

Cow's milk exposure and atopic dermatitis after six months of age

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Abstract

Background About 60% of individuals with atopic dermatitis (AD) develop their first manifestation during infancy. Cow's milk (CM) exposure is considered to be a risk factor for AD.

Objective To evaluate for an association between cow's milk exposure and atopic dermatitis in infants > 6 months of age.

Methods This cross-sectional study consisted of subjects from a previous study and new subjects recruited in order to meet the minimum required number of subjects. Our study population comprised 120 infants, born between 1 February and 30 November, 2012 in Sanglah Hospital, Denpasar. Subjects were divided into CM and non-CM groups and analyzed for their risk of AD. Subjects were included to CM group if they were fed with cow's milk/formula and included to non-CM group if they were breastfeed exclusively in the first six months of life. Other possible risk factors were assessed by multivariate analysis.

Results One hundred twenty subjects were enrolled and analyzed (59 in the CM and 61 in the non-CM groups). The prevalence of AD was 30%. Multiple logistic regression analysis revealed a significant association between CM exposure and AD, with odds ratio (OR) 2.37 (95%CI 1.036 to 5.420; P=0.04). In addition, maternal diet including eggs and/or cow's milk during the breastfeeding period was significantly associated with AD in infants (OR 3.18; 95%CI 1.073 to 9.427; P=0.04).

Conclusion Cow's milk exposure is significantly associated with atopic dermatitis in infants > six months of age. [Paediatr Indones. 2016;56:325-9. doi: 10.14238/pi56.6.2016.325-9].

Keywords: cow's milk exposure; atopic dermatitis; infant

Atopic dermatitis is a chronic inflammatory skin disease that commonly occurs in infants. As the most common atopic disease in infants, 60% of affected individuals develop manifestations during their first year of life.¹ Atopic dermatitis is one of a cluster of diseases termed the "allergic march." Food allergies and AD are typically seen first, followed by asthma and allergic rhinitis in children.^{2,3}

Many studies have shown a correlation between atopic dermatitis and feeding practices in infants.^{4,5} Exclusive breastfeeding, has long been considered to protect against allergies, including AD. The feeding practice of giving formula early in infancy is cause for concern.⁶ Widyanti *et al.* reported that the prevalences of AD in the first three months of life were 17% in the cow's milk (CM) group and 8% in the breastfeeding group. Though the relationship between infant feeding practices and the development of AD in infants remains controversial, the World Health

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Organization recommends exclusive breastfeeding as a means to prevent the development of atopic dermatitis in infants.⁷

The aim of this study was to evaluate for an association between cow's milk exposure and atopic dermatitis in infants > 6 months of age.

Methods

This cross-sectional study was conducted from June to July 2013. It was approved by the Ethics Review Board at Udayana University, Bali. Sampling was conducted consecutively. With an expected AD rate of 35% in the non-CM exposure group,⁸ we needed a minimum of 120 subjects to show an increase of 25% in the CM exposure group, with a power of at least 80% using a two-sided test with a 5% significance level. Some subjects (43) were included from a previous study by Widyanti *et al.*,⁷ i.e., infants born in Sanglah Hospital between February and June 2012, hospitalized in the rooming-in ward, and whose mothers could be contacted via telephone. Subjects' parents provided informed consent. Since only 43 subjects' mothers could be contacted by telephone, we included new subjects who were born between February and November 2012 in Sanglah Hospital to reach the required sample size. Subjects were included to CM group if they were fed with cow's milk/formula, with or without breastmilk, and included to non-CM group if they were breastfed exclusively in the first six months of life.

Data were collected through questionnaires via telephone. Mothers were asked about cow's milk exposure, breastfeeding practice, complementary

feeding practice, solid food introduction, cigarette smoke exposure, maternal diet during breastfeeding, maternal and paternal atopic history, and infant symptoms of AD.

Data were processed with SPSS 16.0 software. Descriptive data are presented in text and tables. Data were analyzed by Chi-square test for bivariate analysis and multiple logistic regression test for multivariate analysis.

Results

During the study period, we enrolled 120 infants, consisting of 59 subjects in the CM exposure group and 61 subjects in the non-CM exposure group. Characteristics of subjects are shown in **Table 1**. Infants' mean age, gender, age at introduction of solid food, as well as maternal and paternal atopic histories were similar between the CM and non-CM groups. Infants in the CM group were more likely to receive cow's milk containing complementary food compared to the non-CM group (85% vs. 46%, respectively). Infants in the CM group were also more likely to receive early complementary food (at age < 6 months) compared to the non-CM group.

The overall prevalence of AD was 30%, with 37% in the CM group and 23% in the non-CM group (**Table 2**). Chi-square test revealed that exposure to CM was associated with AD, with a prevalence ratio (PR) of 2.00, but this result was not statistically significant ($P=0.09$). Cow's milk containing complementary food and maternal diet containing eggs and cow's milk were also associated with AD, with PR 1.60 and 2.63, respectively, but these results

Table 1. Characteristics of subjects

Characteristics	CM group (n = 59)	Non-CM group (n = 61)	P value
Mean age (SD), months	10.6 (2.5)	10.7 (2.8)	<0.01
Male gender, n (%)	27 (46)	30 (49)	0.71
Cow's milk containing complementary food, n (%)	50 (85)	28 (46)	<0.01
Early complementary food, n (%)	21 (36)	15 (25)	0.19
Mean age at introducing solid food (SD), months	5.5 (1.5)	5.8 (1.3)	<0.01
Cigarette smoke exposure, n (%)	40 (68)	30 (49)	0.04
Maternal diet containing egg and/or cow's milk during breastfeeding, n (%)	40 (68)	50 (82)	0.07
Maternal atopic history, n (%)	12 (20)	10 (16)	0.58
Paternal atopic history, n (%)	5 (9)	5 (8)	0.96

were not statistically significant ($P=0.28$ and $P=0.07$, respectively). Cigarette smoke exposure and maternal atopic history were associated with AD (PR 1.97 and 1.82) but these results were not statistically significant ($P=0.11$ and $P=0.22$, respectively). However, exclusive breastfeeding seemed to be protective factor against developing AD, with PR 0.50, but this risk factor was also not statistically significant on bivariate analysis ($P=0.09$).

