



Original article

Breastfeeding and childhood hospitalizations for asthma and other wheezing disorders

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ABSTRACT

Purpose: Observationally in Western settings, breastfeeding is associated with less childhood wheezing disorders but may be confounded by socioeconomic position. We examined the association of breastfeeding with asthma and other wheezing disorders in a developed non-Western setting with unique social patterning of breastfeeding.

Methods: Using Cox regression, we examined the adjusted associations of breastfeeding with public hospital admissions for asthma, bronchitis, and bronchiolitis (*International Classification of Diseases, Ninth Version. Clinical Modification*: 466, 490, and 493) from 3 months to 12 years in a population-representative birth cohort of 8327 Hong Kong Chinese children.

Results: We did not find an association of exclusive breastfeeding for 3 months or more, compared with never breastfeeding, with hospitalization for asthma, bronchitis, and bronchiolitis to 12 years (hazard ratio [HR], 0.89; 95% confidence interval [CI], 0.63–1.25) nor for partial breastfeeding for any length of time or exclusive breastfeeding for less than 3 months (HR, 1.02; 95% CI, 0.86–1.21), adjusted for infant and parental characteristics and socioeconomic position. We also did not find an association of exclusive breastfeeding for 3 months or more with hospitalization for asthma only (*International Classification of Diseases, Ninth Version. Clinical Modification*: 493) (HR, 1.27; 95% CI, 0.82–1.98).

Conclusions: In a large population-representative Chinese birth cohort, we did not find an association of breastfeeding with childhood hospitalizations for asthma and other wheezing disorders.

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Introduction

Asthma and other wheezing disorders is one of the most common chronic diseases in children [1]. Wheezing disorders are most prevalent in developed Western countries and are increasingly prevalent in developing countries as they become more urbanized [2]. Much is unknown about the etiology of childhood wheezing disorders, but wide variations in prevalence between different cities in China suggest that environmental and dietary factors may play an important role [3]. Early exposure to potential dietary allergens may promote the development of asthma and wheeze in infants with atopic predisposition through immune sensitization [4]. On the other hand, dietary constituents such as polyunsaturated fatty acids may have protective effects via immunomodulation [5]. Breast milk is a source of immunomodulatory factors that may promote maturation of the infant's immune

defense mechanisms against atopic disease [6]. However, whether breastfeeding confers protection against childhood wheezing disorders remains a subject of intense debate.

Meta-analyses of observational studies show breastfeeding associated with lower risk of asthma and other wheezing disorders in the first few years of life [7–9]. Conversely, a higher risk of these disorders has also been observed in older children who have been breast-fed [10]. Furthermore, a recent systematic review and meta-analysis of 113 observational studies showed marked heterogeneity among the reviewed studies, possibly due to the varying definitions of asthma and/or wheezing disorders [9]. These studies are predominantly from developed Western settings where socioeconomic position (SEP) is positively associated with breastfeeding [11] and negatively associated with childhood asthma [11–13], making such observations open to residual confounding by SEP. No randomized controlled trials (RCTs) of breastfeeding per se have been conducted. An RCT of breastfeeding promotion in Belarus (The Promotion of Breastfeeding Intervention Trial [PROBIT]), designed to assess the effect of breastfeeding on infections, atopic eczema, and infant growth [14], found no effect of prolonged and exclusive breastfeeding on childhood asthma [15]. The uncertain

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generalizability of a single trial highlights the need for evidence from other contexts with different social patterns of breastfeeding, where estimates may be less confounded.

Hong Kong has a developed postindustrial economy, with a gross domestic product per head and social infrastructure similar to Western Europe or North America [16,17]. Like most developed Western settings, infant formula, mainly cow's milk based, is widely used as a breast milk substitute in Hong Kong [18]. However, contrary to Western settings where breastfeeding mothers tend to be better educated [11], more educated Hong Kong-born mothers tend to initiate and cease breastfeeding earlier, whereas less educated or migrant mothers tend to sustain breastfeeding [17,19]. The prevalence of childhood asthma in Hong Kong approximates that in developed Western countries [20,21], but its association with SEP is less clear [3,20]. Thus, Hong Kong provides a setting with a unique social pattern of breastfeeding to examine the association of breastfeeding with asthma and other wheezing disorders. Here, we took advantage of a large, contemporary, population-representative Hong Kong Chinese birth cohort, "Children of 1997," where we previously found breastfeeding associated with lower risk of hospitalization for respiratory infections in the first 6 months of life [19], to examine prospectively the association of breastfeeding with hospitalizations for asthma, bronchitis, and bronchiolitis up to 12 years of age.

