Invited Commentary

Invited Commentary: Does Breastfeeding Protect Against “Asthma”?

Michael S. Kramer*

* Correspondence to Dr. Michael S. Kramer, 2300 Tupper Street (Les Tourelles), Montreal, Quebec, Canada H3H 1P3 (e-mail: michael.kramer@mcgill.ca).

Initially submitted January 29, 2014; accepted for publication January 31, 2014.

Dogaru et al. have provided the best systematic review and meta-analysis to date of published studies of the association between breastfeeding and childhood asthma. Despite careful analysis of the reviewed studies’ designs and methodological quality features, the authors are unable to explain the enormous heterogeneity ($I^2 = 71\%-92\%$) among the reported findings. This heterogeneity likely stems from the fact that “asthma” is a term used to denote a highly variable phenotype. The reasons for the protective association between breastfeeding and such a heterogeneous phenotype remain unclear, but may reflect nonblinding of feeding histories among observers who assess the outcome, as well as residual confounding, particularly by daycare attendance. The absence of a dose-response relationship based on breastfeeding duration or exclusivity also raises questions about the causal nature of the observed association. Future epidemiologic studies of asthma will require better and finer phenotyping to understand its etiology, including the potential protective effect of breastfeeding.

asthma; breastfeeding; infant feeding; meta-analysis; systematic review

Dogaru et al. (1) have carried out the most detailed, and probably the best, systematic review and meta-analysis of observational studies of the association between infant feeding (in particular, the possible negative association with breastfeeding) and asthma during childhood. They have identified a large number of studies, carefully analyzed them for data quality, and stratified their meta-analysis using different definitions (any vs. exclusive breastfeeding) and durations of breastfeeding, dates of publication, study designs, ages at outcome assessment, and origins (Western vs. non-Western countries). They find consistent evidence of a protective association with breastfeeding, regardless of exclusivity or duration and regardless of whether asthma is defined according to ever versus never, recent asthma, or recent wheezing illness. The authors conclude that breastfeeding protects against asthma and call for future studies to “analyze the mechanisms involved” (1).

As duly noted by the authors, however, the heterogeneity of results among the reviewed studies is striking. As shown in their Web Table 4 available at http://aje.oxfordjournals.org/, the $I^2$ index of heterogeneity, representing the proportion of total variance in the magnitude of association due to between-study variance, ranged from 71% to 92%, depending on the outcome (i.e., asthma ever, recent asthma, or recent wheezing illness). The meta-regression results summarized in their Table 3 indicate that the only study features significantly affecting the odds ratio were the age at assessment of the outcome (particularly for recent wheezing illness) and the date of study publication, with stronger protective effects in studies with outcome assessment at 0–2 years of age and in those published after 1990.

What the authors do not discuss, however, is that asthma itself is extremely heterogeneous. The term “asthma” is used both by parents and physicians to designate quite a variable group of conditions. By definition, asthma is reversible bronchoconstriction, not just wheezing. Very few studies reporting the relationship between infant feeding and asthma have performed spirometry, which would demonstrate whether children labeled as asthmatic have bronchoconstriction and whether such bronchoconstriction is reversible. The strongest meta-analytical findings were found for children whose asthma was ascertained in the first 2 years of life, when most pediatricians and respirologists are reluctant to use the term “asthma” to denote wheezing-associated illnesses. This result suggests that much of the protective association of breastfeeding may be due to its well-established effect on reducing the risk of respiratory tract infection, and particular lower respiratory tract infection, during the period of breastfeeding.
(2, 3). Wheezing-associated infections in the first year or 2 of life are often caused by respiratory syncytial virus and other respiratory viruses. Wheezing among infants and toddlers with these infections usually does not respond to bronchodilators, suggesting that the wheezing may not be a true manifestation of asthma.

As Dogaru et al. (1) point out, early protection against respiratory infection may be 1 of the mechanisms by which breastfeeding protects against later asthma. In this way, breastfeeding (which has no apparent protective effect against respiratory infection once the breastfeeding has ceased) could provide a long-term protective effect. Other mechanisms may involve “programming” of the immune system toward hypersensitivity reactions, particularly of the lung in response to inhaled antigens. These mechanisms have not been clearly established, however, nor have they been shown to relate to differences in infant feeding.

