SpringerLink Header: Otitis (D. Skoner, Section Editor)

The role of breastfeeding in childhood otitis media

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Abstract

Purpose of Review: To summarize the recent literature, both systematic reviews and recently published original studies not included within those reviews, on the relationship between breastfeeding and childhood otitis media (OM).

Recent Findings: There is clear evidence that breastfeeding is associated with a reduced risk of OM in childhood with sound biological plausibility to support that the association is likely causal. Any breastfeeding reduces OM risk in early childhood by 40-50%. Systematic reviews also support a further reduced risk for continued breastfeeding. Recent studies have estimated burden of disease savings if breastfeeding within countries and globally approached WHO guidelines. Cost savings per year for reduced cases of OM by increasing ever and exclusive breastfeeding rates are estimated to be millions of pounds or dollars for UK and Mexico.

Summary: Breastfeeding reduces OM in children. The burden of disease and economic impact of increasing breastfeeding rates and duration would be substantial.

Key Words: Breastfeeding and otitis; otitis media; breastfeeding rates; AOM; breast milk

Abstract:150 words

Body:2582 words

Introduction:

Burden of Otitis Media:

Acute Otitis Media (AOM) is usually caused by either a viral or bacterial pathogen and often treated with antibiotics. Young children are particularly at risk due to limited space in the middle ear and poor drainage from relatively tortuous Eustachian tubes. AOM is often accompanied by significant pain along with fever, acute loss of hearing, and general unwellness. AOM has a number of potential complications. Many AOM-prone children suffer from recurrent episodes in infancy and early childhood. Commonly, on resolution of the acute infection, there is a persistent middle ear effusion (otitis media with effusion-OME) with accompanying hearing impairment. OME can persist, causing longer term hearing impairment and interfering with language development, school performance and behaviour. AOM may result in perforation of the ear drum with chronic discharge (chronic suppurative otitis media). Less common complications include mastoiditis, brain abscess and meningitis.

Globally, there are an estimated 709 million cases of acute otitis media per year, an incidence of 10.85% (1). The peak incidence is in the 1-4-year age group (60.99%) although rates vary from 3.64% in Central Europe to 43.36% in Sub-Saharan Africa (1). The disease burden attributed to AOM in both established and emerging nations is considerable. It is the most common reason for prescription antibiotics in developed countries where AOM is estimated to affect more than 60% of children under one year and more than 80% of children under three years (2-4). There is also a considerable health burden from the sequelae of AOM. It is estimated that there are globally around 31 million cases of chronic suppurative otitis media, and the prevalence rate for AOM induced permanent hearing impairment is 30.82 per 10,000 (1). Furthermore, complications of AOM are estimated to cause the deaths of 21,000 people annually, with mortality rates being highest in the 0-5 year age group (1).

Although updated clinical guidelines have reduced the reliance on antibiotic therapy for mild, early, uncomplicated AOM (5), it is still the most common reason for antibiotic use in many countries (6). Apart from the associated health care burden, this widespread use of antibiotics increases the risk of community antibiotic resistance.

Given the high health care burden, a number of risk factors for AOM have been investigated. The factors currently identified for risk reduction are breastfeeding, avoidance of in utero and childhood passive tobacco smoke exposure, and avoidance of indoor air pollution (1). A recent Lancet mega-review that summarized the evidence on breastfeeding and maternal and child health outcomes from 28 individual systematic reviews, found breastfeeding has many health benefits for both

mothers and children(7). The Lancet findings also confirm the vital role that breastfeeding plays in the prevention of common childhood infectious diseases including AOM.

Breastfeeding and Otitis Media:

Human breast milk is tailor-made for infants (8). Breast milk delivers appropriate nutrition for each infantile developmental stage, and is packed with immune substances that may: directly influence microbial colonization with favourable bacteria; protect against colonization and infection by harmful bacteria and; influence immune programming (9). The WHO recommends exclusive breastfeeding up to the age of 6 months with continued breastfeeding for 2 years and beyond. Despite these recommendations, breastfeeding rates in many countries, especially high-income countries, are poor with rates of only 20% at 12 months (7). Additionally, in children under the age of 6 months, 63%, 61% and 55% are not exclusively breastfeed in upper-middle income countries, low-middle income countries and low income countries respectively (7).

