ORIGINAL ARTICLE

Frequency of Allergic Diseases in 2-Year-Old Children in Relationship to Parental History of Allergy and Breastfeeding

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Abstract

Background: The association between breastfeeding and the risk of atopic diseases in children is controversial. While some studies support the theory of a decreased risk of asthma and allergic diseases due to breastfeeding, others have failed to confirm such a protective effect, and even suggest increased risk. The aim of this longitudinal study was to investigate the association between breastfeeding and the prevalence of atopic diseases in 2-year-old children.
Methods: Data on 1685 children from a birth cohort were collected from questionnaires completed by parents at birth and at 6, 12, and 24 months. By means of logistic regression and considering confounders such as family history and socioeconomic status, we analyzed the association between exclusive breastfeeding and the development of allergic reactions in 2-year-old children.
Results: Exclusive breastfeeding for >4 months was associated with an increased risk of asthma and atopic dermatitis in children without a parental history of allergic diseases (odds ratio [OR]=1.62; 95% confidence interval [CI], 1.02-2.56). Children whose fathers only had a history of allergic disease strongly benefited from exclusive breastfeeding for >4 months (OR=0.39; 95%-CI: 0.18-0.83) whereas those whose mothers only had such a history had an increased risk of asthma and atopic dermatitis (OR: 2.31; 95%-CI: 1.16-4.60).
Conclusion: In children with a family history of allergy, it seems to be important to distinguish between maternal and paternal predisposition as children whose fathers have a history of atopic disease seem to benefit most from breastfeeding for >4 months.

Key words: Breastfeeding. Parental history. Allergy. Children.

Resumen

Antecedentes: La asociación entre la lactancia materna y el riesgo de enfermedades atópicas en niños es motivo de controversia. Mientras que algunos estudios respaldan la teoría de que la lactancia materna reduce el riesgo de asma y de enfermedades alérgicas, otros no han podido confirmar este efecto protector e incluso sugieren que supone un mayor riesgo. El objetivo de este estudio longitudinal fue analizar la asociación entre la lactancia materna y la prevalencia de enfermedades atópicas en niños de 2 años.
Métodos: Se recopilaron datos de 1.685 niños de una cohorte de nacimiento a partir de cuestionarios rellenados por los padres tras el nacimiento y a los 6, 12 y 24 meses. Mediante regresión logística y teniendo en cuenta factores de confusión como los antecedentes familiares y el nivel socioeconómico, se analizó la asociación entre la lactancia materna exclusiva y el desarrollo de reacciones alérgicas en niños de 2 años.
Resultados: La lactancia materna exclusiva durante más de 4 meses se asoció con un mayor riesgo de asma y dermatitis atópica en niños sin antecedentes familiares de enfermedades alérgicas (oportunidad relativa [OR] =1,62; intervalo de confianza [IC] del 95%, 1,02-2,56). Los niños cuyos padres presentaban antecedentes de enfermedades alérgicas obtuvieron claros beneficios de una lactancia materna superior a 4 meses (OR = 0,39; IC del 95% = 0,18-0,83), mientras que los niños cuyas madres tenían antecedentes presentaron un mayor riesgo de asma y dermatitis atópica (OR = 2,31; IC del 95% = 1,16-4,60).
Conclusión: En los niños con antecedentes familiares de alergia, es importante distinguir entre predisposición materna y paterna, dado que los niños cuyos padres presentan antecedentes de enfermedad atópica son los que parecen obtener un mayor beneficio de una lactancia materna superior a 4 meses.

Palabras clave: Lactancia materna. Antecedentes familiares. Alergia. Niños.

Introduction

The effect of breastfeeding on the risk of developing allergic diseases in neonates is increasingly a matter of controversy. While a large number of studies emphasize the protective effect of breast milk, especially in children with atopic heredity who are breastfed for >4 or 6 months [1], the number of publications querying this protective effect is rising. The aim of this study was to investigate the association between the frequency of symptoms of allergic diseases in 2-year-old children and the duration of breastfeeding using data from a birth cohort study carried out in north-west Germany [2].

