

Association between breastfeeding and allergic disorders in Japanese children

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SUMMARY

SETTING: Data on the association between breastfeeding and allergies are conflicting.

OBJECTIVE: To investigate the relationship between the duration and exclusivity of breastfeeding and the prevalence of wheeze, asthma and eczema in young Japanese children.

DESIGN: Study subjects were 1957 children aged 3 years. Data on breastfeeding, allergic symptoms and potential confounders were collected using a questionnaire. Outcomes were defined according to the criteria of the International Study of Asthma and Allergies in Childhood. Adjustment was made for sex, number of siblings, household smoking, paternal and maternal history of asthma, atopic eczema and allergic rhinitis, and paternal and maternal educational levels.

RESULTS: The prevalence values of symptoms of wheeze, asthma and eczema in the previous 12 months were respectively 22.1%, 8.9% and 17.3%. Exclusive breastfeeding for ≥ 4 months vs. < 4 months was associated with a lower prevalence of asthma. The duration of breastfeeding, regardless of exclusivity, for ≥ 6 months tended to be associated with a lower prevalence of asthma. There was no appreciable association between breastfeeding and wheeze or eczema.

CONCLUSIONS: Data from this study indicate that breastfeeding may be associated with a lower prevalence of asthma among young Japanese children.

KEY WORDS: asthma; breastfeeding; cross-sectional studies; eczema; wheeze

EPIDEMIOLOGICAL STUDIES of the relationship between breastfeeding and allergies in children have yielded conflicting results.^{1–17} Some studies have suggested that breastfeeding reduces the risk of allergic disorders,^{1–6} while others have failed to show such a beneficial relationship^{7–12} or have even reported increased allergies among breastfed children.^{13,14} A prospective study in Sweden showed that exclusive breastfeeding for ≥ 4 months reduced the risk of asthma at the age of 4 years.¹ On the other hand, no statistically significant association between breastfeeding and the risk of asthma in children aged 14 years was reported for a birth cohort in Australia.⁹ In a New Zealand birth cohort, breastfeeding for ≥ 4 weeks increased the risk of atopy and asthma.¹³ Examination of a birth cohort in the United Kingdom demonstrated that breastfeeding for ≥ 6 months was protective against wheeze in the first 3 years of life, but not wheeze or atopy at ages 7–8 years.¹⁵ The heterogeneity of these results among studies might be attributed to methodological differences among studies and the immunological complexity of breast milk itself.^{15–17}

To our knowledge, two prospective studies and four cross-sectional studies have assessed the relationship

between breastfeeding and allergies in Japan.^{18–23} The Osaka Maternal and Child Health Study showed no effects of breastfeeding on the risk of wheeze, asthma or eczema during the first 16–24 months of life.^{18,19} On the other hand, a cross-sectional study among schoolchildren showed a positive relation between breastfeeding and the prevalence of asthma,²⁰ and a positive association between breastfeeding and eczema was found in two cross-sectional studies.^{22,23} In a cross-sectional study, there was no association between breastfeeding and asthma, eczema or allergic rhinitis in Japanese university students.²¹ In the present study, we analysed the association between breastfeeding and the prevalence of wheeze, asthma and eczema among Japanese children aged 3 years to provide further evidence on the association between breastfeeding and allergic disorders in Japan.

STUDY POPULATION AND METHODS

Subjects

Data for the present study came from the Fukuoka Child Health Study, a cross-sectional study to investigate the association between various selected factors

and child health problems. On reaching 3 years of age, children in Japan undergo a physical examination performed by the municipal health authorities of the child's area of residence. Eligible subjects for the present study were children aged 3 years who underwent the physical examination offered at all seven public health centres in Fukuoka City, a metropolitan area of Kyushu Island in southern Japan, with a total population of almost 1 414 000. Of the 8269 subjects eligible during the period from June 2006 to January 2007, 8064 parents or guardians were provided with a structured self-administered questionnaire, a brief self-administered diet history questionnaire and a stamped return envelope. A final total of 2109 parents or guardians answered the questionnaires and mailed them to the data management centre (participation rate 25.5%). Our research technicians completed missing answers and/or illogical data by telephone interview. The current study was restricted to subjects who provided complete information on the variables under study, leaving data on 1957 children available for analysis (23.7% of all eligible children).

