

# Exclusive breastfeeding and risk of atopic dermatitis in high risk infant

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## ABSTRACT

Martaviani Budiastuti, Setya Wandita, Sumadiono - *Exclusive breastfeeding and risk of atopic dermatitis in high risk infant*

**Background:** WHO recommends exclusive breast-feeding for 6 months because it is highly beneficial. It has been proven by a number of studies to be advantageous in preventing various infectious diseases. However, its role in preventing allergic diseases especially atopic dermatitis in infant remains uncertain until recently.

**Objective:** To find out whether high risk infant who did not receive exclusive breast-feeding would have a greater risk to suffer from atopic dermatitis.

**Method:** We conducted a case-control study. Data were obtained from Pediatric Outpatient Clinics and Dermatology and Venerology Outpatient Clinics, Dr. Sardjito Hospital Yogyakarta. Case group was high risk infants with atopic dermatitis, while control group was high risk infants but not having the disease. Statistical analysis used *Chi-square* and degree of significance was stated as Confidence Interval (CI) of 95% for each Odds Ratio (OR). Multivariate analysis was performed by using logistic regression method.

**Results:** The study included 88 subjects with 44 subjects for case and control groups as well. Logistic regression showed that not receiving exclusive breast-feeding was statistically significant risk factor to atopic dermatitis in high risk infant {OR 3.72 (95% CI: 1.40-9.90);  $p$  0.01}.

**Conclusion:** High risk infant not receiving exclusive breast-feeding will have greater risk to develop atopic dermatitis.

**Keywords:** exclusive breast-feeding, atopic dermatitis; high risk infants.

## ABSTRAK

Martaviani Budiastuti, Setya Wandita, Sumadiono - *Pemberian ASI eksklusif dan risiko dermatitis atopik pada bayi dengan risiko tinggi.*

**Latar Belakang:** WHO merekomendasikan pemberian ASI eksklusif selama 6 bulan karena cara itu mempunyai manfaat yang amat tinggi. Telah dibuktikan dalam berbagai penelitian bahwa ASI eksklusif mempunyai keunggulan mencegah berbagai penyakit infeksi. Namun demikian, manfaat dalam mencegah penyakit alergi terutama dermatitis atopik masih belum jelas hingga baru-baru ini.

**Tujuan :** Untuk mengetahui apakah bayi dengan risiko tinggi yang tidak mendapat ASI eksklusif mempunyai kemungkinan lebih besar untuk menderita dermatitis atopik.

**Bahan dan Cara:** Dilakukan penelitian kasus-kontrol. Data diperoleh dari Klinik Rawat Jalan SMF Anak dan SMF Penyakit Kulit dan Kelamin RSUP Dr. Sardjito, Yogyakarta. Kelompok kasus adalah bayi dengan risiko tinggi atopik yang menderita dermatitis atopik, sedangkan kelompok kontrol adalah bayi dengan risiko tinggi atopik tetapi tidak menderita dermatitis atopik. Analisis statistik menggunakan uji *Chi-square* dan Interval Kepercayaan (IK) 95% untuk *odds ratio* (OR). Analisis multivariat dilakukan dengan menggunakan metode regresi logistik.

**Hasil:** Penelitian ini melibatkan 88 subjek, masing-masing kelompok 44 subjek kelompok kasus dan 44 subjek kelompok kontrol. Analisis Regresi logistik menunjukkan bahwa tidak mendapat ASI eksklusif pada bayi dengan risiko tinggi atopik merupakan faktor risiko yang bermakna untuk terjadinya dermatitis atopik (OR 3,72, IK 95% 1,40;9,90,  $p < 0.01$ ).

**Simpulan:** Bayi dengan risiko tinggi atopik yang tidak mendapat ASI eksklusif mempunyai risiko lebih tinggi untuk menderita dermatitis atopik.