Participants and Methods

Study Population and Questionnaire Data

Within the scope of a longitudinal study conducted between 1999 and 2000, 3132 mothers of German nationality were interviewed on aspects related to lifestyle and family history of allergic disease. The first survey took place in the obstetric units of 5 participating hospitals in Delmenhorst, Wilhelmshaven, and Leer. Before the mothers were discharged from hospital they completed a baseline questionnaire containing detailed questions on family history of allergic disease, parental education (social class), and a range of lifestyle-related aspects. The mothers were interviewed again at 6 months, 12 months, and 2 years postpartum during the respective preventive check-up visits U5, U6, and U7 that children undergo in Germany. These follow-up interviews included questions about breastfeeding behavior and symptoms of allergic diseases in the children. In total, 1685 mothers (54%) completed the baseline questionnaire and the 3 follow-up interviews. Using this group, we investigated the association between breastfeeding behavior and signs of allergic diseases (eczema, hay fever, bronchial asthma, or allergic/spastic/obstructive bronchitis diagnosed by a physician; itchy rash for >6 months; cracks in the skin under the earlobes) in 2-year-old children. The number of questionnaires analyzed (n=1685) differs from that analyzed in our previous study of this birth cohort (n=1881) [2] because in that case, we only required data from the baseline questionnaire and the last questionnaire (U7 check-up).

Study Variables

Several study variables were established on the basis of the information obtained from baseline questionnaires (completed a few days after birth). Social class was defined by the highest school education achieved by either the mother or the father. We used the following categories: <10 years of formal education, lower class; 10 years, middle class; >10 years, upper class [3]. A hereditary or family predisposition to allergic disease was established on the basis of a reported history of eczema, asthma, or hay fever among the newborn's first-degree relatives [4]. Breastfeeding duration was determined from the information collected at 6 months and 12 months. Only mothers who had exclusively breastfed their children (with no nutritional supplements or milk or tea) were included in the breastfeeding categories. We differentiated between not having breastfed, having breastfed for ≤4 months, and having breastfed for >4 months. Finally, in order to define disease status, we analyzed the answers to the following questions: *a)* "Has the child had physician-diagnosed eczema, an itchy rash for more than 6 months, or cracking of the earlobes (symptoms of eczema)?"; *b)* "Has the child had physician-diagnosed asthma or chronic obstructive bronchitis (symptoms of asthma)?", and *c)* "Has the child had physician-diagnosed hay fever?" If the answer to at least 1 of these questions was yes, the child was considered to have symptoms of allergic disease.

Statistical Analysis

Multiple logistic regression was used to analyze the effect of breastfeeding on the development of atopic diseases in 2-year-old infants. Because breastfeeding behavior and the development of allergic diseases in infants are both strongly associated with social class, we routinely included parental education in our analyses. Further adjustment for sex, place of residence, and parental smoking did not significantly influence the odds ratios (ORs) compared with the results adjusted for parental education alone. Family history of allergic disease, as one of the most important risk factors and confounders, was considered by stratified analyses for children with and without a parental history of atopic disease. The study group was thus stratified into children without a family history, children with a paternal history only, children with a maternal history only, and children with both a paternal and a maternal history. Infants without a parental history but with at least 1 sibling with a history of atopic disease (n=74) were excluded from these stratified analyses. All statistical analyses were performed using the software package SAS, release 8.2 (SAS Institute, Cary, North Carolina, USA).

Results

Table 1 shows the distribution of children with allergic symptoms at the age of 2 years by sex, social class, study center, and family history of allergic disease. Approximately 23% of the 1685 children (n=393) had evidence of allergic disease at the age of 2 years. The majority of these (approximately 70%) had symptoms of eczema, a third had physician-diagnosed asthma or chronic obstructive bronchitis, and only 2 children had physician-diagnosed hay fever. As expected, the appearance of symptoms was strongly influenced by parental predisposition, with maternal predisposition (OR=1.44; 95% confidence interval [CI], 1.12-1.86) having a slightly stronger influence than paternal predisposition (OR=1.30; 95% CI, 0.99-1.71).

Approximately a quarter of all mothers reported not having breastfed their children, with a strong association with social class. In the lower class, 44% of infants had not been breastfed, compared to 27% in the middle class and just 15% in the upper class. Dependent on social class, a family history of allergic disease also seemed to have an effect on breastfeeding duration. The awareness of a genetic predisposition is likely to have prompted more women to breastfeed their child for >4 months in the upper class and in the middle class in particular, where 32.5% of children with a genetic predisposition were breastfed

Table 1. Two-Year-Old Children With and Without Symptoms of Allergic Disease, by Sex, Social Class (Parental Education), Study Center, and Family History