Material and methods

Sources of data

The "Children of 1997" birth cohort is a population-representative Chinese birth cohort ($n = 8327$) covering 88% of all births in Hong Kong from April 1, 1997 to May 31, 1997, described in detail elsewhere [16]. The study was initially designed to investigate the effects of second-hand smoke (SHS) exposure and breastfeeding on infant health services utilization [22,23]. Mother-infant pairs were recruited at the first postnatal visit to any of the 49 government-run Maternal and Child Health Centers (MCHCs) in Hong Kong, where parents of all newborns are encouraged to attend for free preventive care and vaccinations. Baseline characteristics obtained at recruitment included infant feeding, birth characteristics, mother's age, mother's place of birth, parental history of allergies, SHS exposure, and SEP, using a standardized, self-administered questionnaire in Chinese. Follow-up questionnaires were administered at 3, 9, and 18 months. In 2007, a program was instituted to re-establish direct contact with the birth cohort families. Three postal surveys were conducted between 2008 and 2012. Any missing baseline data were updated with each wave of data collection and any discrepancies between waves reconciled.

Hospital discharge data were obtained by record linkage from the Hospital Authority, which oversees all public hospitals and provides inpatient services accounting for about 90% of total bed days and 77% of all admissions in Hong Kong [24,25]. All Hong Kong citizens are entitled to public health care with minimal out-of-pocket payments as the government subsidizes 97% of hospitalization costs in public hospitals [26]. Discharge records include the date of each hospital admission and discharge, name of hospital, principal and secondary diagnoses or reasons for admission, and principal medical procedures.

Exposure: breastfeeding

Information on breastfeeding was obtained from self-administered questionnaires in Chinese completed by the primary caregiver (most commonly mothers), with help as necessary, at the first postnatal (baseline) visit to the MCHCs and subsequent routine

visits when the infants were approximately 3, 9, and 18 months of age. At the first visit, respondents were asked: "How is the infant currently fed?" specified as "exclusively breast-fed," "partially breast-fed," and "only formula-fed." At follow-up visits, respondents were asked: "How has the infant been fed from birth until now?" specified as one of the three original options, or an additional option "initially breast-fed, but now formula-fed," with the age in months when breastfeeding terminated. As respondents who indicated that the infant was "partially breast-fed" did not provide the age when breastfeeding terminated, we were unable to determine the duration of breastfeeding for all breastfed infants. The responses on infant feeding at different ages are summarized in [Supplementary eTable S1](#).

Infants were classified into three groups according to breastfeeding status, that is, "exclusively breast-fed for 3 months or more," "partially breast-fed for any length of time or exclusively breast-fed for less than 3 months," and "never breast-fed," as in our previous studies [17,19,27–29]. Few mothers in this cohort continued any breastfeeding beyond 3 months [19], perhaps because paid maternity leave is 10 weeks. We, thus, categorized breastfeeding into three groups using 3 months as a cutoff. Infants were classified as "exclusively breast-fed for 3 months or more" if at 3 months, or the next available follow-up, they were reported as exclusively breast-fed or if breastfeeding terminated at 3 months of age or more. Because for most exclusively breastfed infants, breastfeeding terminated at 1 or 2 months, making breastfeeding for less than 3 months and partial breastfeeding physiologically rather similar, we combined the two groups into "partially breast-fed for any length of time or exclusively breast-fed for less than 3 months" to reduce misclassification and to be consistent with our previous studies. As sensitivity analyses, we have also separated the two groups into "partially breast-fed for any length of time" and "exclusively breast-fed for <3 months" and re-categorized breastfeeding into "never breast-fed" and "ever breast-fed." As we do not have the age of starting complementary feeding, infants in all three groups may have received breast milk substitutes such as formula, nonmilk liquids, or solid foods.

Outcome: hospitalizations for asthma and other wheezing disorders

Our primary outcome was public hospital admissions for asthma and other wheezing disorders from more than 3 months to 12 years of age. As secondary outcomes, we further considered hospitalizations from more than 3 months to 2 years, more than 2 years to 6 years, and more than 3 months to 6 years to facilitate comparison with a recent systematic review and meta-analysis (which found stronger associations of breastfeeding with lower risk of asthma to 2 years than at more than 2 years) [9] and the PROBIT trial (which examined asthma at 6.5 years) [15]. Finally, we considered hospitalizations from more than 6 years to 12 years to clarify the association beyond early childhood and because the diagnosis of asthma is less reliable in children younger than 6 years [30].

Admissions were coded at discharge according to the *International Classification of Diseases, Ninth Version, Clinical Modification* (ICD-9-CM). We defined asthma and other wheezing disorders as a diagnosis of acute bronchitis and bronchiolitis (ICD-9-CM: 466), bronchitis, not specified as acute or chronic (ICD-9-CM: 490), and asthma (ICD-9-CM: 493). For comparison, we also considered asthma as ICD-9-CM 493 only and bronchitis and bronchiolitis as ICD-9-CM 466 and 490. We included both daypatient and inpatient admissions. Children with no record of hospitalization were assumed to have none, although private hospital admission is possible but not obtainable by record linkage, as in our previous studies [19,31]. We excluded hospitalizations occurring within the

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