Birth Order Effect on Childhood Food Allergy


PURPOSE OF THE STUDY. To determine the relationship between birth order and the prevalence of allergic diseases in childhood.

STUDY POPULATION. The study population included 11,454 children 7 to 15 years of age in Kyoto, Japan.

METHODS. A validated survey was administered to parents of 14,669 children to examine prevalence of allergic rhinitis (AR), atopic dermatitis in childhood and infancy, allergic conjunctivitis (AC), bronchial asthma, food allergy (FA) in childhood and infancy, and wheezing in infancy.

The impact of birth order was examined for 11,454 children with known birth order. FA was categorized as current (at the time of survey) or past; FA during infancy was defined according to symptomatic FA with avoidance of major food allergens at <1 year of age. FA was further subdivided into the following: late FA (onset after age 1 year), early tolerant (gained oral tolerance before age 3 years), and prolonged FA (persistence of disease beyond age 3 years). Logistic regression models were used to compare disease prevalence between different birth order groups. Adjustments were made for confounding variables, including age, gender, gestational age, birth weight, nutrition during infancy, day care attendance before age 1 year, and family history of allergic disease.

RESULTS. First-born children were less likely to be completely breastfed during infancy and less likely to attend day care before age 1 year compared with later-born children. Birth order did not affect the incidence of atopic dermatitis or bronchial asthma. Wheezing in infancy was significantly higher among second-, third-, and later-born children compared with first-born children. Increasing birth order was associated with a statistically significant decrease in prevalence of AR, AC, and FA in childhood and infancy. The relation between birth order and FA showed a decreasing trend in prevalence between first-, second-, and third-born children (4%, 3.4%, and 2.6%, respectively). Prevalence of late FA, early tolerant FA, and prolonged FA was significantly lower in second-, third-, and later-born children compared with first-borns. Higher prevalence remained consistent for first-born children when specific foods were examined.

CONCLUSIONS. The prevalence of atopic dermatitis and bronchial asthma was not affected by birth order whereas the prevalence of AR, AC, and FA decreased with increasing birth order. A reverse trend was demonstrated for wheezing in infancy.

REVIEWER COMMENTS. This cross-sectional examination found a significant protective effect of increasing birth order on some allergic diseases (AR, AC, and FA); however, this effect was not observed for all allergic disorders. Limitations of the study included parental recall bias, lack of confirmation of diagnoses, and limited knowledge of pregnancy and birth history of subjects involved. The trend of decreasing prevalence of FA among later-born children remained consistent regardless of past versus current FA, early- versus late-onset FA, and early tolerant versus persistent FA, and was independent of the food allergen. These findings suggest that future studies should prospectively examine maternal/fetal immunologic changes during first and subsequent pregnancies, the impact of maternal exposures during first and subsequent pregnancies, and the immunologic
Gene Polymorphisms, Breastfeeding, and Development of Food Sensitization in Early Childhood


PURPOSE OF THE STUDY. This study looked at the effect of breastfeeding on the development of food sensitivity (FS) and explored whether this relationship was modified by an array of functional single nucleotide polymorphisms (SNPs).

STUDY POPULATION. The study included children from the Boston Birth Cohort, consisting of multiethnic, predominantly African American mother-infant pairs, participating in a postnatal children’s health study assessing growth, development, and health outcomes.

METHODS. Follow-up visits were scheduled at 6 to 12 months and 2, 4, and 6 years, with blood samples obtained at these times. Breastfeeding history was obtained with a standardized questionnaire. FS was defined as specific IgE of 0.35 kU/L or greater to any of 8 common food allergens (egg white, cow milk, peanut, soy, shrimp, walnut, wheat, and cod). Eighty-eight potentially functional SNPs were genotyped from 18 genes involved in innate immunity or TH1/TH2 imbalance. Logistic regression models were used to test the effects of breastfeeding and gene-breastfeeding interactions on FS.

RESULTS. The children (n = 970) were followed for an average of 2.5 ± 2.2 years. Overall, 37.2% had FS, 76.0% were ever breastfed, and 21.0% were exclusively breastfed for at least 4 months. The prevalence of FS was higher in breastfed children (39.6%) than in those never breastfed (29.4%). With adjustment for pertinent covariates, breastfed children were at 1.5 times higher risk for FS than never breastfed children. The percentages of ever and exclusive breastfeeding were similar in those with and without family histories of allergic disease. Of the 88 SNPs successfully genotyped, 5 revealed statistically significant gene-breastfeeding interaction. Children carrying the GT/TT genotype for an SNP in the IL-12 receptor beta gene had a decreased risk of FS (odds ratio 0.6), but those with the GG genotype had an increased risk of FS (odds ratio 2.0). Similar interactions were observed for SNPs in Toll-like receptor 9 (TLR9) and thymic stromal lymphopoietin (TSLP). Most striking, in the group with exclusive breastfeeding, children carrying the TLR9 TT genotype had odds ratios of 3.3 and 13.2 for breastfeeding <4 months and >4 months respectively.

CONCLUSIONS. The effects of breastfeeding on FS are modified by SNPs in the IL-12 beta receptor, TLR9, and TSLP genes, both individually and jointly. These findings underscore the importance of considering individual genetic variations in assessing this relationship.

REVIEWER COMMENTS. How often have pediatricians and allergists confronted a distraught mother who feels she did everything to avoid allergic disease in her young child by adhering to breastfeeding and delaying the introduction of notoriously allergenic foods? We know now from other studies that the latter tactic is generally the wrong course, and this article might help us understand why prior studies regarding the allergy-prevention benefits of breastfeeding have yielded mixed results.

Parental Eczema Increases the Risk of Double-Blind, Placebo-Controlled Reactions to Milk but Not to Egg, Peanut, or Hazelnut


PURPOSE OF THE STUDY. The authors investigated whether history of parental atopic diseases are associated with a higher risk of reaction to common allergenic foods in children.

STUDY POPULATION. In this Dutch study, 396 children (251 male, 145 female) with suspected food allergy were recruited from a pediatric allergy outpatient clinic. Median age was 5.4 years (range, 6 months to 17.8 years).

METHODS. The parents and children were asked if they each had a previous diagnosis of asthma, allergic rhinitis, atopic dermatitis, or (in the parents) food allergy. Children were identified as having food sensitivity through an elevated ImmunoCap-specific IgE (>0.35 kU/L) to cow’s milk, hen’s egg, peanut, or hazelnut. The children also underwent double-blind, placebo-controlled food challenges (DBPCFC) to the allergenic food, with a period of at least 2 weeks between food and placebo challenges. Logistic regression analysis was used to compare risk of a reaction to each food tested between children whose parents were not atopic and children with 1 or 2 parents with atopic diseases.

RESULTS. More than 90% of the children had been previously diagnosed with atopic disease, most commonly eczema. A total of 553 DBPCFCs were performed with 274 children tested for 1 food, 92 for 2 foods, 25 for 3 foods, and 5 for all 4 foods. Foods tested included cow’s milk (n = 185), egg (n = 110), peanut (n = 198), and
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