

Breastfeeding and Otitis Media: A Review of Recent Evidence

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Abstract Human milk provides infants with antimicrobial, anti-inflammatory, and immunomodulatory agents that contribute to optimal immune system function. The act of breastfeeding allows important bacterial and hormonal interactions between the mother and baby and impacts the mouth, tongue, swallow, and eustachian tubes. Previous meta-analyses have shown that lack of breastfeeding and less intensive patterns of breastfeeding are associated with increased risk of acute otitis media, one of the most common infections of childhood. A review of epidemiologic studies indicates that the introduction of infant formula in the first 6 months of life is associated with increased incidence of acute otitis media in early-childhood. More recent research raises the issues of how long this increased risk persists, and whether lack of breastfeeding is associated with diagnosis of otitis media with effusion. However, many studies suffer from lack of study of younger populations and imprecise definitions of infant feeding patterns. These findings suggest that measures of the association between breastfeeding history and otitis media risk are sensitive to the definition of breastfeeding used; future research is needed with more precise and consistent definitions of feeding, with attention to distinctions between direct breastfeeding and human milk feeding by bottle.

Keywords Breastfeeding · Infant formula · Replacement feeding · Otitis media · Ear infection · Respiratory tract

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infection · Infectious disease · Benefits of breastfeeding · Risks of formula feeding

Introduction

Human milk, unlike infant formula, is a biologically active substance containing antimicrobial, anti-inflammatory, and immunomodulatory agents that function to compensate for the physiologic immaturity of the infant immune system [1, 2]. Infants who are not breastfed exhibit a relative immunodeficiency compared with those receiving human milk, placing them at significantly greater risk of respiratory, gastrointestinal, and other infections [1]. In addition, the act of breastfeeding creates a unique maternal–infant physiology, including important bacterial and hormonal interactions between the mother and child and pressure gradients of suck and swallow that are distinct from those of bottle feeding [1, 3]. Although the differences in health outcomes have been most clearly demonstrated in developing countries, a recent review and meta-analysis determined that replacement feeding in higher-income countries is associated with increased risk of acute childhood infections, atopic diseases, and chronic conditions such as obesity and type 1 and 2 diabetes [4•]. As a result of the decades of research on this and many other infectious and chronic diseases, the World Health Organization currently recommends exclusive breastfeeding for the first 6 months of life and continued breastfeeding up to 2 years and beyond [5].

Immunologic Properties of Human Milk

In addition to secretory IgA and activated T-cell antibodies specific to various enteric and respiratory pathogens present in the maternal–infant environment, human milk supplies the infant with leukocytes and lytic enzymes that are

able to mount nonspecific defenses against bacterial pathogens. Human milk also provides glycoproteins and oligosaccharides that promote the growth of commensal bacteria and inhibit that of pathogens, glycosylated proteins and oligosaccharides that inhibit the binding of pathogenic bacteria to epithelial surfaces, and lactoferrin that competes successfully with pathogens for available iron [1, 2]. It also has been shown to contain biologically active cytokines, chemokines, and colony-stimulating factors with the potential to mediate directly infant immune system function. Although more research would be needed to elucidate the various functions of specific cell-signaling molecules within a recipient infant, demonstrated capabilities within other contexts include their role in enhancing proliferation of thymocytes, activation of leukocytes, regulation of cell proliferation and differentiation in hematopoiesis, and mediation of homeostasis of the infant intestinal barrier [6].

Functional Differences in Feeding Modalities

The breastfed infant has a distinct functional physiology that includes strong negative pressure suck, swallow, and breathing patterns, while the bottle-fed infant rather accepts milk as it flows from the nipple secondary to gravity or mild pressure from the infant's mouth [7]. Hence, bottle feeding may not demand the same level of organization and negative pressure as is required by breastfeeding, and due to pressure gradients and possibly to position during feeding, pooling is more likely to occur in bottle-fed infants. In formula feeding by bottle, the risks that result from the lack of immunologic protection is therefore compounded by the increased risk of milk pooling and differential pressure at the eustachian tube opening.

