Original Research

Is Being Breastfed as an Infant Associated with Adult Pulmonary Function?

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Objective: Breastfeeding reduces the risk of asthma and respiratory infections in infants. Since respiratory infections are associated with reduced pulmonary function in adolescents, pulmonary function impairment may be carried into adulthood. Our aim was to determine whether a history of having been breastfed as an infant is a determinant of adult pulmonary function.

Methods: We analyzed data from a general population sample of residents of Erie and Niagara Counties between September 1995 and December 1999. We calculated forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) prediction equations and used multiple linear regression models to study the association between having been breastfed as an infant and percentage predicted FEV_1 ($FEV_1\%$) and percentage predicted FVC (FVC%) after adjustment for covariates.

Results: Of 2305 subjects, 62% reported having been breastfed. After controlling for age, gender, weight, smoking status, pack-years of smoking, eosinophil counts and dietary factors, there was no association between having been breastfed (yes/no) and $FEV_1\%$ or FVC% (regression coefficients 0.0049, p = 0.46 and 0.0055, p = 0.43, respectively).

Conclusions: We did not find a strong or consistent association between having been breastfed as an infant and pulmonary function in adulthood.

INTRODUCTION

Development of the human lung is not complete at birth. Postnatal lung maturation continues in the early months of life [1,2]. Respiratory infections in the early postnatal period can have adverse effects on pulmonary function during childhood that may persist later in life [3]. Children with asthma, wheezing or more frequent and prolonged respiratory tract infections are likely to have reduced pulmonary functions as adults [4–9].

The immunomodulatory properties of human breast milk are well established [10,11], including those that protect against respiratory syncytial virus [12–14]. In addition, human milk contains IgA that may prevent absorption of antigens in the gastrointestinal tract [15–17]. These properties are believed to be responsible for lower rates of atopic illnesses in infants, such as asthma [18–21], as well as upper and lower respiratory tract illnesses [22–24]. Oddy *et al.* [22] reported a 25% lower risk of developing asthma in infants exclusively breast-fed for the first

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four months of life. Cushing *et al.* [24] reported a 19% reduction in risk of lower respiratory tract illnesses in infants exclusively breastfed for the first 6 months of life. In contrast, some investigators have found an increased risk of atopic illnesses including asthma in breastfed infants [25–28]. For example, Sears *et al.* [27] reported an increased likelihood of asthma at age 9 and 26 years for participants who were breastfed as infants. Thus, the controversy about the possible benefits of breastfeeding on lung disease persists.

A recent systematic review by Kramer *et al.* [29] evaluated twenty independent studies comparing health outcomes in the infant and mother with exclusive breastfeeding for six months or more versus exclusive breastfeeding for at least three months with continued mixed breastfeeding till at least six months of age. No significant reduction in risk of asthma, eczema, or other atopic illnesses was found. The authors concluded that there was no apparent risk in recommending exclusive breastfeeding for the first six months of life, with regard to asthma.

Longitudinal and cross-sectional studies that have reported a protective effect of breastfeeding against asthma and respiratory tract infections have been restricted to children and adolescents. There have been no studies of whether a protective effect of breastfeeding persists into late adulthood, specifically, for adults greater than 35 years and in relation to pulmonary function as an outcome measure. To inform this issue we investigated whether a history of having been breastfed as an infant affects pulmonary function as an adult while adjusting for factors that we previously found to be associated with pulmonary function. These factors were smoking status, cumulative tobacco exposure in pack-years, weight, eosinophil count, education, dietary intake of vitamin E and lutein/zeaxanthin.

MATERIALS AND METHODS

We analyzed data collected from randomly selected participants of a population-based study in Erie and Niagara Counties, New York, between September 1995 and December 1999. We have previously published a detailed description of initial participant recruitment and study methodology [30].

Study Population

In brief, New York State Department of Motor Vehicles and Health Care Finance Association lists were used to randomly select participants aged 35 to 79 years. Of the 6843 subjects for whom we could determine eligibility 4065 agreed to participate (59.4%).

