

Observational Study

Association of breastfeeding with tidal breathing analysis in infants with bronchiolitis

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Institutional review board

statement: The Institutional Review Board of University

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Abstract

BACKGROUND

Tidal breathing flow-volume (TBFV) analysis provides important information about lung mechanics in infants.

AIM

To assess the effects of breastfeeding on the TBFV measurements of infants who recover from acute bronchiolitis.

METHODS

In this cross-sectional study, TBFV analysis was performed in infants with bronchiolitis prior to hospital discharge. The ratio of time to peak expiratory flow to total expiratory time (tPEF/tE) at baseline and after the administration of 400 mcg salbutamol was evaluated.

RESULTS

General Hospital of Alexandroupolis provided approval for this study (IRB No. 23927/2382/02.01.2017).

Informed consent statement:

Parental approval was obtained prior to inclusion for all involved infants.

Conflict-of-interest statement:

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Data sharing statement: The authors confirm that the data supporting the findings of this study are available within the article and its tables/figures. Raw data, without patient's personal information, are available upon reasonable request from the corresponding author.

STROBE statement: The authors have read the STROBE Statement-checklist of items, and the manuscript was prepared and revised according to the STROBE Statement-checklist of items.

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Specialty type: Pediatrics

Country/Territory of origin: Greece

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): C
Grade D (Fair): 0

A total of 56 infants (35 boys), aged 7.4 ± 2.8 mo, were included. Of them, 12.5% were exposed to tobacco smoke and 41.1% were breastfed less than 2 mo. There were no differences in baseline TBFV measurements between the breastfeeding groups; however, those who breastfed longer than 2 mo had a greater change in tPEF/tE after bronchodilation ($12\% \pm 10.4\%$ vs $0.9\% \pm 7.1\%$; $P < 0.001$). Moreover, there was a clear dose-response relationship between tPEF/tE reversibility and duration of breastfeeding ($P < 0.001$). In multivariate regression analysis, infants who breastfed less (regression coefficient -0.335 , $P = 0.010$) or were exposed to cigarette smoke (regression coefficient 0.353 , $P = 0.007$) showed a greater change in tPEF/tE after bronchodilation, independent of sex, prematurity, and family history of asthma or atopy.

CONCLUSION

Infants who recover from bronchiolitis and have a shorter duration of breastfeeding or are exposed to cigarette smoke, have TBFV measurements indicative of obstructive lung disease.

Key Words: Tidal breathing analysis; Lung function; Bronchiolitis; Breastfeeding; Cigarette smoke; Infants

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Core Tip: Assessment of lung function using tidal breathing could be beneficial for infants and preschoolers in whom forced respiratory maneuvers cannot be performed. We examined the correlation between breastfeeding and tidal breathing analysis in infants with bronchiolitis, and demonstrated that those who were exposed to cigarette smoke and/or had a shorter duration of breastfeeding showed tidal breathing alterations indicative of obstructive pulmonary disease.

Citation: Perikleous E, Fouzas S, Karageorgiou A, Steiropoulos P, Nena E, Chatzimichael A, Tsalkidis A, Paraskakis E. Association of breastfeeding with tidal breathing analysis in infants with bronchiolitis. *World J Clin Pediatr* 2021; 10(6): 168-176

URL: <https://www.wjgnet.com/2219-2808/full/v10/i6/168.htm>

DOI: <https://dx.doi.org/10.5409/wjcp.v10.i6.168>

INTRODUCTION

Bronchiolitis is a viral infection of lower airways that is characterized by substantial inflammation, increased mucus production, and necrosis of small airway epithelial cells[1]. It is the leading cause of infant morbidity and mortality worldwide[2], and represents a significant burden for the healthcare system, the family, and society[3]. Infants with co-existing conditions, such as prematurity and cardiopulmonary disorders, are at higher risk of developing more severe bronchiolitis[3]. Moreover, environmental factors such as smoking exposure, indoor and outdoor pollution[4], and lack of breastfeeding[5] may significantly increase susceptibility to the disease.

