Association between obesity and history of atopy with atopic dermatitis in children: A cross-sectional study

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Abstract

Background: The prevalence of atopic dermatitis (AD) has rapidly increased in the past 4 decades and has been mostly observed in children. The prevalence of obesity has also significantly increased worldwide, suggesting that the two conditions may be associated.

Methods: This retrospective analytic study involved a cross-sectional design and used secondary data taken from the medical record of patients who visited the Pediatric Dermatology Subdivision at Dermatology and Venereology Polyclinic Sanglah General Hospital from January 2015 to December 2015. Thirty-two samples were selected.

Results: The prevalence ratio of obesity among subjects with AD was 2.178 (95% CI = 1.034–4.587; p < 0.05), which indicated a significant association between obesity and AD. This study also found a significant association between the history of atopy and AD, and the prevalence ratio was 2.566 (95% CI = 1.099–5.990; p < 0.05). The risk of developing AD among children with obesity was higher than that among children without obesity.

Conclusion: Obesity and history of atopy were significantly associated with AD in children.

Keywords: atopic dermatitis, children, history of atopy, obesity

Background

Atopic dermatitis (AD) or eczema is a chronic and recurrent inflammatory skin disease. Its prevalence has increased rapidly to as high as 20% in children and adolescents and has become a global health issue. Epidemiological data have shown that the prevalence of AD is about 25%–30% of the global population. In Indonesia, the prevalence of AD is approximately 10% of the population, which mostly involves children and individuals in the productive age. According to reports on hospital visits of babies and children in Indonesia, AD ranks first among the 10 skin diseases affecting children.

The etiology of AD is multifactorial. Previous studies found that obesity is related to a disrupted skin barrier function. It also leads to a low degree of chronic inflammatory condition that can affect the AD inflammation pathway. Therefore, obesity can induce or worsen AD. Obesity is a condition marked by excessive fat tissue accumulation inside the body. It can occur at any age, but it is most frequently found in early life until ages 5–6 years old and adolescence. Childhood obesity may also lead to a complex issue.

The increasing prevalence of allergic diseases is associated with genetic and environmental factors. Several studies have proven the association between genetic factors, such as patient and family history of atopy, and AD incidence. The history of atopy may be used as the best predictor associated with atopic diseases (e.g., AD, asthma, allergic rhinitis, and allergic conjunctivitis). The history of atopy is also one of the criteria for establishing the diagnosis of AD based on Hanifin–Rajka and UK Working Party criteria. The history of atopy in an individual likely involves IgE antibody production in response to allergen exposure, leading to the clinical manifestation of atopic diseases, such as asthma, allergic rhinitis, allergic conjunctivitis, or AD.
Various studies have investigated the association between obesity and atopic diseases, including asthma, allergic rhinitis, allergic conjunctivitis, and AD. Several narrative reviews have been conducted to investigate the association between obesity and AD. Obesity is related to the increasing prevalence and severity of AD. Obesity is also known as a modified risk factor and comorbidity of AD. Reducing body weight may prevent or decrease the severity of AD. Obesity may also induce atopic diseases or inflammation. Some studies have found a positive association between obesity and atopic diseases. In addition to obesity, an individual's history of atopy has an important role in AD development. Previous reviews about the association between obesity and history of atopy with AD had a significant implication for public health to control body weight to prevent the occurrence of atopic diseases, especially AD, and observe the history of atopy as one of the risk factors of AD. Our study aimed to investigate the association between obesity and the history of atopy with AD in children in Dermatology and Venereology Polyclinic Sanglah General Hospital.

**Methods**

**Study Subject and Data Source**

This analytic retrospective study involved a cross-sectional design. AD was set as a dependent variable, whereas obesity and history of atopy were used as independent variables. The study population comprised 361 children who visited the Pediatric Dermatology Subdivision of Dermatology and Venereology Polyclinic Sanglah General Hospital from January 1, 2015, to December 31, 2015. The sample of this study included 32 children. This study was conducted from February 2016 to March 2016, and the secondary data taken from patients' medical records were used.

Ethical approval was obtained from the Research Ethics Review Board at the Faculty of Medicine Udayana University/Sanglah General Hospital Denpasar. The inclusion criteria of this study covered 2-to-14-year-old patients who visited Dermatology and Venereology Polyclinic Sanglah General Hospital and patients who were diagnosed with AD and fulfilled the Hanifin–Rajka AD diagnosis criteria. The Hanifin–Rajka criteria consisted of 4 major criteria and 23 minor criteria, which encompassed a set of clinical symptoms and signs, aggravating or environmental factors, abnormal findings from invasive tests, ophthalmic findings, and personal or family history of atopic diseases. These criteria became a standard reference for clinical trials in AD because of their high sensitivity, which was 93% in the study of Williams et al. and 96% in the study of De et al. Patients with incomplete medical records were excluded from this study.