Interview

We conducted an in-depth interview and collected information on lifestyle habits, medical and social history. We asked all participants "Were you breast-fed as an infant?" and recorded

responses as, "Yes", "No" and "Not sure/Don't Know". We assessed usual diet over the 12-month period starting 24 months before the interview and ending 12 months prior to the interview using the 100-item Health Habits and History Food Frequency Questionnaire ("Block" [31]). We calculated individual mean daily nutrient intake using the DietSys nutrition analysis software (version 3.7) [32]. We expressed intake of all nutrients as daily consumption and analyzed lutein and zeaxanthin as lutein/zeaxanthin as previously described [33,34]. In addition, we obtained anthropometric measurements and blood samples.

Pulmonary Function Tests

Trained personnel performed spirometry between 6:30 and 9:30 a.m. following the 1994 American Thoracic Society guidelines [35].

Blood Determinations

Blood samples were obtained between 7:30 and 9:30 A.M. after a fasting of 8 to 12 h. Vitamin measurements were made in the laboratory of the Department of Clinical Laboratory Sciences, School of Health Related Sciences, University at Buffalo, New York. Fat-soluble vitamins were measured in serum by high-pressure liquid chromatography (HPLC) on a Shimadzu LC-7A device with SPD-M6A photodiode array (Shimadzu Scientific Instruments, Inc., Braintree, MA) and expressed as μg/ml. An automated differential cell blood count (including eosinophil counts) was determined at the laboratory of the Kaleida/Millard Fillmore Hospital Center for Laboratory Medicine in Buffalo, New York, using a Coulter Counter (Beckman Coulter, Inc., Fullerton, CA).

Anthropometry

All anthropometric measurements were taken according to a standardized protocol: body weight was measured with participants wearing light clothes and no shoes, using a balance beam scale (Detecto, Inc., Webb City, MO); height was measured without shoes using standardized scales (Perspective Enterprises, Kalamazoo, MI).

Statistical Analysis

Based on values obtained from lifetime non-smokers who were included in this dataset and who did not report a history of chronic lung disease (n = 963), we calculated the following prediction equation for FEV_1 and FVC for men and women: For men:

Predicted $FEV_1 = -1.080 - 0.032 \times$ age (years) $+ 3.741 \times$ height (m) $- 0.537 \times$ race

Predicted FVC $= -3.156 - 0.034 \times$ age (years) $+ 5.558 \times$ height (m) $- 0.597 \times$ race

For women:

Predicted $FEV_1 = 0.007 - 0.028 \times$ age (years) $+2.626 \times$ height (m) $- 0.385 \times$ race

Predicted $FVC = -0.871 - 0.029 \times$ age (years) $+3.655 \times$ height (m) $- 0.603 \times$ race

where race was a dummy variable (Caucasian = 0, African American = 1). We then calculated FEV_1 and FVC as the percentage of predicted value ($FEV_1\%$ and FVC% respectively) for all participants adjusted for age, height and race based on these equations.

For continuous variables with normal distributions, we calculated mean values and standard deviations. Dietary variables were not normally distributed and we used logarithmically transformed variables.

To investigate the association between history of having been breastfed and $FEV_1\%$ and FVC% respectively, we used multiple linear regression analysis. We used forward stepwise regression to select variables for the final model using a p-value ≤0.05. Previously, we found that smoking status, cumulative tobacco exposure in pack-years, weight, eosinophil count, education, dietary intake of vitamin E and lutein/zeaxanthin were important predictors of $FEV_1\%$ and FVC%, respectively [34]. These variables were included in the baseline model. There was no important collinearity. We used the inverse of the variable inflation factor (a statistical quantification of the co-dependence of similar variables as predictors of the outcome of interest) for predictor variables in the fitted model. We investigated non-linear associations of the smoking variables with pulmonary function. There was no important improvement in the total variability explained when we replaced linear terms with polynomial terms. We used SPSS (version 10.0) and STATA (Intercooled version 7.0; College Station, TX) software for statistical analysis.