Breastfeeding and Otitis Media

Several studies have reported an association between lack of breastfeeding and increased risk of otitis media. Acute otitis media (AOM), an inflammation of the middle ear accompanied by symptoms of acute infection, affects more than one third of US children in the first 12 months of life [8] and is responsible for the majority of antimicrobial prescriptions written for children younger than 3 years of age [9, 10]. AOM is often secondary to viral infection of the upper respiratory tract, leading to dysfunction of the eustachian tubes and subsequent microbial colonization of the nasopharynx and the middle ear by agents such as *Streptococcus pneumoniae*, nontypeable *Haemophilus influenzae*, and *Moraxella catarrhalis* [11]. Otitis media with effusion (OME), characterized by the presence of fluid

within the middle ear, may remain following AOM. OME may interfere with hearing and, if persistent, may lead to language delays.

In addition to its role in preventing upper respiratory tract infection, breastfeeding likely protects against AOM through the action of maternal antibodies against middle ear pathogens and interference with bacterial adhesion to the nasopharyngeal epithelium [1, 4••]. Recent evidence also indicates that human milk modulates the infant's own humoral immune response to common OME pathogens by stimulating the production of IgG antibodies specific to whole-cell, nontypeable *H. influenzae* and to its P6 surface antigens [12]. This latter pathway, along with other immunomodulatory functions of human milk, may result in breastfed children retaining protection from AOM pathogens beyond weaning.

There is also indication that the physics of bottle feeding play a role in otitis media risk. A firm tongue-to-palate swallow, which is seen in breastfeeding, is suggested as necessary for the aeration of the eustachian tube [13]. Pressure readings taken during feeding with standard nonvented and undervented bottles have revealed that negative intratympanic pressure is generated in the infant due to the transmission of negative pressure from the bottle to the middle ear. This negative pressure may in turn contribute to eustachian tube dysfunction, predisposing bottle-fed infants to otitis media. This effect was not observed in fully ventilated bottles, which produce suck and swallow actions more similar to those of breastfeeding infants [3]. As the use of a supine feeding position may allow liquid to enter the middle ear [14], an additional risk is seen with bottle propping and other inappropriate feeding patterns common with the use of a bottle. These functional risks apply regardless of whether the bottle contains human milk or other liquids. However, a lack of distinction in most studies between breastfeeding and feeding of expressed milk by bottle disallows consideration of this hypothesis.

Methods

A PubMed search was conducted to identify recent studies that analyzed the association between breastfeeding history and otitis media in children. Studies published in 2010 and early-2011 were reviewed and were included if they contained some measure of breastfeeding as an exposure variable, and included otitis media as an outcome. Those identified were then summarized and grouped by AOM and otitis media with mention of OME. To provide a summary of prior evidence on the breastfeeding–otitis media link, we also include the results of a meta-analysis published in 2009. Where appropriate, results are presented to reflect the risks associated with replacement/supplementary feeding rather than the benefits

of breastfeeding so as to acknowledge the latter as the biological standard.

Results

Breastfeeding and Acute Otitis Media

A recent review and meta-analysis investigating the association between breastfeeding and health outcomes in developed countries determined that infants and young children who had never initiated breastfeeding, as well as those who received some supplementary or replacement feeding in the first 6 months, were at increased risk of AOM. The AOM analysis included data from five cohort studies judged to be of good to moderate methodologic quality. A dose–response relationship was observed between intensity of formula use and AOM risk, with exclusively breastfed infants in the lowest risk category and exclusively formula-fed infants in the highest. According to pooled OR calculations adjusted for potential confounding, infants who received any formula during the first 6 months exhibited twice the odds of developing AOM as infants who were exclusively breastfed (95% CI, 1.40–2.78) [4•, 15]. Differences were also observed between partially and non-breastfed children: those who received no breast milk experienced 1.3 times the odds of developing otitis media as those who were ever breastfed [4•]. The number of episodes of AOM was also correlated with breastfeeding history; never-breastfed infants were at highest risk of experiencing three or more episodes of AOM in infancy [4•].