**Measurement**

All the demographic data of the study subjects were taken from their medical records. Anamnesis and physical examination were performed at the Dermatology and Venereology Residence of Medical Faculty Udayana University/Sanglah General Hospital to establish the diagnosis of AD based on Hanifin–Rajka criteria. Body weight and height were determined upon patient's visit to Dermatology and Venereology Polyclinic Sanglah General Hospital and documented in the medical record. Body weight was measured using a manual body weight scale (kg), while height was measured in a standing position using a height-measuring instrument (in cm). Obesity is clinically defined as a condition in which the body mass index (BMI) of children is more than 95 percentiles on the children's growth and development chart. BMI, which is a clinical standard to define general obesity, was calculated by determining the body weight in kilogram divided by height in centimeter squared. The BMI of the study subjects was identified using age-specific BMI based on a Center for Disease Control and Prevention (CDC) chart for boys and girls aged 2–20 years. A BMI based on a CDC standard is commonly used in clinical practice in the United States; however, percentile is only available for patients aged 2 years or more.

**Data Analysis**

Data were statistically analyzed using SPSS version 20.0. Data analysis included descriptive data analysis to obtain the characteristics of the study subjects. Bivariate analysis involving a chi-square test was performed to obtain the prevalence ratio of obesity and history of atopy in the study subjects with AD.

**Results**

Table 1 shows the characteristics of the subjects in this study including age, gender, body weight, height, BMI, and history of atopy. Most of the study subjects (59.38%) resided in Denpasar. Table 2 presents the significant association between obesity and history of atopy with AD.
Table 1. Characteristics of the Study Subjects with and without Atopic Dermatitis (AD) at the Pediatric Dermatology Subdivision of Dermatology and Venereology Polyclinic Sanglah General Hospital from January 2015, to December 2015

|                              | All subjects | Subjects with AD | Subjects without AD |
|------------------------------|--------------|-----------------|---------------------|
| Number of subjects           | 32           | 19              | 13                  |
| Mean age (year)              | 5.56 ± 0.57  | 6.00 ± 0.79     | 4.92 ± 0.76         |
| Boy                          | 19           | 10              | 8                   |
| Body weight (kg)             | 23.38 ± 1.468| 24.11 ± 2.15    | 22.31 ± 1.81        |
| Height (cm)                  | 106.22 ± 2.734| 106.05 ± 3.82  | 106.46 ± 3.94       |
| BMI (kg/cm²)                 | 20.21 ± 0.54 | 29.71 ± 0.71    | 19.47 ± 0.82        |
| Obesity                      | 18           | 14              | 4                   |
| History of atopy             | 19           | 15              | 4                   |

Table 2. Association Between Obesity and History of Atopy with Atopic Dermatitis

| Atopic dermatitis | p-value | PR  | 95% CI |
|-------------------|---------|-----|--------|
| Yes               | 0.016*  | 2.178 | 1.034 – 4.587 |
| No                |         |      |        |
| History atopy     | 0.006*  | 2.566 | 1.099 – 5.990 |

* Significant association with p < 0.05, PR = prevalence ratio, CI = confidence interval, n = number

Discussion

This cross-sectional study found that obesity was significantly associated with AD in children (PR = 2.178; 95% CI = 1.034–4.587; p < 0.05). Obesity also increased the risk of developing AD by twofold compared with that in individuals without obesity. Individuals with obesity were also more prone to developing AD than individuals without obesity. Individuals with obesity would also visit doctors more often because of their condition. Childhood obesity may be a significant risk factor of developing adulthood obesity and may progress into medical and psychosocial issues. As such, obesity has been declared as one of the risk factors of developing asthma, diabetes, secondary infection, cardiovascular disease, and academic and psychosocial function disturbance.\textsuperscript{11,12}

Some controversies regarding the association between obesity and AD have been noted; nevertheless, some studies have found a positive correlation between obesity and AD. In a study in Canada, Chen et al. obtained a significant association between obesity and atopy with an adjusted odds ratio of 1.33 (1.04–1.71). In 2015, Silverberg et al. found that obesity in children is associated with increased odds of AD and that these AD-predisposing effects are observed when obesity starts before 5 years of age; the highest odds are recorded in the first 2 years and when obesity persists for more than 2.5 years. Obesity is also associated with increased odds of more severe AD and more frequent visits to pediatricians.\textsuperscript{2,4}