	No.	Allergic Disease[a]		*P* Value[b]
		No Symptoms, No. (%)	Symptoms, No. (%)	
Sex				
Boy	837	630 (75.3)	207 (24.7)	
Girl	848	662 (78.1)	186 (21.9)	.17
Parental education				
<10 y (lower class)	324	252 (77.8)	72 (22.2)	
10 y (middle class)	754	587 (77.9)	167 (22.1)	
>10 y (upper class)	607	453 (74.6)	154 (25.4)	.33
Study centre				
Delmenhorst	709	542 (76.4)	167 (23.6)	
Wilhelmshaven	494	377 (76.3)	117 (23.7)	
Leer	482	373 (77.4)	109 (22.6)	.91
Family history[c]				
No	956	772 (80.8)	184 (19.2)	
Yes	729	520 (71.3)	209 (28.7)	<.0001
Maternal history of allergic disease				
No	1288	1009 (78.3)	279 (21.7)	
Yes	397	283 (71.3)	114 (28.7)	.004
Paternal history of allergic disease				
No	1342	1043 (77.7)	299 (22.3)	
Yes	343	249 (72.6)	94 (27.4)	.045
Sibling history of allergic disease				
No	1514	1182 (78.1)	332 (21.9)	
Yes	171	110 (64.3)	61 (35.7)	.0001
Total	1685	1292 (76.7)	393 (23.3)	

[a]Physician-diagnosed asthma or asthma-like bronchitis, hay fever, or eczema; itchy rash for >6 mo or cracking at the earlobes.
[b]Analyzed using the χ^2 test.
[c]History of asthma, eczema, or hay fever in first-degree relatives (mother, father, siblings) of infant.

for >4 months, compared to just 22.8% of those without this predisposition. The association between breastfeeding behavior and the combined effect of social class and family history of allergic disease is shown in the Figure.

On analyzing the association between the prevalence of allergic symptoms in 2-year-old children without allergic predisposition and breastfeeding behavior, we observed a higher proportion of children with symptoms in the breastfed group than in the never-breastfed group (OR=1.30; 95% CI, 0.87-1.93). With regards to the duration of breastfeeding (Table 2), children without a genetic disposition to allergic disease who were exclusively breastfed for >4 months showed a significantly increased risk of developing an atopic disease (OR=1.62; 95% CI, 1.02-2.56).

In contrast to above, the appearance of allergic diseases in 2-year-old children with a family history of atopy was less common in breastfed children than in never-breastfed children (OR=0.86; 95% CI, 0.59-1.24). Nonetheless, when analyzed in greater detail, our data showed very different results depending on the source of parental predisposition. Children with a maternal-only predisposition had a considerably higher risk of allergic disease symptoms at the age of 2 years if they had been exclusively breastfed for >4 months than if they had never been breastfed (OR=2.31; 95% CI, 1.16-4.60). In contrast, children with a paternal-only predisposition had a significantly decreased risk if they had been breastfed for >4 months (OR 0.39; 95%-CI, 0.18-0.83) than if they had never been breastfed. Breastfeeding for ≤4 months seemed to have no influence on increased or decreased risk of allergic disease in children with either a paternal or maternal allergic predisposition. In contrast, breastfeeding, regardless of duration, seemed to have the strongest protective effect on newborns whose father and mother had hay fever, eczema, or asthma. The results for children whose both parents had a history of allergic disease are based on very small numbers so the significantly decreased ORs for both categories of breastfeeding should be interpreted with caution.

An often-discussed explanation for the higher rates of allergies detected in children who have been breastfed for longer is the reversal of cause and effect. In other words, on detecting early signs of atopic disease in their infant, mothers