More recent studies support an association between history of supplementary or replacement feeding and increased risk of AOM in early life. Data collected from a population-based cohort of 926 infants on the Greek island of Crete showed the duration of exclusive breastfeeding to be negatively associated with the risk of developing otitis media in the first year of life ($P < 0.01$), following adjustment for potential confounders [16]. AOM was classified according to parent report of physician diagnosis. When exposure categories were dichotomized to compare infants who had been exclusively breastfed for 6 months with those who had experienced partial or no breastfeeding, exclusive breastfeeding demonstrated an OR of 0.37 (95% CI, 0.13–1.05); this association was of borderline statistical significance. Exclusively breastfed infants also required fewer physician visits for otitis media than non-breastfed infants in this study. No significant differences were observed between partially breastfed (i.e., nonexclusively breastfed) and non-breastfed (i.e., exclusively formula-fed) infants with respect to otitis media risk, and no association was observed between suboptimal breastfeeding and mul-

tiples episodes of AOM. Breastfeeding history was not associated with hospitalizations for AOM in this study. However, interpretation of this finding is complicated by the small number of study infants who were hospitalized and evidence suggesting that hospitalization was influenced by parental anxiety in addition to the severity of the episode itself [17•].

The majority of infants in the Ladomenou et al. [16, 17•] study stopped breastfeeding by 6 months; therefore, while these results suggest that differences in risk between children who were initially exclusively and nonexclusively breastfed persist, it is difficult to determine for what length of time. It is important to note that this study's results differed according to whether exclusive breastfeeding was measured as a continuous or dichotomous variable. This difference highlights the need for consistency in definitions of breastfeeding in epidemiologic research.

Researchers in Finland analyzed cross-sectional data from 221 children aged 1 to 3 years enrolled in urban child care centers to determine the relationship between breastfeeding and the occurrence of recurrent respiratory infections and AOM (≥ 4 AOM episodes in the preceding 12 months) [18]. Partial breastfeeding for 6 months or more was found to be protective, with an OR of 0.20 (95% CI, 0.07–0.56) for recurrent otitis media, with 6 months or less of breastfeeding serving as the comparison group. AOM cases were identified by parental report of physician diagnosis. The average age of the participants was 2.8 years, suggesting that observed differences in otitis media risk persisted beyond weaning. Most children in this sample (62%) were breastfed longer than 6 months; however, interpretation of results is limited by lack of information on whether the breastfeeding pattern was exclusive or partial.

Using data collected from a population-based prospective birth cohort in Rotterdam in The Netherlands, researchers found no association between 3 or more months of breastfeeding and AOM in the second year of life [19]. AOM was defined by parental report of at least one occurrence of fever accompanied by earache for which a physician was visited. Results were controlled for occurrence of AOM during the first year of life. The analysis included 5,323 individuals with information on otitis media; breastfeeding histories were available for 2,371. The results suggest that either no association exists between AOM in the second year of life and method of infant feeding, or that the association exists but is mediated by occurrences within the first 12 months. This study is further limited by the large number of participants with missing data on breastfeeding history, which may have resulted in response bias. Another limitation is the lack of information on breastfeeding exclusivity.

Data collected from 618 Australian Aboriginal children aged 7 years or younger measured the association between

ever-breastfeeding and caregiver report of ear infection within the preceding 2 weeks [20]. The study was designed to investigate the influence of housing conditions on infectious disease but considered the influence of secondary explanatory variables such as infant feeding history. The majority of children in the study (53.9%) were between 3 and 7 years of age. Results revealed no association between ever-breastfeeding and caregiver report of otitis media, although never-breastfeeding was statistically significantly associated with increased risk of respiratory infections. The use of ever-breastfeeding as the exposure category allows the inclusion of a wide variety of feeding patterns, including bottle feeding, potentially limiting the ability to discern differences between groups. The older ages of the study participants meant that most were not at peak risk of AOM.