Permission to perform this study was obtained from the ethics committee of the Faculty of Medicine, Fukuoka University.

Outcome variables

One of the questionnaires included questions on wheeze, asthma and eczema in the previous 12 months based on the International Study of Asthma and Allergy in Childhood (ISAAC) Phase I questionnaire. The definition of wheeze used in this study was determined by a positive response to the question, 'Has your child had wheezing or whistling in the chest in the last 12 months?' A positive response to both the aforementioned questions and another question 'Has your child ever had asthma?' was considered to indicate asthma. For eczema, affirmative answers to all of the following three questions in the ISAAC questionnaire were required: 'Has your child ever had an itchy rash which came and went for at least 6 months?', 'Has your child had this itchy rash at any time in the last 12 months?', and 'Has this itchy rash at any time affected any of the following places: the folds of the elbow, behind the knees, in front of the ankles, under the buttocks or around the neck, ear, or eyes?'

Exposure variables and covariates

Information on the duration of breastfeeding in months and the age in months at which formula milk was introduced was obtained from a structured self-administered questionnaire. Duration of exclusive breastfeeding was defined as the period during which infants were given only breast milk and formula milk had not been introduced. The duration of breastfeeding was defined as the period during which the infants received breast milk, regardless of exclusivity.

Exposure to formula milk in the delivery hospitals was not taken into consideration. The questionnaire also included questions about sex, number of siblings, smoking in the household, paternal and maternal history of asthma, atopic eczema and allergic rhinitis, and paternal and maternal educational level.

Statistical analyses

Logistic regression analysis was used to estimate crude odds ratios (ORs) and 95% confidence intervals (CIs) for allergies relative to breastfeeding. Subjects were categorised into two groups depending on the duration of exclusive breastfeeding (<4 and ≥4 months). Duration of breastfeeding regardless of exclusivity was dichotomised at 6 months (<6 and ≥6 months). The following variables were controlled for in the multivariable model: sex, number of siblings, smoking in the household, paternal and maternal history of asthma, atopic eczema and allergic rhinitis, and paternal and maternal educational level. All statistical analyses were performed using the SAS software package version 9.1 (SAS Institute, Inc, Cary, NC, USA).

RESULTS

The prevalence values of symptoms of wheeze, asthma and eczema in the previous 12 months were

Table 1 Distribution of selected characteristics in 1957 children, Fukuoka Child Health Study, Japan

Variable	n (%)
Male sex	1035 (52.9)
Siblings	
0	603 (30.8)
1	1075 (54.9)
≥2	279 (14.3)
Smoking in household	
Never	1124 (57.4)
Former	124 (6.3)
Current	709 (36.2)
Paternal history of asthma	241 (12.3)
Paternal history of atopic eczema	172 (8.8)
Paternal history of allergic rhinitis	630 (32.2)
Maternal history of asthma	177 (9.0)
Maternal history of atopic eczema	254 (13.0)
Maternal history of allergic rhinitis	783 (40.0)
Paternal educational level, years	
<13	530 (27.1)
13–14	297 (15.2)
≥15	1130 (57.7)
Maternal educational level, years	
<13	541 (27.6)
13–14	792 (40.5)
≥15	624 (31.9)
Duration of exclusive breastfeeding, months	
<4	986 (50.4)
≥4	971 (49.6)
Duration of breastfeeding regardless of exclusivity, months	
<6	391 (20.0)
≥6	1566 (80.0)

respectively 22.1%, 8.9% and 17.3%. Approximately 70% of the subjects had one or more siblings (Table 1). Of the 1957 children, 1124 (57.4%) had not been exposed to smoking in the household. Many more children had parents with a history of allergic rhinitis than parents with a history of asthma or atopic eczema. Just half of the children (49.6%) were exclusively breastfed for ≥ 4 months; 80% were breastfed for ≥ 6 months. Only 2.6% ($n = 51$) of the children were not breastfed at all or were breastfed for < 1 month.

