of age.<sup>17</sup> Infants and young children with AD are more commonly sensitized to foods<sup>18</sup>, whereas children over five years and adults are more commonly sensitized to aeroallergens (dust mite sensitization is most prevalent in both children and adults).<sup>19</sup> And vice versa, food allergies play a role in exacerbating AD in up to 33% of patients with severe AD, 10 – 20% with moderate AD, and 6% with mild AD. Elimination of food allergens in patients with AD and confirmed food allergy can lead to significant AD improvement.

Relation of breast-feeding with IgE as allergic marker in childhood is complex and early production of food-specific IgE is associated with an elevated risk for allergic outcomes. Among children of mothers with high IgE levels, breast-feeding was associated with elevated IgE levels relative to never breast-fed children in that maternal IgE strata. Thus exclusive breastfeeding cause immediate, continuing, and high-volume exposure to antigens, including bacteria and allergens, which might alter inherited predisposition toward IgE production. Other explanation is that breast-feeding associated with lower infections in early life which might stimulate the infant immune system toward an allergic (TH2) rather than an antimicrobial (TH1) response and encourage persistence of the TH2 immunity, particularly in the context of a genetic predisposition toward IgE production.<sup>20</sup> Premature birth (<37 weeks) infants might have higher risk of AD because they have immature skin barrier that cause increased permeability and transepidermal water loss.<sup>21</sup>

Exclusive breastfeeding, household pets during infancy and at present effects on AD is still controversial, where exclusive breastfeeding, household pets (during infancy), and household pets (at

present) were found as both risk and protective factors of AD. Previous studies showed that female gender, asthma, exposure to cigarette smoke (at present), and high family income were significant risk factor for AD, which were not in agreement with our result.

The limitation of this study was our study design was a cross-sectional survey which cannot identify the causal relationship. In addition, the diagnosis of AD was based on a questionnaire, not by detailed history and physical examination. Further investigation by prospective cohort study is required to prove the causal relationship between the development of AD and risk factors in Indonesian children. Because AD might be an 'entry point' for the subsequent development of asthma or allergic rhinitis, children with AD need proper management to prevent

epicutaneous sensitisation leading to systemic immune response. There was no conflict of interest in this study.

### Conclusion

The results of this study showed that allergic rhinitis, history of premature birth (<37 weeks), exclusive breastfeeding, and food allergy were factors associated with AD in Indonesian schoolchildren.

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