## INTRODUCTION

Recently, there is an increased incidence of allergic diseases. In children, allergic diseases cause physical disorders and disturb the children's growth. The most common allergic diseases in children are atopic dermatitis, food allergy, bronchial asthma, and allergic rhinitis.<sup>1</sup>

Atopic dermatitis is a skin disease in the form of chronic and recurrent inflammation with itching as the main symptom and closely related to atopic background, appearing usually at the beginning of children's life.<sup>2</sup> Clinical symptoms of atopic dermatitis are variable from minor to severe symptoms. Around 60% atopic dermatitis in children occurs when they are less than one year old (most common in babies from 2-6 months old).<sup>3</sup> The prevalence of atopic dermatitis in children tends to increase. In The United States, 10-15% atopic dermatitis occur in childhood.<sup>2</sup> Study in India showed that atopic dermatitis was 28.46% of childhood skin diseases and 35-60% symptoms appeared in the first year of life and 48-75% in their first 5 years of life.<sup>4</sup> From the report of baby and children visit in 7 hospitals in Indonesia, atopic dermatitis was on the first list (611 cases) of 10 skin diseases most commonly found in children.<sup>5</sup> In Dermatovenereology Outpatient Clinics, RSUP Dr Sardjito Yogyakarta, in the period of February 2005 to December 2007, there were 73 cases of atopic dermatitis in babies. Atopic dermatitis is the first allergic form that shows a risk of other allergic diseases such as bronchial asthma and allergic rhinitis later in life.<sup>6</sup>

Allergic disease appearing in childhood, especially in infancy, should be prevented as early as possible because children need optimal growth and development processes. That is why, various studies have been conducted to find out the preventive factors of allergic disease incidence. One of the important protective factors is breastfeeding. Breastmilk given exclusively for the first 6 months of life will provide nutritional advantages and protect the

child from allergic diseases. Exclusive breastfeeding for 6 months means to avoid to feed the baby any food known as allergen and as precipitation factor of allergic diseases. Breastmilk being rich in immunoglobulin A (IgA) can help to protect the gastrointestinal tract by binding foreign protein which has a potential to be allergenic and inhibit its absorption. Nutritional contents of breastmilk will stimulate the maturation of gastrointestinal tract, so that it is ready to receive the antigens, maintain normal flora of gastrointestinal tract, and maintain the immunomodulatory factors.<sup>7</sup> Exclusive breastfeeding is expected to be able protective to allergic disease incidence, so that the incidence rate can be decreased, and the disorders they cause, such as growth disorders in childhood, can be decreased.

## MATERIALS AND METHODS

This was a case control study, aimed to know the relationship between exclusive breastfeeding and atopic dermatitis incidence in babies with a high-risk of allergy in their first years of life. This study was conducted in Outpatient Clinics of Pediatric and of Dermatovenereology Department RSUP Dr. Sardjito Yogyakarta from February 2005 until December 2007. The inclusion criteria were babies  $\geq 1$  year old, who have parents or siblings with history of atopy, and with the history of normal birthweight and full term. Exclusion criteria were babies with severe congenital diseases, babies with severe infections, babies in intensive care, and babies whose parents rejected to participate in this study.

Variables of the study consisted of two categories, i.e. independent and dependent variables. The dependent variable was atopic dermatitis incidence. The independent variables were breastfeeding, age, sex, atopic risk in parents, the total number of family members, cigarette smoke exposure, and pets. Other variables measured were parents' age and educational level.

Recruitment of the subjects was conducted by consecutive sampling method. Sample size,

determined by sample size formula for case control study, was 43 subjects. All parents of the subjects were given detailed explanation about this research and signed the informed consent form.

Parents who brought their babies to Outpatient Clinics of Pediatric and of Dermatovenereology Department RSUP Dr Sardjito and whose baby were diagnosed as atopic dermatitis were interviewed. Parents with babies who satisfied the inclusion and exclusion criteria were given detailed explanation about this research, signed the informed consent form, and filled the questionnaire completely. Case group consisted of babies with high-risk allergy who suffered from atopic dermatitis, while control group consisted of babies with high-risk allergy who did not suffer from atopic dermatitis. Subjects in non-risk-factor group were babies with high-risk of allergy who were exclusively breastfed, while subjects in risk-factor group were babies with high-risk allergy who were not exclusively breastfed.