The favorable effects of breastfeeding are indisputable, and no other practice can drastically promote infant's health in the short- and long-term[6]. Comprehensively, there is some evidence of the consistent advantageous impact of breastfeeding on increasing forced vital capacity (FVC)[7]. Early life nutrition with breast milk as the initial food for newborns is considered 'the best' due to its beneficial effects on overall health, along with improved lung function. A previous study showed a link between breastfeeding and lung function in school-age children, namely, greater forced expiratory flow at 50% (FEF50), particularly in those who breastfed longer than 3 mo including children of mothers with asthma[8]. Regarding bronchiolitis, current evidence suggests that breastfed infants have a clear immunological advantage compared with their formula-fed peers[9]; exclusive breastfeeding has been shown to decrease the requirement for oxygen supplementation, the length of hospital stay, and the risk of respiratory failure in infants with more severe forms of the disease[9]. However, despite the clear clinical advantages, less is known about the effects of

Grade E (Poor): 0

Received: May 9, 2021**Peer-review started:** May 9, 2021**First decision:** June 17, 2021**Revised:** June 30, 2021**Accepted:** October 25, 2021**Article in press:** October 25, 2021**Published online:** November 9, 2021**P-Reviewer:** Rodrigues AT**S-Editor:** Gao CC**L-Editor:** A**P-Editor:** Gao CC

breastfeeding on the pulmonary function of infants with acute bronchiolitis.

There is some evidence indicating that tobacco smoke exposure in children decreases lung function and augments airway hyperresponsiveness, predisposing infants to a more severe clinical course of infection compared to unexposed peers[4]. Similarly, studies have shown that maternal smoking during pregnancy is related to bronchiolitis[4,10]. Overall, pregnancy and subsequent parenthood can become major motivators for mothers and caregivers to permanently quit this detrimental practice.

Although lung function testing at bedside is notoriously difficult in infancy[11], recent evidence suggests that tidal breathing flow-volume (TBFV) measurement and analysis are feasible[11,12]. In particular, the ratio of time to peak expiratory flow to total expiratory time (tPEF/tE) decreases in obstructive lung disorders[10], providing important information on the underlying pathophysiological mechanisms and extent of lung injury[11,12].

The aim of this study was to assess the effects of breastfeeding on the lung function of infants who recovered from acute bronchiolitis. We hypothesized that breastfeeding may have favorable effects on baseline tPEF/tE values and/or tPEF/tE reversibility after bronchodilation, independent of other confounding factors.

MATERIALS AND METHODS

Patients

This observational, cross-sectional study was performed between September 2016 and April 2018 in the Pediatric Department of the University General Hospital of Alexandroupolis (Alexandroupolis, Greece). All infants aged 2-12 mo and hospitalized with bronchiolitis were eligible to participate. Bronchiolitis was defined according to the relevant history and physical examination (fever, cough, tachypnoea, chest recession, wheeze or crackles during auscultation)[3]. Infants with genetic disorders, neuromuscular disorders, craniofacial abnormalities, congenital heart disease, a history of significant prematurity (born at < 32 wk gestational age), or requiring intubation and mechanical ventilation after birth were excluded. The study was approved by the local ethics committee, and parental informed consent was obtained prior to enrollment.

Procedures

On the day of hospital discharge, eligible infants underwent TBFV measurements in the pediatric lung function laboratory using the MasterScreen pediatric respiratory system (Jaeger/CareFusion, Hoechberg, Germany). All infants were tested according to relevant European Respiratory Society/American Thoracic Society guidelines[13-15] during natural sleep after feeding. A minimum of 30 s of natural breathing was recorded to acquire a set of at least 10 regular breaths. The ratio of tPEF/tE was automatically calculated by the system at baseline and 10 min after the administration of 300 mcg salbutamol inhaler *via* an appropriate holding chamber. The metadata of the study population were obtained from the medical records. The weight-for-length z-scores were estimated using Centers for Disease Control and Prevention/National Center for Health Statistics norms[16].

Statistical analyses

Continuous variables are expressed as the mean \pm SD standard deviation and compared with the Student's *t*-test or one-way analysis of variance (multiple comparisons). Multivariate regression analysis was used to determine the outcome of breastfeeding in terms of gender, history of prematurity, and family history of atopy. All analyses were performed using IBM SPSS version 25 (IBM Corp., Armonk, NY, United States).