Compared with < 4 months of exclusive breastfeeding, exclusive breastfeeding for ≥ 4 months was significantly associated with a lower prevalence of asthma (Table 2). Adjustment for confounders under study did not appreciably change the result (adjusted OR [aOR] 0.69, 95%CI 0.50–0.96). We found no statistically significant relationship between the duration of exclusive breastfeeding and the prevalence of wheeze or eczema in the multivariate model.

After adjustment for confounders under study, an inverse relation between the duration of breastfeeding and the prevalence of asthma was just short of the significance level (aOR 0.72, 95%CI 0.50–1.06, $P = 0.09$; Table 3). There was no appreciable association of the duration of breastfeeding with wheeze or eczema in the adjusted analysis.

Stratified analysis based on parental allergic history in at least one parent showed that no measurable interactions were found in the association of breastfeeding status with the prevalence of allergic disorders between children with and those without a parental allergic history ($P = 0.63$ and 0.47 for wheeze, 0.67 and 0.57 for asthma, and 0.24 and 0.42 for eczema for homogeneity of OR for exclusive breastfeeding duration and breastfeeding duration, respectively).

DISCUSSION

The present study found that longer exclusive breastfeeding was significantly related to a lower prevalence of asthma, but not to wheeze or eczema. Our results are partially in agreement with a previous meta-analysis of prospective studies showing an inverse association between breastfeeding and asthma,²⁴ but are at variance with a meta-analysis showing a protective effect of breastfeeding against atopic dermatitis.²⁵ On the other hand, a null or positive association between breastfeeding and asthma was shown in previous Japanese studies.^{19–21} These discrepant findings might be attributed to differences in the duration and pattern of breastfeeding and the definition of asthma used in those studies. Furthermore, differences in age

Table 2 Prevalence and odds ratios for allergic disorders according to duration of exclusive breastfeeding in 1957 children, Fukuoka Child Health Study, Japan

	Prevalence <i>n/N</i> (%)	Crude OR (95%CI)	Adjusted OR (95%CI)*
Wheeze, months			
<4	232/986 (23.5)	1.00	1.00
≥ 4	200/971 (20.6)	0.84 (0.68–1.04)	0.84 (0.68–1.05)
Asthma, months			
<4	102/986 (10.3)	1.00	1.00
≥ 4	72/971 (7.4)	0.69 (0.51–0.95)	0.69 (0.50–0.96)
Eczema, months			
<4	178/986 (18.1)	1.00	1.00
≥ 4	160/971 (16.5)	0.90 (0.71–1.13)	0.90 (0.71–1.15)

* Adjustment for sex, number of siblings, smoking in household, paternal and maternal history of asthma, atopic eczema and allergic rhinitis, and paternal and maternal educational level.

OR = odds ratio; CI = confidence interval.

Table 3 Prevalence and odds ratios for allergic disorders according to duration of breastfeeding, regardless of exclusivity, in 1957 children, Fukuoka Child Health Study, Japan

	Prevalence <i>n/N</i> (%)	Crude OR (95%CI)	Adjusted OR (95%CI)*
Wheeze, months			
<6	98/391 (25.1)	1.00	1.00
≥ 6	334/1566 (21.3)	0.81 (0.63–1.05)	0.83 (0.63–1.09)
Asthma, months			
<6	45/391 (11.5)	1.00	1.00
≥ 6	129/1566 (8.2)	0.69 (0.49–1.00)	0.72 (0.50–1.06)
Eczema, months			
<6	70/391 (17.9)	1.00	1.00
≥ 6	268/1566 (17.1)	0.95 (0.71–1.27)	0.95 (0.71–1.30)

* Adjustment for sex, number of siblings, smoking in household, paternal and maternal history of asthma, atopic eczema and allergic rhinitis, and paternal and maternal educational level.