Babies with high-risk allergy were babies who had father/mother/siblings with the history of atopy. The history of atopy (in father/mother/siblings) were the history of allergic diseases such as bronchial asthma, allergic rhinitis, atopic dermatitis, or urticaria. Atopic dermatitis is a chronic and recurrent skin inflammation with itching as the main symptom closely associated with atopy, diagnosis was established in Dermatovenereology Department RSUP Dr Sardjito using Hanifin and Rajka diagnostic criteria. The age of the parents was classified into 2 categories ( $\geq 25$  years old &  $> 25$  years old). The educational level of the parents was classified into 2 categories (junior and senior high school [formal educational length  $\leq 12$  years] and university [formal educational length  $> 12$  years]). Exclusive breastfeeding is a period where babies drink breastmilk only, without any other food intake such as formula milk, cowmilk, or solid food, at least for 6 months or until the baby was included into this study (vitamins, minerals and drugs in the form of drops and syrups were allowed). The total number of family members were the total of family members who lived in the same house with the subjects, this data were classified into 2 categories ( $\leq 5$  people and  $> 5$  people). Cigarette smoke

exposure was the presence or absence of active smokers in the house since pregnancy until the baby was born, so that the baby had a risk to be a passive smoker. Pet was the presence or the absence of pets in the house, especially furry animals, such as cats or dogs.

Data entry and analysis were conducted with SPSS software. Data were presented descriptively in tables to find out the proportion of each variables. Statistic analysis used were chi square with confidence interval (CI) of 95% for each odds ratio (OR) and multivariate analysis was conducted with logistic regression method.

## RESULTS

There were 88 subjects (44 cases and 44 controls). Based on sex, there were 47 (53.4%) males and 41 (46.6%) females. The mean of age of the subjects was  $7.62 \pm 3.53$  months old, while that of the case group was  $7.43 \pm 3.59$  months old, and in control group was  $7.82 \pm 3.49$  months old, with mean difference of 0.39 (95%CI = -1.89-1.16);  $p = 0.61$ .

Mothers with age  $\leq 25$  years old were 63 (71.6%) and with age  $> 25$  years old were 25 (28.4%), while fathers with age  $< 25$  years old were 15 (17.0%) and with age  $> 25$  years old were 73 (83.0%). The formal education of the mothers were 46 (52.3%) university graduates and 42 (47.7%) high school graduates, while the formal education of the fathers were 47 (53.4%) university graduates and 41 (46.6%) were high school graduates.

There were 51 (57.0%) parents who did not give exclusive breastfeeding and 37 (42.0%) gave exclusive breastfeeding. The risk of atopy were in 46 (52.3%) subjects from the mother side and 42 (47.7%) subjects from the father side. There were 38 (43.2%) subjects who had family members  $< 5$  people and 50 (56.8%) subjects who had family members  $> 5$  people. There were 32 (36.4%) subjects exposed to cigarette smoke in their house and 56 (63.6%) subjects were not. There were 27 (30.7%) subjects had pets in the house, while 61 (69.3%) subjects deny having pets (TABLE 1).

TABLE 1. The baseline characteristics

Characteristics	Number (%)	Case	Control	<i>p</i>
Gender				0.76
- male	47/88 (53.4%)	24/47 (51.1%)	23/47 (48.9%)	
- female	41/88 (46.6%)	20/41 (48.8%)	21/41 (51.2%)	
Age (age mean $\pm$ SD <sub>2</sub> in months)	7.62 $\pm$ 3.53	7,43 $\pm$ 3.59	7.82 $\pm$ 3.49	0.61*
Mother age				0.48
- $\leq$ 25 years	63/88 (71.6%)	11/25 (44.0%)	14/25 (56.0%)	
- >25 years	25/88 (28.4%)	33/63 (52.4%)	30/63 (47.6%)	
Father age				0.40
- $\leq$ 25 years	15/88 (17.0%)	9/15 (60.0%)	6/15 (40.0%)	
- > 25 years	73/88 (83.0%)	35/73 (47.9%)	38/73 (52.1%)	
Mother educational level				0.67
- SMP/SMA	42/88 (47.7%)	20/42 (47.6%)	22/42 (52.4%)	
- Academic	46/88 (52.3%)	24/46 (52.2%)	22/46 (47.8%)	
Father educational level				0.83
- SMP/SMA	41/88 (46.6%)	21/41 (51.2%)	20/41 (48.8%)	
- Academic	47/88 (53.4%)	23/47 (48.9%)	24/47 (51.1%)	
Exclusive breastfeeding				0.02†
- No	51/88 (58.0%)	31/51 (60.8%)	20/51 (39.2%)	
- Yes	37/88 (42.0%)	13/37 (35.1%)	24/37 (64.9%)	
Atopic Risk				0.03†
- mother	46/88 (52.3%)	28/46 (60.9%)	18/46 (39.1%)	
- father	42/88 (47.7%)	16/42 (38.1%)	26/42 (61.9%)	
Total family members				0.03†
- $\leq$ 5 people	38/88 (43.2%)	24/38 (63,2%)	14/38 (36,8%)	
- > 5 people	50/88 (56.8%)	20/50 (40,0%)	30/50 (60,0%)	
Smoke exposure				0.18
- Yes	32/88 (36.4%)	19/32 (59.4%)	13/32 (40.6%)	
- No	56/88 (63.6%)	25/56 (44.6%)	31/56 (55.4%)	
Pets in the house				0.26
- Yes	27/88 (30.7%)	15/27 (55.6%)	12/27 (44.4%)	
- No	61/88 (69.3%)	29/61 (47.5%)	32/61 (52.5%)	

