A Study on the Association between Breastfeeding and Allergies in Children 5 Years Old or Younger in the United States

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Abstract

Background: The association between breastfeeding and allergies remains unclear but could be mediated through breast milk's effect on the gut's bacterial population.

Objective: To evaluate if breastfeeding results in a lower prevalence of allergies nationally in children 0 to 5 years old, and to determine if any association is modified as children become further removed from their last breastfeeding.

Methods: This was a cross-sectional study using data from the 2016 National Survey of Childrens Health for children who were 5 or younger. The primary outcome was diagnosis of an allergy ever. Logistic regression was used to determine if different breastfeeding durations showed any association with presenting allergies. A second model with an interaction term between the time elapsed since last breastfed and the duration of breastfeeding tested for effect modification.

Results: As compared to children who were never breastfed, breastfeeding for more than 12 months resulted in an increased prevalence of allergies (PR = 1.70 95% CI:1.20-2.42). Effect modification was present for children breastfeeding 6 to 12 months (p = 0.013). Children in this group that were less than one month removed from breastfeeding showed a 40% reduction in prevalence. This effect was reduced by 1.0% for each month the child was removed from its last breastfeeding.

Conclusions: The results of this study indicate that the association between breastfeeding and allergies may change direction depending on duration. Due to the disease burden caused by allergies, the results merit further investigation under a study design that provides greater strength of evidence.

1 Introduction

Allergies are a common condition where the immune system produces an exaggerated response to an environmental substance known as an allergen that, in most people, has no harmful effect (McConnell, 2007). In the United States, allergies cause significant disease burden in children. In 2016, 7.6 million children were reported to be suffering from a respiratory allergy; 4.5 million from a food allergy; and 8.9 million from a skin allergy (Black & Benson, 2018). Identifying the determinants and deterrents of allergic diseases is crucial to reducing the morbidity they cause in children.

The bacteria colonizing the gut is a driver of the human immune response (Weng & Walker, 2013). This microbe population is known as the gut microbiota, and a balanced diversity is crucial to maintaining a healthy immune system (Walker, 2013). Food intake influences bacterial colonization, and in newborns and infants, milk consumption is the primary driver. When possible, breast milk is preferable to formula milk because of its high-nutrient composition. However, breast milk also contains helpful probiotic bacteria for building a healthy gut microbiota and immune system (Martín, Heilig, Zoetendal, Smidt, & Rodríguez, 2007).

Previous research has shown the benefits of breastfeeding for diseases such as diabetes and intestinal health (Gülden, 2018; Parigi, Eldh, Larssen, Gabrielsson, & Villablanca, 2015; Section on Breastfeeding, 2012). However, the association between allergies and breastfeeding remains unclear,

and studies have reached conflicting results. Ethical concerns prevent the use of randomized control trials to elucidate the relationship as it would be immoral to deny any child the well-established benefits of breastfeeding. As such, research studying the association of breastfeeding with allergies has been mostly observational. A review by Munblit et al. (2017) details the current evidence for an association with several allergic diseases such as eczema, asthma, and food allergy. Different studies have found breast milk to be both increase and reduce the risk of eczema, and in some cases, it showed little to no effect at all (Björkstén et al., 2011; Giwercman et al., 2010; Elbert et al., 2017). The heterogeneity of results is likely due to methodological differences. In particular, the age of the child may influence findings as it is possible that any protection afforded by breastfeeding may wane, and older children are also more likely to be exposed to more risk factors than smaller infants. The association with asthma, while still a source of controversy, has mostly been found to be protective. A meta-analysis by Dogaru, Nyffenegger, Pescatore, Spycher, and Kuehni (2014) of 117 studies found a significant reduction in asthma and wheezing in children who were breastfed. The authors further stratified results by the age the outcome was measured and detected a decreasing trend in the reduction indicating that strength of protection wanes as age increases. Like with eczema, the association of breast milk with food allergies has reached conflicting results (Lodge et al., 2015; Pesonen, Kallio, Ranki, & Siimes, 2006). Inconsistencies may be due to the surrogate markers (clinical history and skin prick test) used to identify food

allergies, as possible misclassification can result in a significant distortion of the effect measures (Munblit et al., 2017).