Almost all the recent literature outlining the links between breastfeeding and OM supports a reduced risk of OM associated with breastfeeding. Since 2013 there have been two systematic reviews, a non-systematic review and four original studies on this subject.

Data Syntheses: Systematic and non-systematic reviews (Table 1)

There have been three reviews published on the impact of BF on OM over the last 4 years

The most recent data synthesis on this topic is our groups 2015 systematic review and meta-analysis by Bowatte et al. (10), commissioned by the World Health Organization as part of the Mega-review recently published in the Lancet (11). Pubmed, Cinahl and Embase databases were searched from inception yielding 24 studies (18 cohorts and 6 cross-sectional). Overall, we found a 43% reduction of the risk of ever having AOM in the first 2 years of life but no reduced risk after the age of 2. In this systematic review, meta-analyses were possible only for particular exposure categories. Infants exclusively breastfed for 6 months compared with those not breastfed or breastfed for periods less than 6 months had a reduced risk of AOM up to the age of 2 years after pooling the ORs of 5 cohort studies (OR 0.57; 95%CI 0.44-0.75). We also found a risk reduction when comparing ever versus never breastfed infants: OR 0.67; 0.56-0.80 (5 studies). An additional meta-analysis was performed on 12 cohort studies in a more versus less exposure grouping. This category included ORs from all studies which compared a greater exposure of breastfeeding (more) to less breastfeeding. The meta-analysis also found a reduced risk of AOM up to 2 years: OR 0.76; 0.67-0.56.

A systematic review by Hornell et al. reviewed the literature published between January 2000 and June 2011 (12). They identified four publications on AOM; two systematic review/meta-analysis (13, 14) and two prospective cohorts (15, 16). After reviewing these publications without performing an overall pooled estimate, the authors concluded that there was convincing evidence of a protective dose and duration of breastfeeding on OM. The publications included in the Hornell et al. systematic review are described in the following sentences. The included systematic review by Ip et al. (13) found a pooled adjusted Odds Ratio from 5 cohort studies for the risk of AOM associated with any breastfeeding of 0.77; 95% CI 0.64-0.91 when compared with never breastfeed infants. Additionally, Ip et al. found some evidence that longer duration of breastfeeding may confer greater protection; the pooled estimate for the risk of AOM associated with 3-6 months exclusive breastfeeding versus

never breastfed was: OR 0.5; 0.36, 0.70. The other included systematic review by Kramer and Kakuma (14) analysed two prospective cohorts with a total of 3762 children finding an increased risk of one or more episode of otitis media in the first 12 months (Risk Ratio 1.28;95%CI 1.04-1.57). One of the two additional cohort studies included in the Hornell et al. systematic review (birth cohort n = 1764) found a non-significant association between distinct lengths of breastfeeding exposure (<1mo, 1-3mo, 4+mo, 4-6mo, 7-11 mo, 12+mo), and prevalence of ear infections in either the first or second 6 months of life. Their findings may have been limited by lack of power in each of the exposure categories. The remaining cohort study on 926 children found that infants exclusively breastfed for six months had fewer infections than partially breastfed or never breastfed children (OR 0.37; 0.13, 1.05).

There was a large amount of overlap between the systematic reviews of Bowatte and Hornell with the Bowatte review including all but studies identified by Hornell along with an additional 15 studies.

A 2013 non-systematic review performed by the American Academy of Pediatric Dentistry, Chicago as an update on the effects of breastfeeding for dental professionals also found that breastfeeding was associated with a reduced risk of OM(17).

Original articles since 2013 (Table 2)

There have been 4 original research articles published since 2013 (18-21). Due to dates of publication (two studies(18, 20)) and inclusion/exclusion criteria (two studies on selected populations)(19, 21), none were included in either of the systematic reviews mentioned above; however, it is unlikely that their inclusion would have affected the direction of associations found as three of these articles found an association between breastfeeding and a reduced risk of AOM.

