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Original article

Breastfeeding and risk of atopic dermatitis up to the age 42 months: a birth cohort study in Japan

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ABSTRACT

Purpose: The purpose of this study was to investigate the association between breastfeeding and atopic dermatitis (AD) up to the age 42 months.
Methods: Data from a nationally representative population-based birth cohort study in Japan were used ($N = 38,757$). Feeding pattern and breastfeeding duration were investigated via questionnaires when infants were aged 6 months. Physician-diagnosed AD during the previous 1 year was ascertained via questionnaires when the children were aged 18, 30, and 42 months. The associations between feeding patterns or breastfeeding duration and physician-diagnosed AD from the age 6 to 42 months, categorized by AD status (no history of AD, episodic AD, and persistent AD), were analyzed using ordered logistic regression adjusted for covariates.
Results: Breastfeeding was positively associated with AD, with dose-response association (P for trend $<$ .001). Exclusively breastfed infants were 1.26 times more likely to have AD (95% confidence interval, 1.12 −1.41) than infants fed formula alone. Furthermore, children with a longer breastfeeding duration were also significantly more likely to have AD (P for trend $<$ .001).
Conclusions: Breastfeeding is associated with an increased risk of AD up to the age 42 months. Further study is needed to elucidate the mechanism underlying the association between breastfeeding and AD.

Introduction

Atopic dermatitis (AD) is one of the most common chronic skin disorders among infants and young children, which is characterized by itchy skin with eczematous changes [1]. The association between breastfeeding and AD has been studied for more than 70 years [2], but the results have been controversial. Although some epidemiology studies including meta-analysis [3] showed that breastfeeding had a protective effect on AD [4–6], other studies suggested that breastfeeding increased the risk of AD [7–9] or that there was no relationship [10–12]. These differences may stem from differences in study design, the definitions of exposure and outcome, sample size, or adjustment for confounders [13–15]. Kramer [14] proposed 12 criteria to assess study designs addressing the relationship between breastfeeding and atopic disease. Those criteria included nonreliance on prolonged maternal recall, strict diagnostic criteria, severity of outcome, assessment of effect in children at high risk, and adequate statistical power. No studies have completely fulfilled these standards thus far [16]. Furthermore, the location of the study may be relevant. Studies in Finland, Denmark, New Zealand, or Japan—countries in which people eat relatively large quantities of fish—showed a positive association between breastfeeding and AD using a prospective study design [8–10,17], suggesting that the contents of the breast milk may be associated with the risk of AD.

The Longitudinal Survey of Babies in the 21st century is a nationwide large birth cohort study implemented by the Ministry of Health, Labour, and Welfare in Japan. It investigated feeding patterns and breastfeeding duration for infants at the age 6 months, and physician-diagnosed AD during the previous 1 year was queried for children at the age 18, 30, and 42 months. Using the data, the association between breastfeeding and AD can be investigated by adopting a prospective design with sufficient statistical power. The purpose of the present study was, therefore, to investigate the association between breastfeeding and the duration of breastfeeding on the development of AD in young children from the age 6 to 42 months in Japan.

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Methods

Study sample

The data used for this study were taken from the Longitudinal Survey of Babies in the 21st century conducted by the Japanese Ministry of Health, Labour, and Welfare from 2001 to 2004. The study sample included all infants born in Japan during the periods of January 10–17, 2001, and July 10–17, 2001 using the birth record list ($N = 53,575$). Questionnaires were mailed to all subjects when the infants were aged 6 months. The subjects were considered to have agreed to participate in the study if they returned the questionnaire to the Ministry. The total number of respondents was 47,015 (response rate, 87.8%). The second and the third questionnaires were mailed in 2002 and 2003 to all subjects who participated in the first survey when the children were aged 18 and 30 months, during which 43,925 and 42,812 subjects responded, respectively (response rates, 93.4% and 91.1%, respectively, of those responding to the first survey). The fourth questionnaires were mailed in 2004 to all subjects who participated in the second or the third survey ($N = 45,072$) when the children were aged 42 months and 41,559 subjects responded (92.2% of those responding to the second or third survey). Because this study focused on breastfeeding and AD up to the age 42 months, subjects without record of breastfeeding status ($n = 308$) and those who did not answer the question about AD in every survey ($n = 1720$) were excluded. We further excluded multiple births ($n = 832$). Therefore, the final sample size for this study was 38,757 (Fig. 1). Because the study was based on an anonymous public use data set with no identifiable information on the survey questionnaire, this study has been exempted from ethical review.