RESULTS

After excluding participants with missing pulmonary function and missing data on key variables, 2305 participants remained for the final analyses (Fig. 1). Participants who were excluded for the final analyses (n = 1062), were more likely to be females (p = 0.005), less educated (p < 0.001) and have lower FEV_1 and FVC (p < 0.001) compared to those included (n = 2305). Participants who answered, "Don't know" to the question about having been breastfed (n = 698) compared to those who answered "Yes" or "No" (n = 2305) tended to be older (p = 0.005), male (p < 0.01), taller (p < 0.001), have higher weight (p = 0.025) and have higher FEV_1 and FVC (p = 0.009).

Table 1 shows that approximately half of the included participants were women and the majority of participants gave a history of having been breastfed. The population included mainly elderly Caucasians. 208 (9%) participants carried a diagnosis of chronic obstructive lung disease (emphysema or
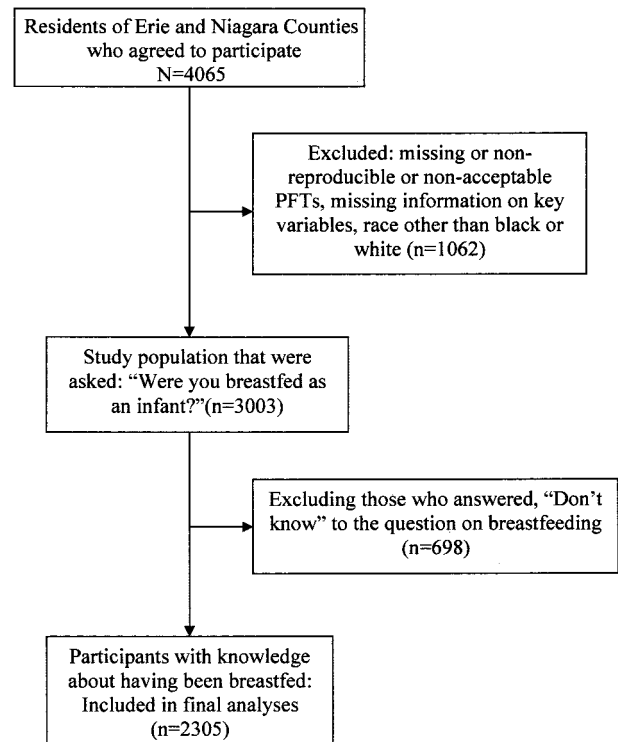

Fig. 1. Flow chart of study participants, Erie and Niagara Counties, New York, 1995–1999.

bronchitis), of whom 136 (65%) gave a history of having been breastfed (p = 0.24). 145 (6%) were diagnosed with asthma of whom 92 (63%) gave a history of having been breastfed (p = 0.64).

The mean $FEV_1\%$ for those who reported having been breastfed was slightly lower compared to that for participants who reported not having been breastfed (93.7% *vs.* 95.3% respectively) but the difference was not statistically significant (p = 0.089). The mean FVC% for participants who reported having been breastfed was similar to that for participants that reported not having been breastfed (96.6% *vs.* 97.4% respectively; p = 0.27).

Fig. 2 shows the distribution of participants who reported having been breastfed by quartiles of $FEV_1\%$ and FVC% respectively. There was a trend towards decreasing frequency of having been breastfed with higher quartiles of $FEV_1\%$ and FVC%, but the difference was not statistically significant after adjustment for smoking history, pack years of smoking, age, gender, height and dietary intake of antioxidants (p = 0.31 and p = 0.87 respectively).

Multiple linear regression analysis on $FEV_1\%$, after adjustment for history of smoking, pack-years of smoking, weight, years of education and dietary intake of cryptoxanthin, did not show an association with having been breastfed as an infant (p = 0.43) (Table 2). Multiple linear regression analysis on FVC%, after adjustment for years of education, pack years of smoking, weight, dietary intake of lutein/zeaxanthin also did

Table 1. Characteristics of Participants, Erie and Niagara Counties, 1995–1999 (n = 2305)

Variable (unit)	Mean (SD*)
Age (years)	58.9 (11.8)
Height (m)	1.68 (0.09)
Weight (kg)	80.06 (17.6)
FVC (liter)	3.75 (1.01)
FEV_1 (liter)	2.86 (0.84)
FVC%[†]	96.9 (16.1)
FEV_1%[†]	94.3 (18.2)
Years of education	13.5 (2.4)
Women %	53.2%
African-American (%)	6.9%
Breastfed (% yes)	62%
History of COPD (%)[‡]	9.1%
History of asthma	6.1%
Smoking	
Never-Smoker (%)	41.5%
Ex-Smoker (%)	44.4%
Current-Smoker (%)	14.1%
Pack-years of smoking	14.4 (20.8)

* SD, standard deviation.