Most recently, Martines et al.(20) performed a case-control study on Sicilian children (204 cases with 204 age and sex matched controls). They found that children who were breastfed were much less likely to develop AOM or Otitis Media with Effusion (OME) following an upper respiratory tract infection (URTI) than those who had never been breastfed ; OR 0.5;95%CI 0.3-0.77.(20)

Ajetunmobi et al. (18) investigated 502,958 children in a retrospective population based Scottish cohort using linkage of birth, death, maternity, infant health, child health surveillance and admission records. They included all single births in Scotland between 1997 and 2009, following the children until March 2012. Based on information collected about feeding at the 6-8 week visit, infants were classified as either: exclusively breastfed, exclusively formula fed, or mixed feeding. Compared with exclusively breastfed children, there was an increased risk of hospitalization for AOM in the first 6 months of life for infants who were exclusively formula fed (Hazard Rate (HR) 2.13; 95%CI 1.26-3.59). This estimate was made following adjustment for a range of socio-economic factors. There was also an increased point estimate for those both breast and formula fed (mixed feeding) compared with exclusive breastfeeding but the 95% confidence interval included 1 (HR 1.5; 0.65-3.48). They also found increased risk of hospitalization within the first year of life for formula fed infants for a large range of illness including: infections (gastrointestinal, upper and lower respiratory tract, urinary, and non-specific fever); asthma; diabetes and dental caries. These increased risks persisted after stratification by area deprivation. There was no increased risk of hospitalization for AOM after the first 6 months of life. The lack of association after the age of 6 months is perhaps expected considering that AOM is usually treated in the community and it is also remarkable that an association was found up to the age of 6 months. The huge population based sample along with the objective ascertainment of prospectively collected exposure and outcome data, contribute to the robustness and importance of this work.

Jenson et al. (19) investigated a population based cohort of 223 Inuit mother-child pairs in two towns on the west coast of Greenland (1999-2007). The primary purpose of this research was to assess the relationship between maternal organochloride exposure and OM in their children. The children were followed up at the age of 4-10 years. They classified breastfeeding status at 6 months as full, partial or not and did not find an association with breastfeeding although point estimates were below 1 suggesting protection for full or partially breastfeed children. It may be that there was little power to detect an association given the number of participants.

The final article by Salah et al. was a retrospective hospital based cohort of 340 children. In a group of children aged less than 2 years attending an outpatient clinic for recurrent AOM (3 or more episodes in 6 months), factors were analysed which predicted further recurrence and treatment failure. They found that breastfeeding duration of less than three months (compared with more than three months) was associated with a significant chance of further recurrence and with treatment failure (failure of antibiotic treatment).

Mechanisms for the protective link between breastfeeding and AOM

Previously it was believed that the protective effect of AOM on breastfeeding was largely mechanical; the suction pressure required and positioning for breast feeding were thought to be advantageous for draining the Eustachian tubes in young infants, thereby preventing AOM. Another slightly older theory that may underlie the reduction in infectious disease enjoyed by breastfed babies is related to the immunomodulatory substances contained in breast milk. This theory has currently been re-invigorated through the recent interest in the human and more specifically the infant gut microbiome. It is now believed a specific symbiotic microbiome which is established early in life and, amongst other functions, is believed to protect the infant against pathogenic infections (22).

Breast milk is known to contain the building blocks for establishment of this microbiome in the form of human milk oligosaccharides (HMOs) along with a distinct breast milk microbiota. HMOs are indigestible sugars most prominent in the colostrum. The milk oligosaccharides from primates are unique in the mammalian kingdom in terms of their diversity and high percentage of fucosylation (23). There are over 200 different types of human HMOs (24) and 50-80% of these are fucosylayted depending on the genetic makeup of the mother (25). They feature prominently in the colostrum (20-25g/L) and taper off in overall percentage for mature breast milk (5-20g/L) (26). Although these HMOs do not provide a source of energy for the infant, their unique branching and diversity makes them a perfect substrate for particular strains of bacteria that are known to be beneficial colonizers of the newborn.