Feeding pattern and breastfeeding duration

Information regarding feeding pattern and breastfeeding duration was obtained in the first survey. Participants were asked about the duration of breastfeeding and formula feeding for the past 6 months. If the mother answered that she had not given any formula, she was included in the category of "exclusive breastfeeding." If she answered that she had given only colostrum or had not given any breast milk, she was included in the category of "formula only." Finally, if the mother answered that she had given both breast milk and formula, she was included in the category of "partial breastfeeding." Thus, we categorized the feeding pattern during the first 6 months of life as "formula only," "partial breastfeeding," or "exclusive breastfeeding." All infants were also categorized into four groups according to the duration of breastfeeding: never, 1–2, 3–5, or 6+ months.

Atopic dermatitis

Information regarding doctor-diagnosed AD was obtained in the second, third, and fourth survey using the following question: "Has your child seen a doctor for AD or eczema treatment in the last

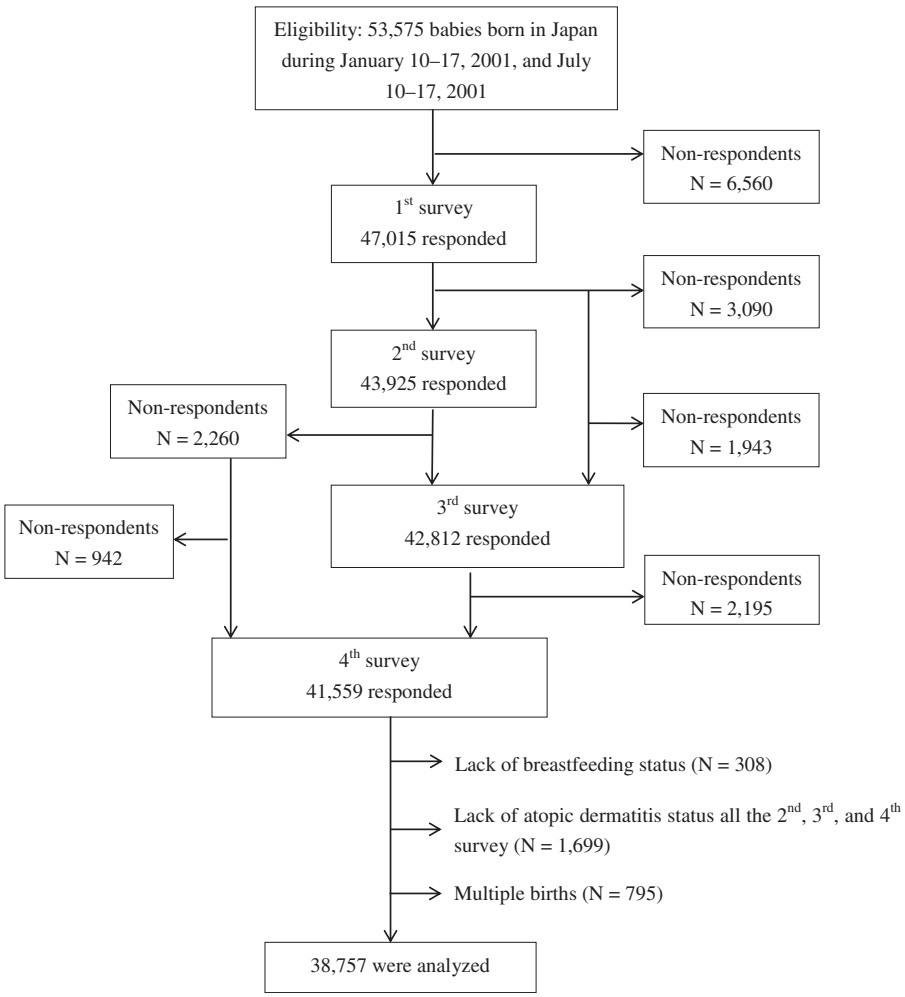

Fig. 1. Flow chart of study participants.