[†] FEV_1%, forced vital capacity in one second in percent of predicted, [†] FVC%, forced vital capacity in percent of predicted. FEV1% and FVC% are calculated by taking the participant's measured FEV1 and FVC values and expressing it as percentage of predicted value, adjusted for age, height, and gender and race.

[‡] COPD, chronic obstructive lung disease (includes history of emphysema and chronic bronchitis) and those that have asthma in addition to COPD.
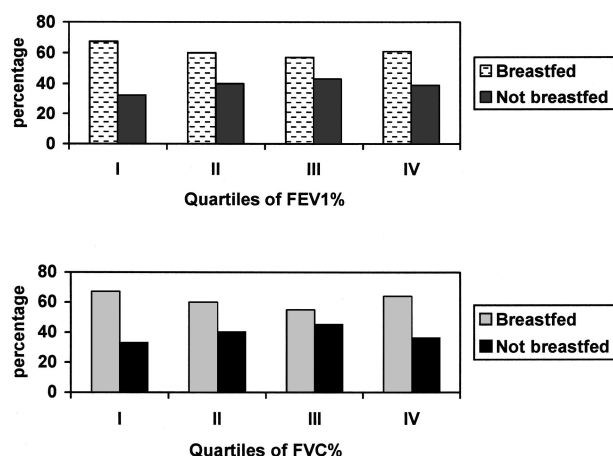
Fig. 2. Histogram of percentage breastfed by quartiles of FEV_1% and FVC%.

not show an association with having been breastfed as an infant (p = 0.46) (Table 2).

Table 3 shows the results of regression on FEV_1% and FVC%, respectively, stratified by smoking history (never, former and current). After adjustment for pack years of smoking, weight, years of education and dietary intake of cryptoxanthin, the relation between having been breastfed and FEV_1% was not statistically significant for never and current smokers (p = 0.07 and p = 0.11, respectively). However, a history of being breastfed was positively associated with FEV_1% for

former smokers (regression coefficient 0.026, p = 0.028) adjusted for the variables listed above. The magnitude of the regression coefficients was similar in the former and current smoker groups, but it was not statistically significant in the latter possibly as a result of the larger error in the current smoker group. Analyses for FVC%, by categories of smoking history did not show any statistically significant association between being breastfed and FVC% even after adjustment, for covariates. However, the regression coefficients showed similar trends to those seen with FEV_1%. When we further stratified by gender, the coefficients for breastfeeding were similar for males and females in all the three smoking status categories.

We analysed the relation between breastfeeding and pulmonary function tests after stratification by history of asthma, chronic obstructive lung disease and being free from either lung disease. There was no statically significant association between FEV_1% and having been breastfed for either those with asthma, COPD or those free of both diseases (p = 0.37, p = 0.23 and p = 0.23 respectively) after adjustment for pack years of smoking, weight, years of education and dietary intake of cryptoxanthin. There was also no statistically significant association between having been breastfed and FVC% for those with asthma, COPD or free of both diseases (p = 0.41, p = 0.27 and p = 0.34 respectively) even after adjustment for smoking history, pack years of smoking, weight, years of education and dietary intake of lutein/zeaxanthin.

DISCUSSION

In this population-based study we observed no important association between having been breastfed as an infant and pulmonary function as an adult. However, when we analyzed this association stratified by smoking history, we found that history of having been breastfed was positively associated with FEV_1% in former smokers (Table 3).

