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Duration and exclusiveness of breastfeeding and school-age lung function and asthma

Evelien R. van Meel, MD [*,†,‡]; Mandy de Jong, BSc [*,†,‡]; Niels J. Elbert, MD [*,§]; Herman T. den Dekker, MD [*,†,‡]; Irwin K. Reiss, MD, PhD [||]; Johan C. de Jongste, MD, PhD [†]; Vincent W.V. Jaddoe, MD, PhD [*,‡,¶]; Liesbeth Duijts, MD PhD [†,‡,||]

[*] The Generation R Study Group, Erasmus MC, University Medical Center Rotterdam, Rotterdam, the Netherlands
[†] Division of Respiratory Medicine and Allergology, Department of Pediatrics, Erasmus MC, University Medical Center Rotterdam, Rotterdam, the Netherlands
[‡] Department of Epidemiology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, the Netherlands
[§] Department of Dermatology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, the Netherlands
[||] Division of Neonatology, Department of Pediatrics, Erasmus MC, University Medical Center Rotterdam, Rotterdam, the Netherlands
[¶] Department of Pediatrics, Erasmus MC, University Medical Center Rotterdam, Rotterdam, the Netherlands

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ABSTRACT

Background: Breastfeeding reduces the risk of asthma in early childhood, but it is not clear whether its effect on respiratory morbidity is still present in later childhood.
Objectives: To examine the associations of any breastfeeding, breastfeeding duration, and breastfeeding exclusiveness with lung function and asthma in school-aged children and whether associations were influenced by respiratory tract infections and maternal or child's atopic status.
Methods: This study of 4,464 children was embedded in a population-based prospective cohort study. Information on breastfeeding was obtained by multiple questionnaires from birth until 1 year of age. At 10 years of age, lung function was measured by spirometry, and information on asthma was obtained by questionnaire. Adjusted linear and logistic regression models were used to examine the associations.
Results: Shorter duration of breastfeeding was associated with a lower forced expiratory volume in 1 second (FEV_1) only (*z* score change, −0.01; 95% confidence interval [CI], −0.02 to −0.00) per month shorter breastfeeding, but not asthma. When categorized, breastfeeding for 2 to 4 months was associated with a lower forced vital capacity (FVC) (*z* score change, −0.11; 95% CI, −0.20 to −0.03) compared with breastfeeding for 6 months or longer. Nonexclusive breastfeeding for 4 months was associated with a lower FVC (*z* score change, −0.08; 95% CI, −0.16 to −0.01) compared with exclusive breastfeeding for 4 months. Results did not materially change after additional adjustment for lower respiratory tract infections and were not modified by maternal history of asthma or atopy, child's eczema, or inhalant allergic sensitization.
Conclusion: Shorter duration and nonexclusivity of breastfeeding were associated with a lower FEV_1 and FVC but not asthma at school-age.

Introduction

Early-life exposures may affect the development and maturation of the respiratory system in early childhood and influence later respiratory health.[1] Our[2,3] and other previous studies[4–10] suggest that prolonged and exclusive breastfeeding reduces the risk of wheezing and asthma in infancy and early childhood, whereas the

Reprints: Liesbeth Duijts, MD, PhD, Department of Pediatrics, Erasmus MC, University Medical Center Rotterdam, Sp-3435, PO Box 2060, 3000 CB Rotterdam, the Netherlands; E-mail: l.duijts@erasmusmc.nl.
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beneficial effect of breastfeeding on lung function[11–18] and asthma in later childhood remains unclear.[19] In a recent meta-analysis[8] of 42 observational studies, ever and prolonged breastfeeding were associated with an up to 12% and 10% reduced risk of asthma at ages 5 to 18 years, respectively, whereas exclusive breastfeeding for longer than 3 to 4 months was not. A systematic review of 5 birth cohorts and 3 cross-sectional studies[20] suggested that prolonged and exclusive breastfeeding improved lung function in children until 18 years of age. However, categorization of breastfeeding duration and exclusiveness differed among studies, effects could not be examined in detail, and heterogeneity was large. More recent studies[16,17,21] were performed mostly in high-risk populations,[16,21] with relatively small sample sizes. Not only are population-based studies on the effect of breastfeeding on lung function and asthma in later childhood scarce, most studies lack prospectively collected, detailed information on breastfeeding. In addition, breastfeeding is associated with a reduced prevalence of lower respiratory tract infections.[22,23] Subsequently, it is suggested that a reduced prevalence of respiratory tract infections may result in less lung damage and a better lung function and less respiratory morbidity later in life.[24] This proposes a possible mediating role for lower respiratory tract infections in the association of breastfeeding with lung function and asthma. Previously, we found that shorter and less exclusive breastfeeding was associated with an increased risk of early wheezing or asthma at 6 years of age, which was partly explained by respiratory tract infections in early and to a lesser extent in later life.[2] The effect of respiratory tract infections on associations of breastfeeding with lung function and asthma at older ages are less known. Lastly, the role of maternal and child's atopic status on the association of breastfeeding with lung function and asthma is not fully clear.[10,11,20]

Therefore, we examined in a population-based prospective cohort study, with detailed information on breastfeeding frequently measured over time, the associations of any breastfeeding, breastfeeding duration, and exclusiveness of breastfeeding with lung function and asthma in school-age children. In addition, we examined whether associations were mediated by lower respiratory tract infections or modified by maternal or child's atopic status.

