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Age and Nutritional Status as Factors Supporting Incidence of Atopic Dermatitis with Complications in Children: A Retrospective and Cross-Sectional Study

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ABSTRACT

Background: AD is a chronic, pruritic inflammatory skin disease that frequently occurs and common in infants and children. **Purpose:** This study aims to analyze the correlation of age, sex, nutritional status, and family history of atopy with the occurrence of AD complications in children. **Methods:** This study used a cross-sectional study design in pediatric AD patients aged 0-18 years. Data were collected from electronic medical records (EMR) of pediatric AD patients at the Dermatology Outpatient Clinic of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, from January to December 2019. The bivariate analysis in this study used the Chi-square test. The statistical test was significant, as indicated by p-value ($p < 0.05$). **Result:** Out of 80 eligible participants, a total of 53.75% of the participants were children aged 1-60 months, and 55% of total were female. In this study, 28.75% of participants had normal nutritional status. A total of 67.5% of patients had no family history of atopy. There was a significant relationship between age and nutritional status with the incidence of AD with complications (p=0.006 and 0.040), but no relation was found between sex and family history of atopy (p=0.444 and 0.644). **Conclusion:** Age and nutritional status have a correlation with the incidence of AD with complications.

Keywords: atopic dermatitis, factors, complications, children, human and disease.

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BACKGROUND

Atopic dermatitis (AD) is defined as a chronic, pruritic, inflammatory skin disease that frequently occurs.[1] AD is common in infants and children and associated with abnormalities in skin barrier function, allergen sensitization, and recurrent skin infections. The prevalence of AD is estimated at 15-20% in children and 1-3% in adults, and the incidence has increased threefold over the last few decades in industrialized countries.[2]

Some of the complications of AD in a more advanced stage include asthma, allergic rhinitis, skin infections, and psychosocial disorders. AD is considered an early stage of atopic march, and children with AD are at increased risk of developing asthma and allergic rhinitis.[3] The appearance of AD often indicate the development of asthma and/or allergic rhinitis (hay fever) in older children.[4] The most common complication of AD, secondary infection, occurs as a result of disruption of the epidermal barrier and altered immune response.[5] Virus, fungi, and bacteria take advantage of the decreased skin barrier function in atopic individuals, colonize the skin, release proinflammatory products (such as superantigens and proteoglycans), and modulate leukocyte activation.[6] In addition, damage to the skin barrier also causes an increase in transepidermal water loss (TEWL) and the pH of the skin becomes more alkaline, thereby causing

changes in the bacterial flora of the skin. In one study, it was found that the higher the severity of AD, the higher the TEWL and pH, both in the lesion area and non-lesion area.[7]

Chronic pruritus (itching), sleep deprivation, and time cost associated with therapy are often aspects of concern for patients and families. AD is associated with poor school performance, low self-esteem, and family dysfunction.[8] The ratio of women to men in AD is 1.14:1. In a study conducted by Ziyab, et al. at Atar-Snir[9], AD in children aged 1-10 years were not affected by sex, but at the age of 10-18 years, AD was more common in girls.[9] As many as 85% of children experience AD before the age of 5 years.[3] The prevalence of several allergic diseases such as AD and asthma is especially high in very young children.[10] AD is mainly seen in infancy, whereas 45% notice the first symptoms in the first 6 months after birth, 60% in the first year of life, and 85% before age 5.[11]

In one study, it was shown that childhood obesity was related to a higher incidence of AD (OR=2.00, 95% CI=1.22-3.26, p=0.006). Obesity was associated with more severe AD manifestations (OR=2.37, 95% CI=1.24-5.37, p=0.010).[12] Children with a history of atopy in 1 or 2 parents, had AD 37.9% and 50%, respectively.[13] A history of atopy in a parent or sibling supports the diagnosis of AD, and is a strong risk factor for the development of the disease. Many risk factors are associated with the development of AD, such as female, obesity, and a family history of atopy.[13]

Based on the explanation above, researchers are interested in analyzing risk factors for complications in AD in children. This study aims to analyze the correlation of age, sex, nutritional status, and family history of atopy with the occurrence of AD with complications in children.

METHODS

This study used a cross-sectional study design in pediatric AD patients aged 1 month - 18 years. Data on characteristics, nutritional status, and diagnosis were obtained from electronic medical records (EMR) of pediatric AD patients at the Dermatology Outpatient Clinic of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, from January to December 2019. The subjects that haven't complete data were excluded. The bivariate analysis in this study used the Chi-square test. The statistical test was significant, as indicated by the p-value ($p < 0.05$). Measurement data was analyzed with IBM SPSS statistical software version 25 (IBM Corp., Armonk, NY, USA). This study was approved by the Ethics Committee of Dr. Soetomo General Academic Hospital.