During lung development, pulmonary function increases through childhood and adolescence before it plateaus and then declines in adulthood [36]. Weiss *et al.* [37] predicted that a girl developing asthma at age seven would experience a 7% reduction in FEV_1 by age 15. Roorda *et al.* [38] followed 10-year old children (n = 406) with asthma for nearly 15 years and reported that respiratory symptoms persisted or recurred in the majority of participants. Similarly, there is evidence that lower respiratory tract infections in childhood are important predictors of poorer pulmonary function as adults [39–40]. For example, Shaheen *et al.* [39] found reductions in FEV_1 and FVC of 0.39 and 0.60 litres, respectively, in an adult population who had a history of pneumonia before the age of two years.

There is evidence that breastfeeding confers a protective effect against asthma and respiratory infections in childhood and adolescence [18–24]. Therefore, one might hypothesize that asthma and a higher risk of respiratory illnesses as a child would predispose to poorer pulmonary functions as adults.

Table 2. Multiple Linear Regression Coefficients for Regression on FEV$_1$% and FVC%, Erie and Niagara Counties, New York, 1995–1999 (N = 2305)

Variable (unit)	β	FEV$_1$% 95% CI[‡]	β	FVC% 95% CI[‡]
Breastfed (yes/no)	0.0055	−0.0087, 0.020	0.0049	−0.0083, 0.018
Pack Years of smoking (one pack-year)	−0.0027***	−0.0031, −0.0023	−0.0010***	−0.0013, −0.00076
Weight (one kg)	−0.00066**	−0.0010, −0.0002	−0.0014***	−0.0017, −0.0010
Years of Education (one year)	0.0061***	0.0031, 0.009	0.0060***	0.0033, 0.0087
Smoking status (never, former, current)	0.0060*	0.00013, 0.011	–	–

Forward stepwise regression used to select variables for the final model for FEV1% and FVC% respectively.

FEV1% and FVC% are calculated by taking the participant's measured FEV1 and FVC values and expressing it as percentage of predicted value, adjusted for age, height, and gender and race. All variables included in the final models respectively are shown. Dietary variables were log transformed to increase normality.

[‡] 95% confidence interval * p < 0.05, ** p < 0.01, *** p < 0.001.

Table 3. Multiple Linear Regression Coefficients for Regression on FEV$_1$% and FVC%, Erie and Niagara Counties, New York, 1995–1999 Stratified by Smoking Status (N = 2305)

	Never smokers (n = 956)			
	FEV$_1$%		FVC%	
Variable (unit)	β	95% CI[‡]	β	95% CI[‡]
Breastfed (yes/no)	−0.017	−0.037, 0.0019	−0.0084	−0.028, 0.011
Weight (one kg)	−0.0013***	−0.0018, −0.0007	−0.0016***	−0.0022, −0.0011
Years of Education (one year)	0.0072***	0.0032, 0.011	0.0070***	0.0031, 0.011
	Former smokers (n = 1024)			
	FEV$_1$%		FVC%	
Variable (unit)	β	95% CI[‡]	β	95% CI[‡]
Breastfed (yes/no)	0.026*	0.0028, 0.050	0.019	−0.0013, 0.040
Pack Years of smoking (one pack-year)	−0.0021***	−0.0027, −0.0016	−0.0008***	−0.0012, −0.00037
Weight (one kg)	−0.00081*	−0.0014, −0.0001	−0.0017***	−0.0023, −0.0012
Years of Education (one year)	0.0043	−0.00031, 0.009	0.0044*	0.0003, 0.0086
	Current smokers (n = 325)			
	FEV$_1$%		FVC%	
Variable (unit)	β	95% CI[‡]	β	95% CI[‡]
Breastfed (yes/no)	0.033	−0.0080, 0.074	0.016	−0.017, 0.050
Pack Years of smoking (one pack-year)	−0.0032***	−0.0043, −0.0022	−0.0014**	−0.0023, −0.000586
Weight (one kg)	0.00082	−0.0004, 0.0020	−0.0003	−0.0013, 0.0006
Years of Education (one year)	0.0078	−0.0011, 0.016	0.0067	−0.0006, 0.014

Variables from the final model for FEV1% and FVC% respectively. FEV1% and FVC% are calculated by taking the participant's measured FEV1 and FVC values and expressing it as percentage of predicted value, adjusted for age, height, and gender and race. All variables included in the final models respectively are shown. Dietary variables were log transformed to increase normality.