Although there is a growing literature on the establishment of the infant gut microbiome and its importance for protection from gastrointestinal morbidity along with its capacity to correctly educate the infants immature immune system, less is known about the microbiome of the naso-pharynx and its potential effect on protection from AOM. Recently, Biesbroek et al (27) investigated the nasopharyngeal microbiome in 101 exclusively breastfed and 101 exclusively formula fed infants.

They discovered a distinctly different bacterial community composition in the nasopharynx between the two feeding modes; with breastfed children having increased representation of *Dolosigranulum* and *Corynebacterium Sp.* and reduced representation of *Staphylococcus, Prevotella* and *Veillonella sp.* at 6 weeks of age.

Literature concerning cost savings from reduced AOM linked to increased breastfeeding

Given the convincingly positive findings for breastfeeding in relation to OM, some of the recent literature has focussed on reductions in OM and cost savings which could be achieved through greater uptake and continuation of breastfeeding. Pokhrel et al. (28) assessed the potential economic impact, from the point of view of the National Health Service, from improving breastfeeding rates in the U.K. Breastfeeding rates in the UK are comparatively low internationally with only 55% of infants breastfed at 6 weeks and only 23% exclusively (2010). They assessed the economic impact in terms of 4 acute childhood conditions in the first year of life: gastrointestinal illness, lower respiratory tract infections, AOM and necrotising enterocolitis, finding that for women who have initiated breastfeeding for the first week, an increase in breastfeeding duration up to 4 months would save 11 million pounds per year. For AOM these costs were based solely on the costs of treating AOM in primary care and did not appear to take into account the cost of complications, hospitalizations or the costs for parents who would need time off work to care for their children. Specifically, for AOM the cost saving was estimated to be between 0.28 and 1.16 million pounds per year depending on whether exclusive breastfeeding rates at 6 months increased to 21% OR 65% respectively. McIsaac et al. (29) studied potential reductions in common childhood infections in Aboriginal Canadians where AOM reduction may be arguably greater due to the increased prevalence of severe AOM in this population and relative decrease in breastfeeding when compared with general Canadian infants . They found a 5.1% to 10.6% reduction in OM in Aboriginal infants if they received any breastfeeding. The preventable proportion of infectious disease in Aboriginal infants was 1.5-2 times greater than the non-Aboriginal Canadian infants. Arantxa Colchero et al. (30) investigated the costs of inadequate breastfeeding in Mexican infants who experience very low rates of exclusive breastfeeding at 6 months; only 14% in 2012. They found if exclusive breastfeeding rates increased to 95% at 6 months and 95% partial breastfeeding between 6 and 12 months, then the savings related to reduced AOM could be between 0.5 and 15.4 million US dollars per year. This estimate increased when the cost of infant formula is added: 289.9 million dollars per year. Furthermore, the economic modelling from the Lancet mega-review using the Lives Saved Tool to estimate global impacts of increasing exclusive breastfeeding for 95% of all children at 1 month, and 90% at 6 months with partial breastfeeding of 90% between 6 and 23 months found a possible prevention of 823,000 deaths in children under the age of 5. This was largely from prevention of infectious disease in low-income countries (11).

Conclusions:

There appears to be little doubt that breastfeeding is beneficial for protecting infants from a range of infectious diseases including AOM. In addition, there are a number of other economic and health related reasons for promotion of breastfeeding in line with the WHO guidelines. Governments globally should promote and support breastfeeding through campaigns and measures designed to educate and support mothers, families and communities.

Compliance with Ethics Guidelines

Conflict of Interest

Drs. Lodge, Bowatte, Matheson, and Dharmage declare no conflicts of interest relevant to this manuscript.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