Few published studies are available on the association between infant feeding practices and severity of AOM. Researchers in the United States conducted a prospective, longitudinal study of 128 children 6 to 35 months of age to assess the association of various risk factors with the reported severity of AOM symptoms [21]. Researchers combined parental reports of earache, fever, irritability, restless sleep, and poor feeding into a total symptom severity score. The association between ever-breastfeeding and the symptom severity score did not achieve statistical significance. Again, the interpretation is limited by the use of ever-breastfeeding as the exposure category.

History of Breastfeeding and Otitis Media with Effusion in Older Children

In a case–control study of 138 children in rural India aged 11 months to 7 years, researchers included both acute suppurative otitis media and OME diagnoses. They found no difference in otitis media risk between those who had been breastfed for longer than 6 months and those who had been breastfed for less than 6 months [22]. Limitations of this study included the small number of infants who were breastfed for less than 6 months and the lack of data on exclusivity. In another study, data collected on 1,740 primary school children in Istanbul, Turkey, showed no association between breastfeeding for the first 6 months of life and a current diagnosis of persistent OME [23]. The children ranged in age from 5 to 12 years (mean age, 8.5 years). In a third study, a case–control study of 100 Brazilian children aged 4.2 to 10.8 years with chronic upper airway obstruction due to enlarged tonsils or adenoids, researchers failed to find a significant association between a history of exclusive or partial bottle feeding and a diagnosis of OME. Due to the specialized nature of the population, many of whom experienced signs of anatomic obstruction

of the eustachian tubes, these last results have more limited generalizability [24].

Given the older ages of the children in these studies, it is possible that intervening variables obscured the expected impact of breastfeeding on incidence of otitis media. Prospective study would enhance interpretation of these associations.

Discussion

Recent evidence from various regions supports an association between formula feeding—presumably bottle feeding—and increased risk of AOM in infancy and early-childhood. Epidemiologic studies indicate that infants who receive formula in the first 6 months of life are at increased risk of developing AOM in early-childhood compared with those who are exclusively breastfed. These studies also indicate a dose–response relationship between breastfeeding exclusivity and duration and reduction in risk of AOM. Although not all findings are consistent, studies that included only children of preschool age or younger and that utilized precise measures of breastfeeding consistently demonstrated this association. These results are concordant with a recent prospective study in Hong Kong indicating that never-breastfed children are at increased risk of hospitalization for respiratory infection in the first 6 months of life, a category that included, but was not limited to AOM [25].

The studies conducted after 2009 do not provide additional insight into how long the protective effect of breastfeeding against otitis media might continue. In children older than 12 months of age, there is some indication that the infant feeding and later otitis media association may be mediated by occurrence of otitis media episodes in the first 12 months of life. Measures of the association between infant feeding and AOM appear to be sensitive to the definitions of feeding patterns used. Future research should attempt to utilize standard and precise definitions of breastfeeding and other infant feeding practices over time, distinguishing between exclusive and partial breastfeeding and bottle use, as well as between breastfeeding and human milk feeding by bottle. Where possible, information on the type of feeding bottle used and the position in which the infant is fed, as well as any bottle propping or bottle holding by the infant would also be valuable.

The studies presented here suffered from several limitations commonly found in infant feeding research. Due to the inability to randomly assign individuals to feeding groups, these studies are observational and may suffer from residual confounding from factors that are difficult to isolate (e.g., caregiver characteristics). This limits the

interpretation of causality. Furthermore, the interpretation of these results is complicated by variable and imprecise definitions of breastfeeding and by differences in the age groups studied.

Conclusions

Recent epidemiologic evidence confirms that introduction of infant formula in the first 6 months of life is associated with increased risk of otitis media when compared with 6 months of exclusive breastfeeding. However, there remains a need to further explore the association of infant feeding with otitis media and OME later in childhood, controlling for intervening variables in the interval. Further research is needed to examine these associations utilizing standardized and precise definitions of infant feeding practices, including consideration of the differences that may occur when duration of exclusive or partial breastfeeding is included. Finally, today, with the increasing practice of human milk expression and later feeding by bottle, it is also becoming important to differentiate among breastfeeding at the breast, bottle feeding of human milk, and bottle feeding of other milks and formulas.

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Ms. Abrahams reported no potential conflicts of interest relevant to this article.

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