\* mean difference 0.39 (95%CI = -1.89;1.16), *p* = 0.61† *p* < 0.05 (statistically significant)

The statistically significant relationships between independent variables and the incidence of atopic dermatitis were: not exclusively breastfeeding (OR = 2.86, 95%CI = 1.19;6.89), but

also the risk of atopy from the mother side (OR = 2.53, 95%CI = 1.07;5.97), and total family members  $\geq$  5 people (OR = 2.57, 95%CI = 1.08;6.13) (TABLE 2).

TABLE 2. The relationship between independent variables and the incidence of atopic dermatitis

Variable	Case	Control	p	OR (95%CI)
Gender			0.76	OR 1.09 (0.47;2.53)
- male	24	23		
-female	20	21		
Exclusive breastfeeding			0.02*	OR 2.86 (1.19;6.89) †
- No	31	20		
- Yes	13	24		
Atopic risk			0.03*	OR 2.53 (1.07;5.97) †
- mother	28	18		
- father	16	26		
Total family member			0.03*	OR 2.57 (1.08;6.13) †
- ≤ 5 people	24	14		
- > 5 people	20	30		
Smoke exposure			0.18	OR 1.81 (0.75;4.37)
- Yes	19	13		
- No	25	31		
Pets in the house			0.26	OR 1.65 (0.68;3.99)
- Yes	15	12		
- No	29	32		

\* : p < 0.05 (statistically significant)

† : OR > 2

The statistically significant results were further analyzed with multivariate analysis with logistic regression. Variables affecting the incidence of atopic dermatitis were: not exclusively breast-

feeding (OR = 3.72, 95%CI = 1.40;9.90), but also total family members ≥ 5 people (OR = 3.32, 95%CI = 1.24;8.86) (TABLE 3).

TABLE 3. The relationship between independent variables and the incidence of atopic dermatitis with logistic regression

Variable	Cases	Control	p	OR (95%CI)
Exclusive breastfeeding			0.01	OR 3.72 (1.40;9.90)
- No	31	20		
- Yes	13	24		
Atopic risk			0.07	OR 2.36 (0.94;5.92)
- Mother	28	18		
- Father	16	26		
Total family members			0.02	OR 3.32 (1.24;8.86)
- ≤ 5 people	24	14		
- > 5 people	20	30		

## DISCUSSION

The babies suffered from atopic dermatitis in Outpatient Clinics of Dermatovenereology Department RSUP Dr. Sardjito in February 2005 until December 2007 were 73 cases. This study covered 44 babies with the diagnosis of atopic dermatitis as case group and 44 babies who had high risk of allergy but not suffered from atopic dermatitis as control

group. Atopic dermatitis is a chronic and recurrent skin inflammation, and in severe case there is itching which causes the baby to be irritated, has secondary infection and causes growth and development disorders. Atopic dermatitis is the first form of allergy which indicates the risk of other allergic diseases such as bronchial asthma or allergic rhinitis later in life.<sup>6</sup>

The pattern of allergic diseases in babies and children illustrated in “Allergic March” shows that



atopic dermatitis and food allergy commonly appear at the early years of childhood, and then followed by allergic rhinitis and bronchial asthma. The youngest age in this study was 2 months old. This is consistent with the opinion of Blauvelt about the age when the atopic dermatitis occurred was around 2-6 months old.<sup>8</sup> The severity level of the first allergic disease could predict the persistency and the progressivity of the next allergic diseases.<sup>9</sup>