12 months?" If participants answered "yes" in the second, third, and fourth surveys, the infant was categorized as having "Persistent AD." If participants answered "yes" once or twice among the three surveys, the infant was categorized as having "Episodic AD." Furthermore, if participants answered "no" in all three surveys, the infant was categorized as having "no history of AD."

Confounders

Data regarding a child's sex, birth weight, and gestational age were obtained from their birth records. Family demographics and lifestyle were investigated in the first survey, including parental age, parental smoking habits, whether the infant was living with grandparents, the number of siblings at birth, and maternal anxiety during child rearing. Socioeconomic status (SES) variables were obtained from the first survey, including the maternal working status at 6 months postpartum, and from the second survey, with respect to parental education. Household income was averaged using data from all the four surveys. Details of the distribution of these confounders are shown in Table 1.

Analyses

Ordered logistic regression was used to investigate associations between feeding pattern or breastfeeding duration and AD, which was categorized on the basis of AD persistence (i.e., no history, episodic, or persistent). For the multivariate analysis, we use three models. Model 1 adjusted for the child's demographics (sex, birth weight, and gestational age); model 2 adjusted for the child's demographics plus family demographics and lifestyle (parental age, parental smoking habits, whether living with grandparents, number of siblings at birth, and maternal anxiety during child rearing); and model 3 adjusted for the child's demographics, family demographics and lifestyle, plus SES (parental education and household income). The associations between breastfeeding duration and AD were also investigated using ordered logistic regression.

For sensitivity analysis to avoid the bidirectional association between breastfeeding and AD (e.g., young children with allergic symptoms were more likely breastfed by mothers who believe breastfeeding would prevent further exacerbation of allergic symptoms [15,18]), we focused on subjects without allergic symptoms (physician-diagnosed AD or bronchial asthma, based on questionnaire response) during the age 6–12 months ($N = 31{,}322$) and investigated the association between feeding pattern or breastfeeding duration and AD at the age 18–42 months using ordered logistic regression because breastfeeding is finished after the age 18 months in most cases. All analyses were performed using STATA SE statistical package, version 12 (Stata Corp., College Station, TX).

Results

In total, 1402 (3.6%) and 8787 (22.7%) of young children had persistent and episodic AD up to the age 42 months, respectively. Furthermore, 8679 (22.4%), 27,861 (71.9%), and 2217 (5.7%) of children were exclusively, partially, or not breastfed for the first 6 months of life. More than half of the children were breastfed for 6 months or more. With respect to crude association, exclusive breastfeeding and a breastfeeding duration of 6+ months were more likely present among infants with persistent AD (26.0% and 62.3%, respectively) compared with infants with no history of AD (21.7% and 55.0%, respectively). In addition, sex, maternal age, paternal smoking habits, living with grandparents, older siblings, maternal anxiety during child rearing, maternal education, paternal education, maternal work status, and average household income were associated with AD status (Table 1).

The odds ratio (OR) of feeding pattern during the first 6 months of life with respect to having AD from the age 6 to 42 months is shown in Table 2. Exclusive and partially breastfed infants were 1.35 and 1.18 times significantly more likely to have AD (95% confidence interval [CI], 1.21–1.51; and 1.07–1.31, respectively) than infants fed formula alone, after adjusting for the child's demographics. The P for trend demonstrated significance ($P < .001$). Further adjustment for family demographics and lifestyle (model 2) and SES (model 3) attenuated the point estimate (OR of exclusive breastfeeding, 1.33 and 1.26 for models 2 and 3, respectively), but P for trend remains significant ($P < .001$ for both).