RESULT

We obtained data of total 185 AD patients at the Dermatology and Venereology Outpatient Clinic from the period January – December 2019. Among them, 86 (46%) are pediatric patients aged 1 month – 18 years, 76 (41%) are adult patients, 12 (7%) are pre-elderly (aged 45–59 years), and the remaining 11 (6%) are elderly patients (aged ≥ 60 years). We exclude 6 patients with incomplete data. As shown in Figure 1, the number of eligible participants is 80.

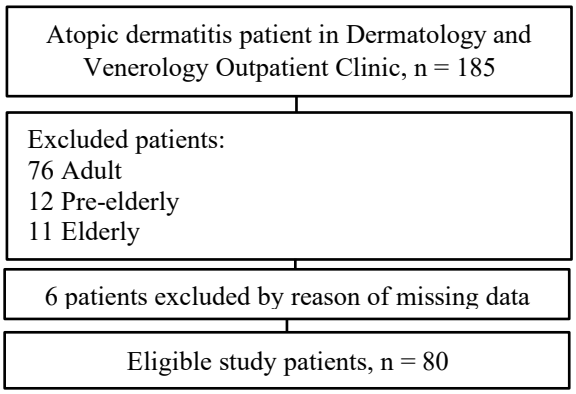

Figure 1. Participant selection process.

The characteristics of participants are shown in Table 1. A total of 53.75% of the participants are children aged 1-60 months, and 55% of the total is female. Nutritional status is calculated based on the table of BMI per age of participants, based on Minister of Health Regulation (PERMENKES) No. 2 in 2020. In this study, 28.75% of participants have normal nutritional status. A total of 67.5% of patients have no family history of atopy, and 76.25% of participants have AD without complications.

As shown in Table 2, there is a significant relation between age and the incidence of AD with complications (OR = 4.626; p = 0.006). There is no relation between sex and AD with complications. Most female participants experience AD without complications (79.5%), compared to 72.2% of male participants (OR = 0.669; p = 0.444). Similarly, 73.1% of participants with a family history of atopy and 77.8% of participants without a family history of atopy experience AD without complications (OR = 1.289; p = 0.644). There is a significant relation between nutritional status and the incidence of AD with complications (OR=0.331; p=0.040).

Table 1. Characteristics of participants

Characteristics	n (%)
Sex	
Male	36 (45)
Female	44 (55)
Age (months)	
1-60	43 (53.75)
61-120	25 (31.25)
121-216	12 (15)
Nutritional status	
Severely wasted	9 (11.25)
Wasted	0 (0)
Normal	23 (28.75)
Possible risk of overweight	4 (5)
Overweight	22 (27.5)
Obese	22 (27.5)
Family history of atopy	
Yes	26 (32.5)
No	54 (67.5)
AD with complications	
Yes	19 (23.75)
No	61 (76.25)
Diagnose	
AD + allergy	1 (1.25)
AD + secondary infection	11 (13.75)
AD + pyoderma	1 (1.25)
AD + scabies	2 (2.5)
AD + scabies + acanthosis nigricans	1 (1.25)
AD + xerosis cutis	3 (3.75)
AD only	61 (76.25)

*AD = Atopic Dermatitis

Table 2. Analytical results.

Variables	AD with complications		OR	*p*
	No	Yes		
Age			4.626	0.006*
≤ 60 months	38 (88.4)	5 (11.6)		
> 60 months	23 (62.2)	14 (37.8)		
Sex			0.669	0.444
Male	26 (72.2)	10 (27.8)		
Female	35 (79.5)	9 (20.5)		
Family history of atopy			1.289	0.644
Yes	19 (73.1)	7 (26.9)		
No	42 (77.8)	12 (22.2)		
Nutritional status			0.331	0.040*
Normal	14 (60.9)	9 (39.1)		
Not normal	47 (82.5)	10 (17.5)		

*Significant if $p > 0.05$

AD = Atopic Dermatitis

DISCUSSION

In this study, the data revealed, 88.4% of children aged ≤ 60 months had AD without complications, while 62.2% children aged > 60 months had AD without complications. The number of patients who develop AD with complications was increase along with age. There are several possible causes. AD is a multifactorial disease, caused by interactions between genetic susceptibility genes that result in the breakdown of the skin barrier, damage to the immune system, and increased immune response (sensitization) to allergens and microbial antigens.[4] Meanwhile, children's immune systems are immature and especially susceptible to bacterial infections.[14] In one study, it was found that children aged 5 years had significantly higher Th17/Th2 inflammatory cytokines.[15]