In this study, baby who had not exclusively breastfed would have an increased risk to suffer from atopic dermatitis (OR = 3.72, 95%CI = 1.40-9.90, p = 0.01). This was consistent with the studies of Schoetzau *et al.*<sup>10</sup> and Kull *et al.*<sup>11</sup> Exclusive breastfeeding for 6 months means to avoid giving additional food containing allergenic proteins, especially for babies with high-risk atopy. Breastmilk contains various immunologic components which control inflammatory process. Secretoric IgA in breastmilk may protect the gastrointestinal tract by binding the foreign allergenic proteins and prevent the absorption. Nutritional contents in breastmilk may also stimulate the maturation of gastrointestinal tract, so that it will be more ready to receive antigens, maintain gastrointestinal tract normal flora, and maintain the immunomodulatory factors.<sup>7</sup>

Total family members  $\geq 5$  people in this study was significantly associated with the incidence of atopic dermatitis (OR = 3.32, 95%CI = 1.24;8.86, p = 0.02). This was consistent with the theory of "hygiene hypothesis" by Strachan, which suggested that a family with smaller number of family members would be more seldom to have infection than the bigger family, so that Th1 immune response would be decreased, while Th2 response would be increased, and it would facilitate the occurrence of allergic diseases.<sup>12</sup>

This study used retrospective design, so that it had several weaknesses. Common biases in retrospective study are classification, information, and confounding bias.<sup>13</sup> In this study, cases and controls were chosen from the same population, i.e. patients who visited the Outpatient Clinics in RSUP Dr Sardjito Yogyakarta. The diagnosis of atopic dermatitis in the case group was established by peers in Outpatient Clinics of Dermato-venereology Department, while control group, consisted of babies with high-risk allergy but not suffered from atopic dermatitis, was obtained from Outpatient Clinics of Pediatric Department in RSUP Dr Sardjito Yogyakarta.

Skin prick test (SPT) and specific IgE level measurement may help to identify the specific allergens that precipitate atopic dermatitis and are associated with the status of atopy in parents and patients.<sup>14</sup> Genetic factors have big roles in the incidence of allergic diseases in children. The result of the previous studies illustrated the pattern of genetic inheritance. If both parents are atopy, their child will have 40-60% risk to have atopy; if both parents are atopy with the same manifestations, then their child will have 50-80% risk to have atopy; if one of the parents has atopy, then the child will have 20-40% risk to have atopy; if one sibling has atopy, then the child will have 25-35% risk to have atopy; but if no parents or siblings had atopy, then the child will have 5-15% risk to have atopy.<sup>15</sup> The criteria of atopy in this study was taken from the data in the questionnaires. The weaknesses of this study were: no SPTs and IgE level measurements conducted to determine the status of atopy. This study used data of patients and risk factors of atopic dermatitis by asking the parents of the patients to fill the questionnaires.

Researchers tried to identify the variables acting as risk factors of atopic dermatitis and the confounding variables. Independent variables measured were exclusive breastfeeding, risk of atopy in fathers/mothers/siblings, the total number of family members in the same house, cigarette smoke exposure, and pets in the house. Confounding variables in this study was the age of the subjects. Confounding variables are variables associated to independent and dependent variables, so that subjects chosen in this study were from age group until 1 year old, because according to the theory, in atopic dermatitis, 35-60% symptoms would appear in the first year of life and exclusive breastfeeding in that age period could affect the incidence of atopic dermatitis.<sup>4</sup>

Multivariate analysis with logistic regression showed that babies who were not exclusively breastfed would have an increased risk of atopic dermatitis (OR = 3.72, 95%CI = 1.40;9.90, p = 0,01), and total family members  $\geq 5$  people was a risk of atopic dermatitis incidence (OR = 3.32, 95%CI = 1.24;8.86, p = 0.02). These two results were statistically significant, but clinically the difference must be analyzed further because the low values of 95%CI (1.40 and 1.24) were too near to value of 1. Anyhow, the far distance of upper values of 95%CI (9.90 and 8.86) from value

of 1 clearly showed a tendency that the difference were clinically conclusive and a study with bigger sample size will confirm that the difference is clinically conclusive.

A further study have to be conducted with a more careful planning, more detailed identification of confounding factors, and a better study design (cohort design), to assess the strength of the causal-effect relationship.

## CONCLUSION

Babies with high risk of allergy who were not exclusively breastfed would have an increased risk to have atopic dermatitis. This result may be used as information for counselling on the advantages of exclusive breastfeeding, especially in babies with a high-risk of allergy.

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