Methods

Design and Cohort

This study was embedded in the Generation R Study, a population-based prospective cohort study from early fetal life until young adulthood in Rotterdam, the Netherlands. A detailed description of the study design has been published previously.[25] The study has been approved by the Medical Ethical Committee of the Erasmus MC, University Medical Center Rotterdam. Written informed consent was obtained from parents or legal representatives of all participants. Children were excluded from the current analyses if the parents or legal representatives did not give consent for participation in this phase, if they were twins, if information on breastfeeding was missing, and if information on lung function and asthma were missing. As a result, a total of 4,464 mothers and their children were included for the current analyses (eFig 1).

Breastfeeding Duration and Exclusiveness

Data on breastfeeding were collected using questionnaires administered at 2, 6, and 12 months after birth. Response rates varied from 71% to 82%. The duration of breastfeeding was assessed by asking whether mothers ever breastfed their child and at what age they stopped breastfeeding. Children were classified as never breastfed and ever breastfed. Among those who were breastfed, duration of breastfeeding was categorized into 4 groups: less than 2 months, 2 to 4 months, 4 to 6 months, and 6 months or more. Breastfeeding duration was also measured continuously by using the number of months a child was breastfed as a continuous variable. Exclusivity of breastfeeding was defined by the age of introduction of infant formula, other drinks, or food and categorized into nonexclusive breastfeeding for 4 months and exclusive breastfeeding for 4 months. Analyses that focused on breastfeeding duration and exclusiveness were performed among children who were ever breastfed.

School-age Lung Function and Asthma

At 10 years of age (mean [SD] age, 9.8 [0.3] years), children visited our research center. Spirometry was performed according to the American Thoracic Society and European Respiratory Society recommendations.[26] Lung function measures included forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC), FEV_1/FVC, and forced expiratory flow after exhaling 75% of FVC ($FEF_{75\%}$) and were converted into sex-, height-, age-, and ethnicity-adjusted *z* scores according to the Global Lung Initiative reference data.[27] Children were asked to stop the use of short- and/or long-acting bronchodilators 8 to 48 hours before spirometry, respectively, if they did not have asthma symptoms. A current acute asthma attack or respiratory tract infection was a contraindication for spirometry. Questionnaires based on the International Study on Asthma and Allergy in Childhood (ISAAC) Questionnaire[28] at 10 years of age provided information on ever asthma (no or yes) and current wheezing (no or yes), and information on asthma medication use (no or yes) was obtained during the visit at the research center. Current asthma (no or yes) was defined as ever diagnosis of asthma with wheezing or medication use in the past 12 months at 10 years of age.

Covariates

Information on maternal characteristics included educational level, history of asthma or atopy, pet keeping, damp patches or mold in the house, parity, psychiatric symptoms defined using the Global Severity Index,[29,30] body mass index (BMI) at intake, and smoking during pregnancy and were obtained from multiple questionnaires completed by the mother during pregnancy. Midwife and hospital registries at birth provided information on child's sex, gestational age at birth, and birth weight. We collected information about child's ethnicity and daycare attendance by questionnaires during the first year of life. Information on physician-attended lower respiratory tract infections was obtained by multiple questionnaires at 6 months to 6 years of age. Lower respiratory tract infections included bronchitis, bronchiolitis, and pneumonia and were categorized into early ($\leq$3 years) and late (3–6 years) lower respiratory tract infections. At 10 years of age, information on ever diagnosis of eczema was obtained by questionnaire. Allergic sensitization for the 5 most common inhalant allergens (house dust mite, grass, birch, cat, and dog; ALK-Abelló B.V., Almere, the Netherlands) was determined by a skin prick test at the age of 10 years, using the scanned area method.[31]

Statistical Analysis

First, for the loss to follow-up analysis, we compared characteristics of children included and not included in the study using *t* tests for normal distributed continuous variables, Mann-Whitney tests for nonnormal distributed continuous variables, and χ^2 tests for categorical variables. Second, we used linear and logistic regression models to examine the associations of ever breastfeeding and duration and exclusiveness of breastfeeding with lung function and asthma, respectively. Analyses were adjusted for potential confounders, which were (1) selected from literature, (2) if they were related to breastfeeding and asthma or lung function,