This study can be placed within the conceptual framework for microbiome-related health and disease and will examine the association between breastfeeding and allergies in children up to 5 years old in the United States. Using data from the 2016 National Survey of Childrens Health, I conducted a cross-sectional study to determine if breastfed children presented a lower prevalence of allergies. Additionally, I evaluated if effect modification was present to see if protection changed as children became further removed from breastfeeding.

2 Materials and Methods

2.1 Sample

The data for this study comes from the 2016 National Survey of Children's Health which collected information on children ages 0 - 17 from a national sample of 364,150 households. The methodology for the survey is available from the U.S. Census Bureau (U.S. Census Bureau, 2018). To be included in the analysis, a child had to be 5 or younger, and the respondent had to have provided an answer to survey question number A6 regarding the diagnosis of an allergy. In total, 14,458 records were available.

2.2 Data Preparation

2.2.1 Outcome and Exposure

No recoding was necessary for the outcome, and the presence of an allergy was captured as *yes* or *no* in the survey. For this analysis, exposure to breastfeeding is measured by duration. A categorical variable was coded to indicate how long an infant has been breastfeeding, or how long it was breastfed before stopping. Depending on duration, children were grouped into the following categories: *never, less than 6 months, 6 to 12 months*, and *>12 months*.

2.2.2 Other Covariates

Variables for the child's sex, race, the presence of a smoker in the child's household, and access to nutritious meals were taken directly from the survey with no need for recoding. Missing values for sex and race were imputed in the original data (U.S. Census Bureau, 2018). Two measures regarding infant nutrition were coded as variables indicating the age when formula and solid foods were introduced, respectively. Possible values are *never or not yet; earlier than 6 months* and *6 months or after*. The time elapsed since the infant stopped breastfeeding was measured by calculating the child's age in months and subtracting the month the infant stopped breastfeeding. If the child was still breastfeeding, then no time was considered to have elapsed. Since no exact value for a child's month-age was captured in the survey, an

estimate was generated by adding 1 to its year-age and multiplying by 12. In other words, the month-age for all children was rounded to the next year. If a child was less than a year old, then survey items indicating ages under 4, 6, 9 and 10 months were used following the same policy of rounding up. For example, any child reported to be less than 4 months old was rounded up to 4. A summary of the variables used in this study is presented in **table 1** in appendix A.

2.3 Statistical Analysis

A univariate analysis was done to compare the characteristics of children with and without allergies. Statistical differences were evaluated using a Chi-square test with an alpha of 0.05. To examine the main effect of breastfeeding duration on allergies, a multivariate analysis was done by building a logistic regression model and adjusting for sex, race, the presence of a smoker in the child's household, access to nutritious meals, ages when formula and solid foods were introduced and time elapsed since the child stopped breastfeeding. To assess whether any protection conferred against allergies wanes as children become further removed from breastfeeding, a second model with an interaction term between the time elapsed since last breastfed and the duration of breastfeeding was built. All statistical analysis applied NSCH sampling weights to obtain nationally representative results.

2.4 Ethical Considerations

IRB approval was obtained for using data from the 2016 National Survey of Children's Health.

3 Results

Table 2 shows the weighted distribution of the exposure and other covariates in children with and without allergies for nationally weighted sample ($N = 23,658,317$). Chi-square tests indicated significant differences for *breastfeeding duration* ($p = 0.04$), *time of first solids* ($p = 0.03$), *race* ($p = 0.001$) and *access to nutritious meals* ($p<0.0001$). Children breastfed longer than 12 months had the highest prevalence of allergies for the group (18.4%), and an increasing trend in the percentage of children presenting the outcome is observed as solid foods are introduced at earlier ages. A similar trend is found when measuring access to nutritious meals, with children whose parents reported sometimes or often not being able to afford enough to eat presenting the highest prevalence of allergies (22.2%). The average months since last breastfed was also found to be significantly different under a two-sample t-test. Children with allergies were on average approximately 9 months further removed from their last breastfeeding compared to children without allergies.