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•• Of major importance

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Table 1. Reviews of Breastfeeding and otitis media in past 4 years							
Authors &	Study Type & inclusion	Population & numbers	Exposure & how	Outcome & how Ascertained	Measured effect		
Date &	criteria		ascertained				
Country							
Hornell et al	Systematic review	Population	Duration of both any	Grade of evidence ;	Convincing evidence of a		
2013		Nordic countries	and exclusive	convincing/probable/limited-	protective dose/duration effect		
	Short and long term	Number	breastfeeding	suggestive/limited-no conclusion	of breastfeeding on acute otitis		
	effects of breastfeeding	60 quality assessed	Introduction of		media		
	and introduction to	papers	foods other than	Quality Assessment Tols(QAT) from			
	solids	13 SLR/MA; 41	breast milk	the NNR5 secretariat-included	Recommend unchanged nnr		
		prospective cohort; 6		modified AMSTAR	2004 exclusive breastfeeding 6		
	Inclusion	from PROBIT trial; 13			months and continued partial		
	Published since January	reports			breastfeeding thereafter		
	2000, human subjects			Ip SLR (grade A) 5 cohort studies			
	Search date June 2011	4 of these on AOM – 2		BF signif reduction in AOM			
	English or Nordic	prospective cohorts					
	language	and 2 SLR/MA		Pooled adjusted OR s:			
	Noraic study			ever vs never BF 0.77 (95%CI: 0.64,			
	population			0.91)			
	EXClusion			EX BF 3 - 6 months vs never:			
	formulas og			0.50 (0.36, 0.70)			
	iormulas eg			Drespective schort studies:			
	Supplemented (LC-			Fisk at all birth schort 1764			
	PUFA), Dreast milk			Fisk et al – Dirth conort 1764			
	high rick mothers and						
	childron			$12 \pm m_0$ = oar infactions 0 6mo and			
	If only definition over vs			6-12 months. Non significant			
	nover			association by Bf duration and prev			
				of ear infections $0-6$ and $6-12$			
				months			
				Ladomenou et al			
				Ex bf for 6 months, fewer infections			

				than partially and nonBF- adj OR	
				0.37 (0.13, 1.05)	
Bowatte et	Systematic Review and	Population	Ever versus never	Childhood Hospitalization for AOM	Reduced risk AOM in first 2
al	Meta-analysis	24 studies (USA or	breastfeeding	until March 2012 (Follow-up period	years of life (not after 2)
2015		Europe)		varied between 2.25 years and 15	Ex BF 6 months – 43%
	Exclusion	18 cohort	More versus less	years)	reduction in ever AOM in first 2
	OME	6 cross-sectional	breastfeeding		years
	Non-english	Number		Ascertainment	
			Exclusive BF for 6	Linkage of birth, death, maternity,	EX BF 6 months vs other OR
			months versus	infant health, child health	0.57; 0.44-0.75 (5 cohorts)
				surveillance and admission records	0.59, More vs Less BF Or 0.67
					0.76 (12 cohorts)
					Ever vs Never BF or 0.67 ;0.56,
					0.80 (5 studies)
Salone et al	A narrative review:	Includes: peer	Not given: OM is a	Not given	Compared with formula-fed
2013	studies published from	reviewed articles,	small part of health		children, the health advantages
	January 1999 - March	systematic review and	outcomes assessed		associated with breastfeeding
	2011	meta-analyses, and			include a lower risk of acute
		reports from major			otitis media
		nongovernmental and			
		governmental			
		organizations			

Table 2. Origin	Table 2. Original Studies on the link between Breastfeeding and Otitis media- published in last 4 years					
Authors &	Study Type & inclusion	Population & numbers	Exposure & how	Outcome & how Ascertained	Measured effect	
Date &	criteria		ascertained			
Country						
Martines et	Case-Control	Population	Breastfeeding ever	Current AOM or EOM	Risk of OM	
al		Sicilian children,	Yes vs No			
2016		Palermo		ENT specialist on history and		
	Inclusion	Sep 2012 – June 2013		otoscopy	breastfed vs non-breastfed	
Sicily	Children attending ED					
	in Palermo with URTI	Number	Ascertainment		Chi square – 10.16 95%	
	then having OM	204 children(106 males	Questionnaire	Ascertainment	(p=0.0014)	
	diagnosed (either Acute	and 98 females)	(recall)	Questionnaire (recall)		
	otitis media-AOM or	204 age and sex				
	Otitis media with	matched healthy			OR 0.5 CI (0.3, 0.77)	
	effusion EOM) within	children				
	21 days and age/sex				This appears to be an	
	matched controls				unadjusted estimate	
Ajetunmobi	Retrospective	Population	Infant feeding at 6-	Childhood Hospitalization for AOM	Risk of hospitalization for OM	
et al	population –based	Single births in	8week age review	until March 2012 (Follow-up period		
2015	Birth Cohort	Scotland 1997-2009	1. Exclusive	varied between 2.25 years and 15	Compared with exclusive	
			breastfeedin	years)	breastfeeding (baseline)	
Scotland	Exclusion	Number	g			
	Congentital anomalies,	502,948	2. Formula	Ascertainment	All ages:	
	non-Scottish residents		feeding	Linkage of birth, death, maternity,	Mixed fed HR 1.04 (0.95- 1.14)	
			3. Mixed	infant health, child health	Formula fed HR 1.03 (0.97-	
			breast and	surveillance and admission records	1.09)	
			formula		≤6months	
			feeding		Mixed fed HR 1.5(0.65-3.48)	
					Formula fed HR 2.13 (1.26-	
			Ascertainment		3.59)	