OR = odds ratio; CI = confidence interval.

at diagnosis among study populations might produce conflicting results. The relationship between breastfeeding and asthma might vary with the age of the child.^{13,26} From a longitudinal study in New Zealand, it was observed that breastfeeding for ≥ 4 weeks increased the risk of asthma in mid-childhood, with effects persisting into adulthood.¹³ In a US cross-sectional study, breastfeeding was inversely associated with the prevalence of asthma before 24 months of age.²⁶ This protective relationship was no longer evident in breastfed children who were diagnosed with asthma after 24 months of age, however.²⁶

The mechanisms of the protective effect of breastfeeding against asthma are not well understood. The physical exercise caused by suckling at the breast might result in increased elasticity and efficiency of the lung parenchyma, resulting in increased lung capacity and increased airflow.²⁷ In a UK cohort study, forced vital capacity, forced expiratory volume in 1 second and peak expiratory flow were significantly increased in children breastfed for at least 4 months compared with children who were not breastfed.²⁷ Other feasible mechanisms are the immunostimulatory properties of breast milk, which might enhance the immature immunological system of the infant and strengthen its host defence mechanisms against infective or other foreign agents.^{28–30} In addition, the immunosuppressive factors in breast milk might downregulate inflammation and prevent the development of allergies.³⁰ Oddy et al. observed a significant inverse association between the dose of transforming growth factor beta-1 received through breast milk and the risk of wheeze in the first year of life, although concentrations of interleukin-10, tumour necrosis factor- α and the soluble form of cluster of differentiation 14 (CD14) were not related to wheeze.²⁹ Alternatively, prolonged breastfeeding might be associated with a lifestyle that has a protective effect against asthma.¹

The lack of an association between breastfeeding and eczema in the current study might be attributed to unknown active substances in breast milk that obscure any beneficial effect of breastfeeding. Dioxins and polychlorinated biphenyls (PCBs) are lipophilic compounds that are present in human milk. A study in the Netherlands showed that plasma PCB levels were 3.6 times higher in breastfed children than in their formula-fed peers, and that the breastfeeding period and breast milk PCB levels were significantly positively related to plasma PCB levels in the breastfed group.³¹ In Dutch preschool children, perinatal exposure to PCBs and dioxins was associated with changes in the T-cell lymphocyte population, although PCB exposure was not related to the prevalence of asthma or bronchitis.³²

In the current study, observed relationships between breastfeeding and the prevalence of wheeze, asthma and atopic eczema were not modified by parental al-

lergic history. Several studies have investigated the relationship of breastfeeding with allergic disorders in children with or without a family history of allergies, but did not show consistent results.^{1,6,10,11,13,15,18,19,21,22} However, a review concluded that the protective effect of breastfeeding against the development of atopic disease appears even stronger in children with an atopic heredity.³³

This study had methodological strengths. Study subjects were homogeneous with respect to age and geographic background, and we could control for relevant confounding variables. On the other hand, some limitations may have affected our results. Of the 8296 eligible subjects in Fukuoka City, only 1957 (23.7%) were included in this analysis, leading to a potential for selection bias. We were not able to assess a difference between participants and non-participants because information on the personal characteristics of non-participants, except for age, was not available. Our subjects were not representative of Japanese children in the general population. In particular, the educational levels of the subjects' parents in the present study were higher than in the general population. According to the 2000 population census of Japan, the proportions of men aged 35–39 years in Fukuoka City with <13, 13–14, ≥ 15 and unknown years of education were respectively 39.6%, 8.0%, 43.3% and 9.1%.³⁴ The corresponding figures among men in the present study were respectively 27.1%, 15.2%, 57.7% and 0.0%. Among women aged 30–34 years in Fukuoka City, the percentage of <13, 13–14, ≥ 15 and unknown years of education were respectively 41.3%, 34.4%, 16.1% and 8.3%.³⁴ The corresponding figures among women in the present study were respectively 27.6%, 40.5%, 31.9% and 0.0%. The present population might have had a greater awareness about health than the general population, which could have driven the results. In the current study, we observed no association between breastfeeding and the prevalence of wheeze. Because our definition of wheeze using ISAAC criteria among children aged 3 years was crude, it might be difficult to detect a significant inverse association between breastfeeding and wheeze. In the current study, data on breastfeeding were collected retrospectively, which might lead to recall bias. However, most of the questionnaires were completed by the mother, and it is unlikely for a mother not to remember the breastfeeding history of her child. Parents of children with allergic disorders might have reported a longer duration of breastfeeding than actually occurred. This type of differential exposure misclassification could lead to bias toward a positive direction. However, in the current study, the parents or guardians were informed of the main purpose of the study, which was to investigate the association between various selected factors and child health problems, but no special attention was paid to breastfeeding. Blinding of the

specific study question was likely to reduce information bias. It is also possible that mothers tend to breastfeed longer if the child has had onset of an allergic disorder, particularly eczema, before weaning, which might introduce a bias toward a positive direction. This might have masked a possible inverse association between breastfeeding and eczema in the current study.