Similarly, the OR of breastfeeding duration during the first 6 months of life and the development of AD from the age 6 to 42 months, derived from ordered logistic regression, is shown in Table 3. Infants who were breastfed for at least 6 months were 1.32 times more likely to have AD (95% CI, 1.11–1.38) than infants fed formula alone after adjustment for the children's demographics (model 1). The OR was lower if the breastfeeding duration was shorter (OR, 1.13 and 1.03 for 3–5 months and 1–2 months, respectively), yielding a strong dose-response association (P for trend $< .001$). Further adjustment for family demographics and lifestyle (model 2) and SES (model 3) attenuated the point estimate (OR of 6 months breastfeeding: 1.30 and 1.24 for models 2 and 3, respectively), but P for trend remains significant ($P < .001$ for both).

Before sensitivity analysis, we investigated the association between young children with and without allergic symptoms from the age 6 to 18 months with respect to the distribution of feeding pattern and breastfeeding duration and found that young children with allergic symptoms from the age 6 to 18 months are more likely to be breastfed and for a longer duration ($P = .001$ and $P < .001$; data not shown). Therefore, further sensitivity analysis (i.e., among young children without allergic symptoms from the age 6 to 18 months) was performed. We then confirmed that exclusively breastfed infants were 1.35 times more likely to have AD (95% CI, 1.13–1.60) than infants fed formula alone, after adjustment for covariates measured in this study (model 1; Table 4). Furthermore, young children breastfed for at least 6 months were 1.33 times more likely to have AD (95% CI, 1.13–1.57) than infants fed formula alone, after adjustment for covariates (model 1; Table 5). Both ORs were slightly attenuated in model 2 and model 3 but remained significant. P for trend also demonstrated significance for both feeding pattern and breastfeeding duration, suggesting a dose-response association ($P < .001$ in models 1, 2, and 3).

Discussion

We discovered that breastfeeding for 6 months of life is associated with an increased risk of AD up to the age 42 months, using a nationwide, population-based, prospective large birth cohort study in Japan. More specifically, young children breastfed exclusively or for at least 6 months were 1.26 or 1.24 times more likely to have AD up to the age 42 months compared with formula-fed young children, respectively. Furthermore, among children without allergic symptoms from the age 6 to 18 months, we found positive associations between breastfeeding (terminated before the age 18 months in most cases) and occurrence of AD after the age 18 months, suggesting that reverse causation (to have AD → breastfeeding) is unlikely. Our study meets 11 of 12 criteria suggested by Kramer [14], although there was one unmet criterion, that is, the assessment of effects in children at high risk of AD, which was not possible due to lack of information on parental allergic history.

Table 1
Characteristics of study population ($N = 38,757$)