On multivariate analysis, cow's milk exposure was significantly associated with atopic dermatitis, with OR 2.37 (95%CI 1.036 to 5.420; $P = 0.04$). Maternal diet containing egg and cow's milk was also associated with atopic dermatitis with OR 3.18 (95% CI 1.073 to 9.427, $P = 0.04$) (Table 3).

the first months of life.⁹ In our study, we found that cow's milk exposure was associated with atopic dermatitis in infants after six months of life

Atopic dermatitis is generally the first atopic disease occurring in the first year of life. Atopic dermatitis is associated with respiratory and intestinal manifestations later in life, indicating that this first manifestation of atopic disease is a predictive factor for the development of asthma, eczema, and food allergies. Atopic dermatitis affects approximately 5 to 20% of children worldwide. In the vast majority of cases, atopic dermatitis has an onset before five years of age, and prevalence data in children shows a slight female to male preponderance.¹⁰ We found the prevalence of atopic dermatitis to be 30% in

Table 2. Risk factors for atopic dermatitis

Variables	Atopic dermatitis (n=36)	No atopic dermatitis (n=84)	PR	95% CI	P value
Cow's milk exposure, n (%)					
Yes	22	37 (44)	2.00	0.900 to 4.427	0.09
No	14	47 (56)			
Gender, n (%)					
Male	16	41 (49)	0.84	0.383 to 1.838	0.66
Female	20	43 (51)			
Exclusive breastfeeding, n (%)	14	47 (56)	0.50	0.263 to 1.272	0.09
Cow's milk containing complementary food, n (%)	26	52 (44)	1.60	0.683 to 3.751	0.28
Early complementary feeding, n (%)	11	25 (30)	1.04	0.444 to 2.428	0.93
Cigarette's smoke exposure, n (%)	25	45 (54)	1.97	0.860 to 4.511	0.11
Maternal diet containing egg and cow's milk during breastfeeding, n (%)	31	59 (66)	2.63	0.916 to 7.538	0.07
Maternal atopic history, n (%)	9	13 (59)	1.82	0.698 to 4.747	0.22
Paternal atopic history, n (%)	2	8 (80)	0.56	0.113 to 2.772	0.47

Chi-square test

Table 3. Multivariate regression logistic analysis of the risk factors for atopic dermatitis

	OR	95% CI	P value
Cow's milk exposure	2.37	1.036 to 5.420	0.04
Maternal diet containing egg and cow's milk during breastfeeding	3.18	1.073 to 9.427	0.04

Discussion

Exposure to allergens early in life influences the development of allergen-specific immune responses.⁸ Cow's milk, as the first allergen introduced to infants, has been associated with increasing risk of developing atopic diseases later in life. Early exposure to cow's milk has long-lasting effects on humoral antigen-specific responses, indicating less effective tolerance-inducing mechanisms in the intestinal mucosa during

120 subjects, with 37% in the CM exposure group and 23% in the non-CM group. Females were more likely to experience atopic dermatitis compared to males (32% vs. 28%, respectively).

Exclusive breastfeeding is considered to be a protective factor against atopic diseases. This protective effect may operate through several mechanisms. Immune modulators and anti-inflammatory components found in human breast milk contribute to this protective effect.¹¹ IgA and sIgA in breast

milk have the potential to lessen hypersensitivity reactions.¹² In our study, however, exclusive breastfeeding (a minimum of 6 months breastfeeding without supplementation) was not associated with atopic dermatitis.

In 2000, the American Academy of Pediatrics suggested that lactating mothers with infants at high risk of developing AD should avoid peanuts and tree nuts, and should consider eliminating eggs, cow's milk, and fish from their diets. Food allergens such as peanuts have been detected in breast milk.¹³ In contrast, a Cochrane review of 4 trials with 334 pregnant women did not find adequate evidence that avoidance of eggs, milk, and other antigenic food during lactation prevented AD in children.¹⁴ In our study, we found that maternal diet containing egg and/or cow's milk was associated with atopic dermatitis in their infants.

Maternal atopy poses a higher risk for infantile AD than does paternal atopy. Whether this is due to genetic or congenital factors or both is uncertain.¹⁵ Maternal history of atopy was found to be two times more frequent than paternal history of atopy. The children of affected mothers were reported to contract atopic disease in the same proportion as the children of affected fathers. A possible dose-response effect in polygenic inheritance is assumed.¹⁶ The presence of parental history of atopic symptoms doubled the incidence of atopic symptoms in the children if one of the parents was affected, and tripled the incidence if both parents were affected.¹⁷ However, in our study, we found that maternal atopy was not associated with the incidence of atopic dermatitis.

In conclusion, cow's milk exposure and maternal diet containing egg and cow's milk in breastfeeding mothers are associated with atopic dermatitis in infants > 6 months of age. Avoidance of cow's milk through exclusive breastfeeding and maternal diet free of egg and cow's milk when breastfeeding should be promoted to prevent atopic dermatitis in infants. Further investigation needs to address the incidence of atopic dermatitis in the next period of life.

Conflict of Interest

None declared.

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