[‡] 95% confidence interval * p < 0.05, ** p < 0.01, *** p < 0.001.

While there it is theoretically possible that a protective effect of breastfeeding on adult pulmonary function exists, there are several possible explanations for our finding of a lack of a consistent association. Lung maturation continues postnatally and breast milk may contain substances that are important for postnatal lung development. However, as lung maturation levels off in early adulthood, the protective effect of breastfeeding may also be lost. In addition, other lifestyle factors, such as smoking, occupational and environmental exposures, may be stronger contributors to deterioration of pulmonary functions, mitigating the protective effects of breastfeeding present earlier in life.

Other studies have shown no beneficial effect of breastfeeding on lung function in children; moreover, some studies reported an increase in risk of asthma and respiratory illnesses during this period [25–28]. This latter observation would support the absences of a beneficial effect of breastfeeding on

pulmonary function in adulthood. However, to our knowledge, such inferences have never been explored. Our study maybe the first one to address the question of an association between having been breastfed and adult pulmonary function.

Stratification by history of asthma, COPD or being free from either of these lung diseases did not show any significant association. Such findings may be of importance, because asthma and COPD are leading causes of hospital admissions and mortality, particularly in the elderly [41–44].

The finding that history of having been breastfed was positively associated with FEV$_1$% in former smokers (regression coefficient 0.026, p = 0.028) is not easily explained. One could speculate that smokers have a greater rate of pulmonary function decline and breastfeeding may have a protective effect on smoking induced lung injury later in life. The presence of this association only among former smokers may be a function of

the sample size of the strata, as there were nearly three times as many former smokers as current smokers in our study population. Alternatively, this association may be a chance phenomenon because we have investigated multiple associations in this dataset. In particular, the fact that such relation was not seen with FVC% precludes us from drawing strong conclusions.

Factors that strengthen our study results are the careful evaluation of extensive lifestyle, dietary and demographic variables. However, the cross-sectional design raising the possibility for errors in recall are important limitations of our study, but in regards to recall error we believe participants were unaware of the study hypothesis. There have been no studies to our knowledge that have tested the reliability of recall about breastfeeding 35 to 79 years later, and hence the response of the participants should be evaluated with caution. Another limitation is that we were unable to evaluate other important risk factors such as maternal smoking, exclusivity and duration of breastfeeding, why breastfeeding was stopped, family history of atopic illnesses. All of these factors may be associated with childhood asthma and respiratory infections. However, studies have not found a dose-response relation between duration of breastfeeding and decrease or increase in risk of asthma [19,27]. Another limitation is that we excluded 1062 participants from the analyses due to missing data because they were unable to recall whether they had been breastfed. These participants had significantly poorer lung functions. Hence, our analysis may have been underpowered to detect statistically significant trends between breastfeeding and lung function (such as the negative association between FEV% and having been breastfed with a $p = 0.089$).

In analyzing dietary factors, we did not measure fatty acid intake. Although there is limited data in humans on the association between dietary fatty acid intake and lung function, evidence from animal studies suggests that fatty acid intake may affect tissue levels of prostaglandins, particularly prostaglandin E2 in lung, kidney and liver [45]. In addition, we may have had insufficient power to detect a difference of the magnitude we observed between those participants who were breastfed and those who were not. Based on the mean difference in FEV_1 between the breastfed and not breastfed group of approximately 2%, we observed that the power of our study was 0.74. Finally, since impaired pulmonary function is associated with increased mortality, our cohort may not include participants who died early because of impaired pulmonary function. If breastfeeding had a positive effect on lung function, a greater proportion of those who died and were not included in this study *would not* have been breastfed. Only a long-term population-based cohort study can resolve this question.

In summary, we did not observe a protective effect of breastfeeding on adult pulmonary function. The observation that having been breastfed was associated with slightly higher pulmonary function in former smokers needs to be further explored. Because publication bias may exist for reporting positive associations [46], our study adds important information on breastfeeding and adult lung function. Data from long-term populations based studies are needed to further explore the hypothesis that having been breastfed may be associated with better lung function in adulthood.

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