Above and beyond the heterogeneity of the outcome, the way that Dogaru et al. (1) present their data does not provide evidence of a clear dose-response relationship between breastfeeding and later asthma. Unfortunately, all of the data analyses are shown using dichotomized categorizations of infant feeding: ever versus never breastfed (both for any breastfeeding and for exclusive breastfeeding) or dichotomized durations of breastfeeding. The authors never show any analyses in which 3 or more categories of duration are presented, which would permit an assessment of a dose-response relationship with duration. As shown in their Table 3, exclusive breastfeeding (vs. any breastfeeding) was not independently associated with a significant protective association, which is some evidence against a dose-response relationship. With an outcome as heterogeneous as asthma, the absence of a dose-response relationship does not necessarily invalidate the observed association. In other words, it is conceivable that any degree of breastfeeding affords some protection. But if that is the case, it is then surprising that more breastfeeding versus less breastfeeding shows a protective association of similar magnitude to that of any versus no breastfeeding.

Measurement bias could explain the positive associations observed in many studies. Most of the studies reviewed by the authors used a cohort design, which means that nonblinding of the observers who assessed the presence or absence of asthma with respect prior feeding history might have influenced the way that parental history or physical findings at the time of interview or examination were elicited or labeled. According to Dogaru et al. (1), the presence or absence of blinded outcome ascertainment could not be assessed in the majority of published studies.

Residual confounding is another important consideration. The fact that the association under study was, if anything, slightly weaker in Western countries than in non-Western countries suggests that confounding by socioeconomic status may not be important. But daycare attendance may be a potential source of confounding that was not evaluated by the authors and may not have been assessed or reported in many of the studies reviewed. Continued breastfeeding of infants who attend daycare is not impossible, but it is difficult. A mother who returns to work during her child’s infancy and places her infant in daycare for most of the day is likely to find it challenging to continue breastfeeding. Daycare attendance is known to be strongly associated with increased risk of infections, including respiratory syncytial virus and other wheezing-associated respiratory infections. Those infections, irrespective of breastfeeding history, may be early markers or even causes of subsequent asthma.

Where does this leave us? The high-quality systematic review and meta-analysis by Dogaru et al. (1) of previous studies of breastfeeding and “asthma” makes a useful contribution to the literature. But difficulty remains with the outcome, especially given the authors’ painstaking but unsuccessful efforts to understand the sources of heterogeneity in findings among the reviewed studies. Problems in understanding the epidemiology of asthma are similar to those in understanding the etiology of other imprecisely defined, highly heterogeneous conditions such as preterm birth, attention deficit/hyperactivity disorder, and chronic fatigue syndrome. Until more clarity is established by subdividing recurrent wheezing and wheezing-associated respiratory infections into more homogeneous phenotypes, it will be difficult to understand the etiology of these various conditions, not only with respect to infant feeding but also to genetic and other potential environmental determinants.

Breastfeeding has well-established benefits in reducing infectious morbidity and, in low- and middle-income countries, death from infections (4, 5). Even in high-income settings, risks of necrotizing enterocolitis among preterm infants (6) and of sudden infant death syndrome (2) are clearly reduced by breast milk and/or breastfeeding, and the evidence for breastfeeding’s role in accelerating cognitive development is also very strong (7, 8). Protection against some phenotypes characterized by wheezing and against other atopic and immunological diseases may also eventually be proven to be among breastfeeding’s health benefits. But better and finer phenotyping of these conditions will be necessary to understand their etiologies, including the potential protective effect of breastfeeding.

ACKNOWLEDGMENTS

Author affiliations: Department of Pediatrics, McGill University Faculty of Medicine (Michael S. Kramer); and Department of Epidemiology, Biostatistics, and Occupational Health, McGill University Faculty of Medicine (Michael S. Kramer).
Conflict of interest: none declared.

REFERENCES