Characteristics	No history of AD ($n = 28,568$, 73.7%)	Episodic AD ($n = 8787$, 22.7%)*	Persistent AD ($n = 1402$, 3.6%)†	P (χ^2 test)
	n (%)	n (%)	n (%)	
Feeding pattern				
Formula only	1715 (6.0)	433 (4.9)	69 (4.9)	<.001
Partial breastfeeding	20,648 (72.3)	6244 (71.1)	969 (69.1)	
Exclusive breastfeeding	6,205 (21.7)	2110 (24.0)	364 (26.0)	
Breastfeeding duration (mo)				
Never	1715 (6.0)	433 (4.9)	69 (4.9)	<.001
1–2	5484 (19.2)	1474 (16.8)	200 (14.3)	
3–5	5652 (19.8)	1600 (18.2)	260 (18.5)	
6+	15,717 (55.0)	5280 (60.1)	873 (62.3)	
Sex				
Male	14,643 (51.3)	4653 (53.0)	809 (57.7)	<.001
Female	13,925 (48.7)	4134 (47.1)	593 (42.3)	
Birth weight (g)				
<2500	2100 (7.4)	595 (6.8)	85 (6.1)	.15
2500–4000	26,132 (91.5)	8096 (92.2)	1303 (92.9)	
4000+	329 (1.2)	95 (1.1)	14 (1.0)	
Gestational age (wk)				
<37	1181 (4.1)	317 (3.6)	46 (3.3)	.11
37–42	27,123 (95.0)	8386 (95.5)	1341 (95.7)	
42+	246 (0.9)	82 (0.9)	15 (1.1)	
Maternal age (when the child was aged 6 mo)				
<30	12,416 (43.5)	3759 (42.8)	568 (40.5)	.03
30–39	15,530 (54.4)	4860 (55.3)	794 (56.6)	
40+	622 (2.2)	168 (1.9)	40 (2.9)	
Paternal age (when the child was aged 6 mo)				
<30	8621 (30.2)	2637 (30.0)	432 (30.8)	.52
30–39	16,818 (58.9)	5217 (59.4)	835 (59.6)	
40+	3129 (11.0)	933 (10.6)	135 (9.6)	
Mother's smoking habits (when the child was aged 6 mo)				
No	24,154 (84.9)	7494 (85.7)	1205 (86.4)	.09
Yes	4285 (15.1)	1254 (14.3)	189 (13.6)	
Father's smoking habits (when the child was aged 6 mo)				
No	10,659 (38.0)	3431 (39.7)	544 (39.7)	.01
Yes	17,417 (62.0)	5206 (60.3)	828 (60.4)	
Living with grandparents (when the child was aged 6 mo)				
No	22,356 (78.3)	6983 (79.5)	1083 (77.3)	.03
Yes	6212 (21.7)	1804 (20.5)	319 (22.8)	
Older siblings				
0	14,168 (49.6)	4485 (51.0)	649 (46.3)	.002
1	10,457 (36.6)	3188 (36.3)	553 (39.4)	
2+	3943 (13.8)	1114 (12.7)	200 (14.3)	
Maternal anxiety during child rearing (when the child was aged 6 mo)				
Scarcely not	11,095 (38.9)	2994 (34.1)	426 (30.4)	<.001
Some	15,658 (54.9)	5169 (59.0)	838 (59.8)	
Very much	1750 (6.1)	606 (6.9)	137 (9.8)	
Maternal education				
<High school	1396 (4.9)	370 (4.2)	58 (4.2)	<.001
High school	11,270 (39.7)	3098 (35.4)	477 (34.3)	
Some college	11,845 (41.7)	3829 (43.8)	611 (43.9)	
College+	3899 (13.7)	1449 (16.6)	246 (17.7)	
Paternal education				
<High school	2174 (7.7)	586 (6.8)	98 (7.1)	<.001
High school	11,162 (39.7)	3254 (37.5)	553 (40.0)	
Some college	4439 (15.8)	1407 (16.2)	201 (14.6)	
College+	10,358 (36.8)	3420 (39.5)	529 (38.3)	
Maternal work status (when the child was aged 6 mo)				
Not working	21,070 (74.6)	6484 (74.5)	994 (71.5)	.01
Full-time work, with childcare leave	2892 (10.2)	976 (11.2)	169 (12.2)	
Full-time work, without childcare leave	1546 (5.5)	427 (4.9)	79 (5.7)	
Other	2752 (9.7)	819 (9.4)	149 (10.7)	
Average income per year (the first, second, and fourth survey); million yen				
<2.5	2505 (8.8)	602 (6.9)	135 (9.6)	<.001
2.5–5.0	12,030 (42.1)	3648 (41.5)	576 (41.1)	
5.0–7.5	9444 (33.1)	3028 (34.5)	451 (32.2)	
7.5–10	3047 (10.7)	1029 (11.7)	153 (10.9)	
10+	1542 (5.4)	480 (5.5)	87 (6.2)	

* Episodic AD cases were defined as those diagnosed with AD at least once from the age 6 to 42 mo.
† Persistent AD cases were defined as those diagnosed with AD every year from the age 6 to 42 mo.