One study evaluated spontaneous histamine release from basophils in children with and without AD aged 0.3-8 years. As a result, children with AD, with and without IgE antibody sensitivity to food allergens, showed "basophil hyperactivity".[16] However, the diagnosis of AD is still based on clinical grounds, and so far, no reliable biomarker has been found to distinguish AD from other diseases. Several new findings related to subsets of T lymphocytes, cytokines, and chemokines, have the potential to be biomarkers, such as serum levels of CD30, interleukin (IL)-12, -16, 18, -31, and others.[17] In a study measuring IL-31 levels in AD patients, it was found that serum IL-31 levels in AD patients with severe AD tend to have higher serum IL-31 levels than patients with moderate or mild severity, and patients with moderate severity tend to have higher IL-31 levels than patients with mild severity.[18]

In a study conducted by Hong *et al*. (2012)[10], the prevalence of AD is especially high in children 0-3 years and 4-6 years, but the prevalence decreases with age. AD generally causes itching and sleep disturbances, affecting both boys and girls, but more common in children under 10 years of age. In pediatric AD, xerosis is more common, causing rough, flaky, and cracked skin. Lichenification or thickening of the skin, is more common in children over 10 years of age and adults.[19] Excoriations and crusting are also common and can lead to secondary infection.[12]

This study did not find a significant relation between sex and the incidence of AD with complications. Female and male participants, 79.5% and 72.2%, respectively, had no complications. Often, the prevalence of sex depends on the demographics factors of an area. AD in pre-school children did not show any significant difference in terms of sex dominance.[20] In one study, positive skin test results

were found to be more common in men. Meanwhile, clinically asymptomatic sensitization is more common in women.[21] In another study examining sex hormone levels in boys and girls, the prevalence of AD in children was slightly higher in boys than in girls, but after puberty, it was the opposite, so the balance of sex hormone-modulating effects on immune responses and the skin barrier may possibly affect the course of DA.[22]

This study did not find a significant association between a family history of atopy and the incidence of AD with complications. 73.1% and 77.8% of participants, with and without a family history of atopy, respectively, had no complications. In a study conducted by Wen et al. (2009)[23], a history of atopy in parents can be used to calculate the predictive probability of AD up to 70.1% in men with maternal education level > 12 years, both parents with AD, renovating and painting of house during pregnancy, and mold on the walls at home, but the lowest probability (3.1%) was also found in girls who did not have the factors above.

There is a complex inherited pattern for allergic disease (AD, asthma, allergic rhinitis), so a detailed family history of atopy, including childhood and adult experiences, is important for identifying and classifying risk and disease phenotypes.[24] A family history of atopy alone is not a diagnostic criterion for AD but can help confirm the incidence of AD.[25] Genetic and epigenetic variations may be key to the molecular taxonomy of AD and provide the background for personalized management of AD patients.[26]

This study found a significant relation between nutritional status and the incidence of AD with complications. According to Zhang and Silverberg (2015)[27], overweight or obese children have a higher likelihood of suffering from AD (OR=1.32; 95% CI=1.15-1.51). This relevancy is significant in North America and Asia, but not in Europe. It is possible that an increase in Body Mass Index (BMI) predisposes to AD. Obesity is a proinflammatory condition, and AD is a chronic inflammatory dis (ease.[28] Adipose tissue is considered an endocrine organ, and leptin/estrogen (found at higher concentrations in women) can modulate the Th2 dominance frequently found in allergic inflammation diseases such as AD.[29] Furthermore, obesity is associated with an increased prevalence and severity of AD, obesity is a modifiable risk factor for AD, so controlling body weight may prevent or cure AD.[12]

Limitations in this study were the limited number of participants, incompleteness and variety of data, and difficulty of data collection due to the COVID-19 pandemic. There may be uneven distribution of data and bias in the calculations because there are participants who were excluded from the analysis due to incomplete data. Further research is needed by adding more data quantities and variables to improve accuracy. From 80 participants, more than half of total were female, children aged ≤ 60 months, had no family history of atopy, and more than three quarters had AD without complications.

This study found a significant relation between age and nutritional status with the incidence of AD accompanied by complications, while sex and family history of atopy did not show a significant relation.

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