			Linkage of birth, death, maternity, infant health, child health surveillance and admission records		Adjusted for parental factors, delivery and infant health characteristics, features of health care system – exact variables unclear and deprivation area index, maternal ethnic and religious background
Jenson et al	Population based	Population	Breastfeeding status	ОМ	Risk of OM in first 4 years of
	cohort	400 mother –child	at 6 months		life
2013		pairs(400 pregnant		Ascertainment	compared with no
Greenland	(primary aim to assess	women aged 16-46)	1. Full	Ear examinations with	breastfeeding at 6 months
	the effects of	living in three towns	2. Partly	tympanometry and gradings:	
	organochloride	on west coast of	3. No	1. Chronic otorrhea (>14 days)	Full breastfeeding:
	exposure in mothers on	Greenland	.	2. Chronic perforation	HR 0.85 (0.47-1.54)
	otitis media in their	(Nuuk, Ilulissat,	Ascertainment	(>3months)	Doubly have offered in a
	children)	Mantisoq) 1999-2007	Mothers interviewed	3. Circular atrophy	Partly breastfeeding
		Number	at 6 months	4. Wyringoscierosis	HR 0.90 (0.54-1.49)
		Number		5. Diffuse atrophy	Estimates adjusted for say
		living in Nuuk and		7 Eibrosis	estimates adjusted for sex,
		Ilulissat and 223 (85%)		7. FIDIOSIS 8. Unknown (ear way	OM mothers history of
		of these children		obstructing	smoking
		followed up at 4-10		view/uncooperative)	SHOKING
		vears		9 Normal	
		years			
				OM history	
				-	
				Ascertainment	
				medical records	
Salah et al.	Retrospective	Population	Breastfeeding	Recurrent AOM	Recurrent AOM

2013	hospital-based cohort	Recurrent AOM	duration	(≥3 episodes in 6 months) at age 3-	
		patients <2 years	> 3months versus <	24 months	Unadjusted – Chi square
	Exclusion	attending outpatient	3 months	Otoscopy – congested and/or	5.7 episodes of AOM (SD +-1.9)
	Chronic otitis media	Pediatric		bulging eardrum, or otorrhea and	in infants breastfed < 3months
	with effusion,	Otolaryngology Unit,	Ascertainment	presence of acute signs of infection	cf 5.1 episodes AOM (SD 1.6)
	Typanostomy tube	Cairo University	Review of hospital	(fever, pain, irritability)	in infants breastfed > 3 months
	insertion	Hospital (May 2011-	charts	Treatment failure	(p=0.005)
		April 2012)		Persistence or worsening of AOM	
				for up to 1 week following initial	Treatment failure
				treatment (antibiotics)	Logistic regression(with
		Number			unknown inclusion of other
		340			variables) showed that short
					breastfeeding (<3 months) was
					a "significant risk factor" for
					treatment failure (p=0.006)

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Title: The Role of Breastfeeding in Childhood Otitis Media

Date: 2016-09-01

Citation:

Lodge, CJ; Bowatte, G; Matheson, MC; Dharmage, SC, The Role of Breastfeeding in Childhood Otitis Media, CURRENT ALLERGY AND ASTHMA REPORTS, 2016, 16 (9)

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