The present study is consistent with the findings from Japan that used cross-sectional design [19,20] and prospective design [9]. Because the previous prospective study in Japan [9] was based on a relatively small sample size ($N = 763$) and a low follow-up rate (76.1%), they concluded a null association between breastfeeding and AD, although the point estimate of OR was positive and similar

Table 2
ORs for breastfeeding patterns during the first 6 mo with respect to AD from the age 6 to 42 mo using ordered logistic regression analysis ($N = 38,757$)

Feeding pattern	Model 1	Model 2	Model 3
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Formula only	Reference	Reference	Reference
Partial breastfeeding	1.18 (1.07–1.31)*	1.16 (1.05–1.29)*	1.11 (1.00–1.24)
Exclusive breastfeeding	1.35 (1.21–1.51)†	1.33 (1.19–1.49)†	1.26 (1.12–1.41)†
P for trend	<.001	<.001	<.001

Model 1: adjusted for child's sex, birth weight, and gestational age. Model 2: adjusted for variables used in model 1 plus maternal age, paternal age, maternal smoking habit, paternal smoking habit, living with grandparent(s), older siblings, and maternal anxiety during child rearing. Model 3: adjusted for variables used in model 2 plus maternal education, paternal education, maternal work status at 6 mo postpartum, and average household income.
* $P < .01$.
† $P < .001$.

Table 4
ORs for feeding pattern with respect to AD from the age 18 to 42 mo among children without allergic symptoms from the age 6 to 18 mo using logistic regression ($N = 31,322$)

Feeding pattern	Model 1	Model 2	Model 3
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Formula only	Reference	Reference	Reference
Partial breastfeeding	1.20 (1.02–1.42)*	1.20 (1.01–1.41)*	1.15 (0.97–1.36)
Exclusive breastfeeding	1.35 (1.13–1.60)†	1.35 (1.13–1.61)†	1.29 (1.08–1.55)†
P for trend	<.001	<.001	.001

Model 1: adjusted for child's sex, birth weight, and gestational age. Model 2: adjusted for variables used in model 1 plus maternal age, paternal age, maternal smoking habit, paternal smoking habit, living with grandparent(s), older siblings, and maternal anxiety during child rearing. Model 3: adjusted for variables used in model 2 plus maternal education, paternal education, maternal work status at 6 mo postpartum, and average household income.
* $P < .05$.
† $P < .01$.

to our study (OR, 1.27; 95% CI, 0.83–1.95) [9]. Furthermore, the prevalence of AD in the present study (26.3% up to the age 42 months) is similar to that of the previous study in Japan [9] (18.6% up to the age 24 months), although there were differences in the follow-up period and diagnostic criteria (our study used physician diagnosis, whereas previous study [9] used the International Study of Asthma and Allergies in Childhood [ISAAC] questionnaire). Therefore, because our study is a larger prospective study, we add to the literature that the association between breastfeeding and AD is generalizable in Japan.

Another study also discovered positive association between breastfeeding and AD among children without atopic heredity in Finland [17], in Denmark [10], and in a case-control study in New Zealand [8], where fish consumption is relatively high as in Japan [21], suggesting that maternal fish intake may explain the association between breastfeeding and AD, especially among children without allergic heredity. A previous study reported that maternal fish intake during pregnancy was associated with AD and asthma in infants [22]. Fish contains polychlorinated biphenyls (PCBs), and PCBs are transferred to human milk [23,24]. A study in Netherland showed that breastfed infants showed 3.6 times higher plasma PCB levels than formula-fed infants [25]. Because PCB influence the immune system [26,27], breastfeeding may play a role in inducing AD through exposure to PCB.

Alternatively, the hygiene hypothesis [28] may explain the association between breastfeeding and AD. That is, breastfeeding may be a risk factor for AD because it reduces the effect of exposure to bacteria or endotoxins [29] on the immune system, such that the infant does not fully develop mature immune response mechanisms such as the shift from Th-2 dominance in infants to Th-1 in later childhood. Because we have adjusted for the number of siblings as a proxy of the hygiene situation in the house and the association remains significant, the hygiene hypothesis is not likely to explain the association. However, because we do not have information regarding infections at the age 6 months, it is not possible to adjust for infection at the age 6 months to confirm an independent effect of breastfeeding on AD. In addition, breastfeeding may affect the balance of gut flora, which is associated with the development of AD [30–32]. Further study is needed to elucidate the mechanism underlying how breastfeeding is associated with the development of AD.