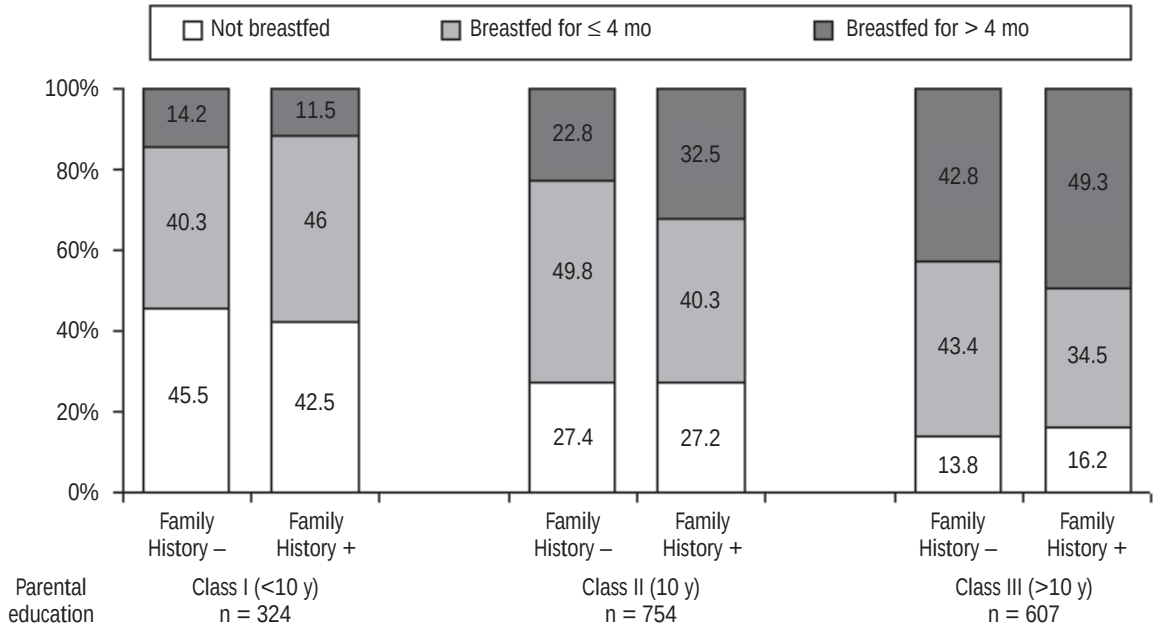

Figure. Breastfeeding behavior by social class (parent education) and family history of allergic diseases.

Table 2. Duration of Breastfeeding and Symptoms of Allergic Disease in 2-Year-Old Children by Family History of Atopic Disease

	Allergic Disease[a]			
	No Symptoms, No. (%)	Symptoms, No. (%)	OR[b]	95% CI
No parental predisposition[c]				
Not breastfed	218 (84.5)	40 (15.5)	1	
Breastfed for ≤4 mo	357 (81.9)	79 (18.1)	1.15	(0.75-1.75)
Breastfed for >4 mo	197 (75.2)	65 (24.8)	1.62	(1.02-2.56)
Paternal but no maternal predisposition				
Not breastfed	42 (65.6)	22 (34.4)	1	
Breastfed for ≤4 mo	67 (66.3)	34 (33.7)	0.97	(0.50-1.88)
Breastfed for >4 mo	76 (81.7)	17 (18.3)	0.39	(0.18-0.83)
Maternal but no paternal predisposition				
Not breastfed	58 (74.4)	20 (25.6)	1	
Breastfed for ≤4 mo	93 (76.2)	29 (23.8)	0.98	(0.50-1.92)
Breastfed for >4 mo	68 (60.7)	44 (39.3)	2.31	(1.16-4.60)
Paternal and maternal predisposition				
Not breastfed	8 (50.0)	8 (50.0)	1	
Breastfed for ≤4 mo	30 (83.3)	6 (16.7)	0.18	(0.05-0.69)
Breastfed for >4 mo	26 (78.8)	7 (21.2)	0.26	(0.07-0.99)

Abbreviations: CI, confidence interval; OR, odds ratio.
[a]Physician-diagnosed asthma or asthma-like bronchitis, hay fever, or eczema; itchy rash for >6 mo or cracking at the earlobes.
[b]Adjusted for parental education.
[c]History of asthma, eczema, or hay fever in newborns' parents (mother, father, or both); 74 infants with a sibling history of allergic disease only were excluded from the analysis.

feel compelled to prolong breastfeeding (which would explain the higher number of children with allergic symptoms within the subgroup of children breastfed for >4 months). To control for such an effect in the present study, we conducted an additional analysis excluding children with reported symptoms of allergic disease in the first 12 months of life (6-month and 12-month visits). In other words, we carried out an additional restricted analysis comprising only children who showed symptoms of allergic disease for the first time between 13 and 24 months and all children without allergic disease. Our aim was to exclude breastfeeding durations of >4 months that might have been prompted by signs of allergic disease during the child's first months of life. The number of children included (and consequently the power of the analysis) was considerably reduced by this selection, but the results remained almost unchanged in terms of tendency.

We also studied possible modifying effects on prolonged breastfeeding related to social class and parental predisposition to allergic disease (see Figure 1) by stratifying the data in Table 1 by social class. This produced a table with many small cell counts, particularly for the lower social class, and resulted in very unstable stratum-specific ORs, which is why we have not shown these results. Nevertheless, we found no significant differences between ORs for breastfeeding duration by family history of allergic disease across the 3 categories of social class.

Discussion

The main strength of the present study is its prospective design, which allowed us to ask parents about confounders such as family history of allergies and education during the baseline survey. We collected data on breastfeeding behavior at 6 months and 12 months and on symptoms of allergic diseases at 6 months, 12 months, and 2 years. We are therefore likely to have eliminated undesirable effects such as recall bias or bias due to misclassification of exposure. Our study, nonetheless, also has limitations. Specifically, breastfeeding behavior, and disease status in particular, were based on parental information only, with no assessment of objective outcomes such as serum immunoglobulin (Ig) E levels or skin prick tests.