Point estimates from a bivariate analysis (**table 3**) revealed that, compared to children that were never breastfed, children breastfeeding for less

than 6 months or 6 to 12 months had a reduced likelihood of presenting allergies, with only the result for the latter group being significant (PR = 0.71 95% CI: 0.54-0.93). Children breastfeeding more than 12 months had a prevalence ratio close to the null (PR = 1.03 95% CI:0.75-1.40).

Time of first solids, race, access to nutritious meals and the *number of months since last breastfed* were included in a multivariable logistic model (**table 3**). After adjusting, the prevalence ratio for children breastfeeding 6 to 12 months compared to *Never* was no longer found to be protective (PR = 1.00 95% CI: 0.75-1.33), and children breastfeeding more than 12 months were found to have a 70% increased likelihood of allergies (PR = 1.70 95% CI:1.20-2.42).

Inclusion of an interaction term between *breastfeeding duration* and *months since last breastfed* revealed that effect modification is present with borderline significance ($p = 0.046$). Further inspection found the term to be significant only for children who had a breastfeeding duration of 6 to 12 months ($p = 0.013$). When the number of months removed from breastfeeding is zero then a 40% reduction in prevalence is observed. Each month that a child becomes further removed from breastfeeding decreases the observed effect by 1.04%.

The results presented here come from a complete case analyses with listwise deletion. Missing data was addressed through multiple imputations; however, no significant differences were observed in the measures.

4 Discussion

The results indicate that breastfeeding for less than six months does not influence the development of allergies. When breastfed for 6 to 12 months, the association with allergies is modified by the number of months removed from the last breastfeeding episode with each passing month decreasing the protection conferred by approximately 1.0%. The result is consistent with what was observed in the meta-analysis by Munblit et al. (2017) where protection declined as age groups increased. Unlike in the meta-analysis, this study did not examine age groups but rather the months removed from breastfeeding which implicitly considers age. Only using the child's age to evaluate how far removed they were from breastfeeding would not have accounted for children who stopped breastfeeding at older ages.

Previous studies have generally examined breastfeeding as binary with few considering how long the exposure lasted. In this study, breastfeeding was categorized by the duration to evaluate any differences in the results for children who were meeting or exceeding the current breastfeeding recommendations. Treating breastfeeding as an ordinal variable did not reveal any dose effect. Rather than strictly increasing or decreasing, prevalence ratios for the categories form a U-shape with the highest prevalences observable at the lowest and highest exposure durations. This result is indicative of a changing relationship between breastfeeding and allergies and could help explain the conflicting findings of previous studies where the duration of exposure was

not considered.

The association of breastfeeding with allergies mediated through the gut microbiota has not been thoroughly investigated. This study contributes to the clarification of this relationship by adjusting for covariates that may alter the human gut microbe population (i.e., access to nutritious meals, age of first solid foods and first formula), but have not typically been considered. A large sample size was used for the analysis and the results presented are nationally representative.

This study is not without limitations. The data used comes from the 2016 National Survey of Children's Health which asks respondents if the child has been diagnosed with an allergy, but does not specify the type. This broad definition does not allow respiratory, food and skin allergies to be analyzed separately, and instead forces the assumption that the association will behave in the same way for all types of allergies. The inconsistent findings from previous studies indicate that this is not the case and as such, treating allergies as a single group is likely introducing bias. Misclassification is another source of bias that may be occurring. The results from the univariate analysis found access to nutritious meals to be highly associated with allergies (p¡0.0001). The survey question for this variable dealt with food insufficiency, but, to my knowledge, did not specify what is considered nutritious. Without a clear definition, respondents are likely to provide subjective answers according to their own definitions resulting in information bias. Lastly, the results from this study likely present residual confounding. Information about the health

of the mother was not available and therefore, could not be controlled for.