The results of this study were consistent with previous findings, which demonstrated the association between obesity in children and AD in adolescents; other studies have revealed a significantly high risk of AD in individuals with a high BMI.\textsuperscript{6,12} Previous studies also found that obesity has become an epidemic in the United States and may have contributed to the increasing prevalence of AD. The prevalence of AD has increased by more than twice over the past 5 decades. Similarly, the prevalence of obesity doubled in children and adolescents in the United States between 2007 and 2008. This study also revealed that obesity might contribute to the increasing prevalence of AD.\textsuperscript{1}

The mechanism of the association of obesity and AD remains unknown, although several mechanisms likely involved in the pathogenesis of this association have been proposed. For example, alterations in leptin activities in individuals with obesity interfere with the immune system. This condition subsequently triggers the immune system to elicit an inflammatory response. In

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individuals with obesity, leptin induces macrophage and cytokine activation. Another study has shown that obesity may affect adipokines, which contribute to the pathogenesis of AD. Furthermore, increased levels of cytokines, such as TNF-α, IL-6, and IL-12, are commonly found in individuals with obesity. Several studies have found increasing level of Th2, IL-4, and IL-13 in individuals with asthma and obesity, thereby confirming the interaction between obesity and bronchial asthma incidence. Obesity may induce a prolonged inflammation process, which leads to increased C-reactive protein (CRP), proinflammatory cytokine, and leptin levels. CRP is an inflammatory marker that also plays an important role in the pathogenesis of AD in individuals with obesity.¹ ² ⁶

The results of this study found that 78.9% of the subjects with AD also had a history of atopy. Several longitudinal studies have supported this finding and stated that the history of atopy is related to the incidence of AD. One-third of patients with AD will likely suffer from asthma in the future, and the remaining proportion will possibly have allergic rhinitis. Other studies have shown that 34.1% of children with AD have asthma, while 57.6% of children with AD have a history of rhinitis. Furthermore, about 43% and 45% of individuals with AD have rhinitis and asthma, respectively. In a study in Turkey, 21% of children with asthma also have AD, ¹² ¹³ ¹⁵ ¹⁶

This study found a significant association between the history of atopy and AD, and the prevalence ratio was 2.566 (95% CI = 1.099–5.990; p < 0.05). This prevalence ratio showed that the risk of having AD in individuals with a history of atopy increased by 2.5 times compared with that in individuals without a history of atopy. Individual with a history of atopy will more likely have AD compared with individual with no history of atopy. In a study in France, asthma is correlated with rhinitis and AD (OR = 0.72 and 0.24). In another study performed in Turkey in 2008, asthma is significantly associated with rhinitis and AD. Subjects with AD have a history of asthma (28.1%) and a history of rhinitis (56.3%; OR = 2.41 and 4.26). A cohort study in New Zealand has also revealed a significant correlation between asthma and AD (OR = 2.4; 95% CI = 1.3–4.6).¹³ ¹⁶ ¹⁷

Similar to the findings of this study, previous results indicated that individuals with a history of atopy are more likely to have AD than individuals without a history of atopy. In a nested case-control study on 2,201 school children aged 5–14 years in East Germany, 75% of children with AD have a history of atopy and had more than one positive radioallergosorbent test (RAST) compared with children without AD (35%).¹⁴ ¹⁸

The association between history of atopy and AD is possibly attributed to a genetic basis in all these atopic diseases. Several studies have revealed the relation of chromosomal AD with asthma in chromosomes 5, 11, and 13. Immunologic characteristics such as increased IgE and eosinophil levels have also been observed in these atopic diseases.⁸ ⁹

This study had several weaknesses. The sample size was limited, so the results of this study might not represent the actual population. This study involved a cross-sectional design, which might not confirm the causal association between obesity and the history of atopy with AD. The history of atopy was also not categorized in this study. In future studies, the history of atopy should be classified into the history of asthma and allergic rhinitis to provide more informative and more specific findings. The relation of obesity and history of atopy with the severity of AD should be examined. Body weight control measures that may reduce the AD incidence in a population should also be considered. Further studies should be performed to identify the pathway involved in the pathogenesis of AD and determine the role of obesity and history of atopy in AD.

Conclusion

This cross-sectional study found a significant association between obesity and history of atopy with AD. Early interventions that aimed to reduce the body weight of children with obesity and lower their risk of having AD should be audited and verified in the future. Counseling should also be provided to their parents to increase the awareness of the increasing risk of having AD in children who suffer from obesity and children with history of atopy.

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