In conclusion, our results indicate that exclusive breastfeeding for ≥ 4 months was associated with a reduced prevalence of asthma in young children. In Japan, this is the first epidemiological study to support the protective effect of breastfeeding against asthma. Further studies, particularly prospective studies, are needed to be able to draw conclusions about the question of the protective effect of breastfeeding on the development of asthma as well as the influence of breastfeeding on the development of eczema.

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RÉSUMÉ

CONTEXTE : Les données concernant l'association entre l'allaitement maternel et l'allergie ne sont pas concordantes.

OBJECTIF : Investiguer la relation entre la durée et les caractères exclusifs de l'allaitement maternel et la prévalence d'une respiration sifflante, de l'asthme et de l'eczéma chez de jeunes enfants japonais.

SCHEMA : Ont été inclus dans l'étude 1957 enfants âgés de 3 ans. Les données concernant l'allaitement maternel, les symptômes allergiques et les facteurs confondants potentiels ont été recueillis grâce à un questionnaire. Les résultats ont été définis selon les critères de l'International Study on Asthma and Allergies in Childhood. On a pratiqué un ajustement pour le sexe, le nombre de frères et sœurs, le tabagisme au domicile, les antécédents maternels et paternels d'asthme, d'eczéma atopique et de rhinite allergique ainsi que pour les niveaux d'éducation paternel et maternel.

RÉSULTATS : Les valeurs de prévalence des symptômes de respiration sifflante, asthme et eczéma au cours des 12 mois précédents ont été respectivement de 22,1%, 8,9% et 17,3%. Une prévalence plus faible de l'asthme est en association avec un allaitement exclusif pendant une période de ≥ 4 mois par comparaison avec un allaitement de < 4 mois. La durée de l'allaitement exclusif ou non de ≥ 6 mois a tendance à être en association avec une plus faible prévalence de l'asthme. On n'a pas trouvé d'association appréciable entre l'allaitement et la respiration sifflante ou l'eczéma.

CONCLUSIONS : Les données de cette étude indique que l'allaitement maternel peut être en association avec une plus faible prévalence de l'asthme chez les jeunes enfants japonais.

RESUMEN

MARCO DE REFERENCIA: Existen datos contradictorios sobre la asociación entre la lactancia materna y la aparición de alergias.

OBJETIVO: Investigar la correlación entre la duración y exclusividad de la lactancia natural y la prevalencia de sibilancias, asma y eccema en los niños pequeños en el Japón.

MÉTODOS: Se estudiaron 1957 niños de 3 años de edad. Se administró un cuestionario con el fin de recoger datos sobre la lactancia materna, los síntomas de alergia y los posibles factores de confusión. Las variables de evaluación se definieron según los criterios del Estudio Internacional sobre el Asma y las Alergias en la Niñez (ISAAC). Se recogió información sobre el sexo, el número de hermanos, el tabaquismo en el domicilio, los antecedentes maternos y paternos de asma, al eccema atópico y la rinitis alérgica y el grado de educación de los padres.

RESULTADOS: Durante los 12 meses previos a la encuesta, la prevalencia de sibilancias fue 22,1%, de asma 8,9% y de eccema fue 17,3%. La lactancia natural exclusiva durante ≥ 4 meses se asoció con una menor prevalencia de asma, cuando se comparó con una lactancia materna exclusiva durante < 4 meses. La duración de la lactancia materna, sin condición de exclusividad, durante ≥ 6 meses, tendió a asociarse con una menor prevalencia de asma. No se observó una asociación evidente entre la alimentación natural y presencia de sibilancias o eccema.

CONCLUSIONES: Los resultados del estudio indican que la alimentación natural se puede asociar con una menor prevalencia de asma en los niños japoneses de corta edad.