This analysis used a cross-sectional design and, as such, the results should be considered at the appropriate level of strength of evidence provided by this type of study. Cross-sectional studies do not allow causality to be inferred mainly because temporal precedence of exposure to outcome cannot be established. Nevertheless, the results obtained here merit further consideration under a study design that offers a higher strength of evidence and addresses the limitations previously noted. A longitudinal study design, such as a Cox proportional-hazards model would provide a better understanding on the relationship between breastfeeding and allergies, and is a suggested direction of any future research.

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A Tables and Figures

Table 1: Study variables

Variable	Values	Type
Allergies	1 - Yes 2 - No	Dependent
Breastfeeding duration	0 - Never 1 - <6 months 2 - 6 to 12 months 3 - >12 months	Independent
First formula	0 - Never fed formula 1 - Before 6 months 2 - 6 months or after	Control
First solids	0 - Never been fed solid foods 1 - Before 6 months 2 - 6 months or after	Control
Sex	1 - Male 2 - Female	Control
Race	1 - Hispanic 2 - White, non-Hispanic 3 - Black, non-Hispanic 4 - Multi-racial/Other, non-Hispanic	Control
Smoker in household	1 - Yes 2 - No	Control
Access to nutritious meals	1 - We could always afford to eat good nutritious meals 2 - We could always afford enough to eat but not always the kinds of food we should eat 3 - Sometimes or often we could not afford enough to eat	Control
Months since last breastfed	0 - 72	Control

Table 2: Weighted distribution of covariates among children 0-5 with and without allergies. Except where noted, values indicate percentages.

	Present allergies (weighted N = 3,842,908)	**No allergies** (weighted N = 19,815,409)
Breastfeeding duration∗		
Never	896,013 (18.0%)	4,081,665 (82.0%)
<6 months	1,462,154 (16.7%)	7,303,552 (83.3%)
6 to 12 months	710,604 (13.5%)	4,563,701 (86.5%)
>12 months	614,342 (18.4%)	2,725,052 (81.6%)
First formula		
Before 6 months	2,801,536 (17.0%)	13,672,663 (83.0%)
6 months or after	274,079 (18.3%)	1,225,300 (81.7%)
Never	668,792 (13.9%)	4,152,650 (86.1%)
First solids∗		
Before 6 months	2,774,147 (17.1%)	13,443,713 (82.9%)
6 months or after	720,855 (16.5%)	3,642,073 (83.5%)
Never	149,389 (9.3%)	1,460,096 (90.7%)
Sex		
Male	98,773 (15.7%)	255,846 (84.3%)
Female	109,671 (16.8%)	243,217 (83.2%)
Race∗		
Hispanic	779,757 (14.3%)	4,670,977 (85.7%)
White, non-Hispanic	2,025,807 (16.2%)	10,454,495 (83.8%)
Black, non-Hispanic	634,480 (22.8%)	2,154,550 (77.2%)
Multi-racial/Other, non-Hispanic	402,864 (13.7%)	2,535,387 (86.3%)
Smoker in household		
Yes	655,829 (18.9%)	3,129,239 (81.1%)
No	2,817,207 (15.9%)	16,576,756 (84.1%)
Access to nutritious meals∗		
Always	2,301,338 (14.4%)	13,659,427 (85.6%)
Not always	1,154,256 (20.3%)	4,546,878 (79.7%)
Could not afford enough to eat	293,981 (22.2%)	1,029,471 (77.8%)
Months since last breastfed∗ $\bar{X}(SE)$	42.7 (0.8)	34.0 (0.48)

∗ Indicates a statistical difference with a p-value <0.05

Table 3: Crude and adjusted prevalence ratios for allergies under different breastfeeding duration.

	Crude		**Adjusted**$*$	
	PR	95% CI	PR	95% CI
Breastfeeding duration				
Never	1.00	-	1.00	-
<6 months	0.91	(0.71 - 1.17)	1.16	(0.89 - 1.51)
6 to 12 months	0.71	(0.54 - 0.93)	1.00	(0.75 - 1.33)
>12 months	1.03	(0.75 - 1.40)	1.70	(1.20 - 2.42)

$*$ Model adjusted for *Time of first solids, race, access to nutritious meals* and the *number of months since last breastfed*.