Other studies have reported a protective effect of breastfeeding on AD [4–6]. A previous study that reported a protective effect of breastfeeding on AD, assessed at 12 months [4], precluding a longer protective effect of breastfeeding on AD. Another observational study reported that a protective effect of breastfeeding on AD was found for the early onset of AD (age < 2 years) but not for a later onset of AD [5]. Furthermore, a longer follow-up study reported that breastfeeding is no longer protective for AD in subjects aged 9–21 years [29].

Several limitations need to be addressed. First, because AD was assessed as doctor-diagnosed AD (which is not always based on the same criteria), misclassification might occur. Previous studies ascertaining AD prevalence use the ISAAC questionnaire

Table 3
ORs for breastfeeding duration during the first 6 mo with respect to AD from the age 6 to 42 mo using ordered logistic regression analysis ($N = 38,757$)

Breastfeeding duration (mo)	Model 1	Model 2	Model 3
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Never	Reference	Reference	Reference
1–2	1.03 (0.92–1.16)	1.02 (0.91–1.14)	0.99 (0.88–1.12)
3–5	1.12 (1.00–1.25)	1.10 (0.98–1.24)	1.06 (0.95–1.19)
6+	1.32 (1.19–1.47)*	1.30 (1.17–1.45)*	1.24 (1.11–1.38)*
P for trend	<.001	<.001	<.001

Model 1: adjusted for child's sex, birth weight, and gestational age. Model 2: adjusted for variables used in model 1 plus maternal age, paternal age, maternal smoking habit, paternal smoking habit, living with grandparent(s), older siblings, and maternal anxiety during child rearing. Model 3: adjusted for variables used in model 2 plus maternal education, paternal education, maternal work status at 6 mo postpartum, and average household income.
* $P < .001$.

Table 5
ORs for breastfeeding duration with respect to AD from the age 18 to 42 mo among children without allergic symptoms from the age 6 to 18 mo using logistic regression ($N = 31,322$)

Breastfeeding duration (mo)	Model 1	Model 2	Model 3
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Never	Reference	Reference	Reference
1–2	1.06 (0.89–1.27)	1.06 (0.88–1.27)	1.03 (0.85–1.24)
3–5	1.13 (0.95–1.35)	1.14 (0.95–1.36)	1.09 (0.91–1.31)
6+	1.33 (1.13–1.57)*	1.33 (1.13–1.58)*	1.28 (1.08–1.52)*
P for trend	<.001	<.001	<.001

Model 1: adjusted for child's sex, birth weight, and gestational age. Model 2: adjusted for variables used in model 1 plus maternal age, paternal age, maternal smoking habit, paternal smoking habit, living with grandparent(s), older siblings, and maternal anxiety during child rearing. Model 3: adjusted for variables used in model 2 plus maternal education, paternal education, maternal work status at 6 mo postpartum, and average household income.
* $P < .01$.

[33], which reports higher prevalence than physician-diagnosed prevalence [34]. Thus, our AD classification may capture more severe cases than the ISAAC assessment, suggesting our OR would be an underestimate of the association. Second, because we did not have data regarding parental allergic history, it was not possible to adjust or stratify the data for parental allergic history in this investigation of the association between breastfeeding and AD. The Longitudinal Survey of Babies in the 21st century is aiming to investigate the status of children born in 2001 to develop countermeasures to the falling birth rate. Parental allergic history was not included in the survey questionnaire. Third, the definition of exclusive breastfeeding in this survey differs from the World Health Organization definition [35]. We are not collecting data on the use of solid foods, water, or other liquids, so the number of infants in the exclusive breastfeeding category may be overestimated. Fourth, although the sample size was large, it was not a representative sample of the Japanese population because it included only infants born in January and July, and the months of birth were not adjusted due to the lack of data. Thus, possible differences related to seasonal variation of birth may have been missed.

Conclusions

In conclusion, breastfeeding is associated with an increased risk of AD up to the age 42 months, using a nationwide, population-based, prospective large birth cohort study in Japan. Moreover, among children without allergic symptoms from the age 6 to 18 months, we found positive associations between breastfeeding and occurrences of AD after the age 18 months. Further study is needed to elucidate the mechanism by which breastfeeding was associated with the development of AD.

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