Nonetheless, our results are in concordance with some recently published reports showing, on the one hand, that breastfeeding might be preventive or more preventive for infants with some kind of genetic disposition [5,6,7] and, on the other hand, that prolonged breastfeeding in children without a family history of allergy could be a risk factor for the onset of allergic disease [7,8]. An enormous number of epidemiological studies have been published on this topic, but their results seem to show inconsistencies regarding the association between breastfeeding and the risk of atopic disease in children. The reasons for the sometimes contradictory findings are manifold and are probably related to study design (cross-sectional, case-control, cohort), outcome measures (eczema, asthma, wheeze, atopic sensitization, etc), the age of children (newborns up to adults), the reversal of cause and effect [9], and not least of all, the absence of an adequate statistical consideration of family history. A recently published review summarizes the current situation: "Although breastfeeding is strongly recommended for its multiple benefits on child health, most recent studies do not confirm the 'conventional wisdom' that breastfeeding is protective against allergy and asthma." [10]

Our findings are consistent to a certain extent with results from a publication from 1999 which hinted at a correlation between disease in children and breastfeeding that was dependent on maternal predisposition to allergy [11]. In that study, Wright et al showed that children of mothers with an increased IgE level also had significantly increased IgE values when they were breastfed for >4 months compared to children breastfed for <4 months ($P<.01$). The authors also showed that in the group of children of mothers who had a low IgE level, compared to never-breastfed infants, those who had been breastfed had lower IgE values at the ages of 6 years ($P<.02$) and 11 years ($P<.08$). These results suggest an interaction between maternal asthma—expressed by IgE status—and the effect of breastfeeding duration. In the same direction, Snijders et al [12] concluded from their own birth cohort study (KOALA) that "… the relationship between breastfeeding and infant eczema in the first 2 years of life may be modified by maternal allergic status, because a protective effect of breastfeeding duration on eczema seemed to be present mainly for mothers without allergy or asthma…". Nevertheless, Snijders et al did not find any association between breastfeeding and eczema for children whose mothers had a history of allergy or asthma, in contrast to our findings and to results reported from the Tucson Children's Respiratory Study [13], where exclusive breastfeeding for ≥4 months among infants whose mothers had a history of asthma increased the risk for developing asthma (OR=8.7; 95% CI, 3.4-22.2).

Assuming that breastfed children with a positive maternal history of atopic diseases have a higher risk for eczema, one must ask what mechanisms could be responsible for such an effect. Hatakka et al [14] saw the components of breast milk as a possible explanation, proposing that the maturation of the immune system would be enhanced by the intake of human milk incorporating immunomodulatory components such as cytokines, IgA, and bifidobacteria and lactic for the infant's gut.

Indeed, according to those authors, atopic mothers may have higher cytokine and soluble CD14 levels in their breast milk, which would affect the development of atopic disease. This would mean that prolonging breastfeeding might have a protective effect. This suggestion was based on a previously published paper from the KOALA study that found a somewhat higher concentration of soluble CD14 in the breast milk of mothers with an allergic history than in that of mothers without such a history [15], but no association was found between the concentration for soluble CD14 and infant atopic outcome. While Rothenbacher et al [16] found no association between maternal atopic history and soluble CD14 concentrations in breast milk, they did mention an association between duration of exclusive breastfeeding and soluble CD14 levels (P for trend, .005). Unfortunately their results concerning the risk of atopic dermatitis in association with breastfeeding are not very helpful for a comparison with our study, since they used children that had been breastfed for <3 months as a reference category. Interestingly, the lowest ORs were found in children who had not been breastfed, regardless of whether their mothers had atopic disease or not.

In summary, our results suggest that it might be useful in epidemiological studies to differentiate between maternal and paternal history of allergic diseases to investigate possible interactions between breastfeeding duration and diverse aspects of parental heredity on the development of childhood allergies. Perhaps our results are just artefacts but if further investigations could confirm these results, advice to mothers regarding breastfeeding behavior could change.

Acknowledgments

We are especially grateful to all the families for their participation in the study. Part of the study was presented and published as an abstract at the annual meeting of the German Association of Epidemiology in Freiburg, Germany. The study was funded by the Bundesministerium für Bildung, Wissenschaft, Forschung und Technologie (BMBF), 53170 Bonn, Germany (No: 01 EG 9812 / 9).

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Manuscript received May 25, 2009; accepted for publication August 26, 2009.

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