RESULTS

A total of 56 infants (35 boys), aged 7.4 ± 2.8 mo, were included in this study. Their characteristics are presented in Table 1. Of them, 21.4% were born prematurely, 12.5% were exposed to tobacco smoke (during pregnancy and/or after birth), and 16.1% had a family history of asthma or atopy. No breastfeeding was reported in 7 infants (12.5%), whereas 23 infants (41.1%) were breastfed less than 2 mo (Table 1).

There were no differences in baseline TBFV measurements between infants who did not breastfeed or breastfed less than 2 mo (Group 1) and those who breastfed longer

Table 1 Characteristics of the study population

Characteristics	
<i>n</i>	56
Age (mo)	7.4 ± 2.8
Male sex, <i>n</i> (%)	35 (62.5)
Body weight, kg	7.3 ± 1.6
Body length, cm	65 ± 8.1
Weight-for-length z-score	-0.2 ± 2.0
Gestational age, wk	37.9 ± 1.5 (range 35-41)
Prematurity (< 37 wk)	12 (21.4)
Breastfeeding	
No	7 (12.5)
< 2 mo	16 (28.6)
2-6 mo	12 (21.4)
> 6 mo	21 (37.5)
Smoking exposure	
In pregnancy	5 (8.9)
After birth	7 (12.5)
In pregnancy and/or after birth	7 (12.5)
Family history of asthma/atopy	9 (16.1)

Values are mean ± SD or number of cases (%).

than 2 mo (Group 2) (Table 2). Conversely, infants in Group 1 had a significantly higher change in tPEF/tE after bronchodilation compared with those in Group 2 ($12\% \pm 10.4\%$ vs $0.9\% \pm 7.1\%$; $P < 0.001$) (Figure 1A). The tPEF/tE reversibility was also higher in infants exposed to tobacco smoke during pregnancy and/or after birth (Figure 1B). There was a clear dose-response relationship between the reversibility of tPEF/tE and the duration of breastfeeding ($P < 0.001$) (Figure 2).

Multivariate regression analysis showed that infants who breastfed less (beta -0.335, $P = 0.010$) or were exposed to cigarette smoke (beta 0.353, $P = 0.007$) had a greater change in tPEF/tE after bronchodilation, independent of sex, prematurity, and family history of asthma or atopy (Table 3).

DISCUSSION

In this study, we demonstrated that infants who recovered from acute bronchiolitis and had a shorter duration of breastfeeding or were exposed to cigarette smoke, had TBV measurements indicative of obstructive lung disease. Specifically, these infants had a greater percent change in tPEF/TE after bronchodilation, and this effect was independent of other confounding factors such as premature birth and family history of asthma or atopy. Interestingly, there was a clear dose-response relationship between tPEF/tE reversibility and the duration of breastfeeding. Moreover, infants who were exposed to cigarette smoke showed a greater change in tPEF/tE after bronchodilation, independent of sex, prematurity, and family history of asthma or atopy.

Early life exposures may affect the outgrowth of pulmonary system, resulting in an immediate impact on later lung function. Previous studies have highlighted the key role of breastfeeding in terms of larger lung volumes at school age[8,17], suggesting the influence of breastfeeding on respiratory health. In addition, studies have shown that extended and exclusive breastfeeding reduces the risk of wheezing and asthma during infancy, early childhood[17-20], and even in youth[21], functioning as a shield against allergic predisposition. In a recent study of 555 children, forced expiratory volume in 1 s and FVC markedly increased in accordance with breastfeeding duration

Table 2 Baseline tidal breathing flow-volume values according to breastfeeding duration

	BF < 2 mo (n = 23)	BF ≥ 2 mo (n = 33)	P value
Tidal volume, mL/kg	8.6 ± 1.8	8.3 ± 2.1	0.580
Respiratory rate, bpm	46.8 ± 20	44.7 ± 18.4	0.687
Expiratory time, s	0.57 ± 0.21	0.55 ± 0.22	0.735
tPEF/tE, %	35.4 ± 15.5	41.3 ± 13.7	0.139

Values are mean ± SD. BF: Breastfeeding; TBFV: Tidal breathing flow-volume; tPEF/tE: Time to peak expiratory flow to total expiratory time.

Table 3 Factors affecting the % time to peak expiratory flow to total expiratory time change after bronchodilation

	Regression coefficient β	P value
Breastfeeding duration	-0.335	0.010
Cigarette smoke exposure	0.353	0.007
Male sex	0.005	0.974
Prematurity	0.031	0.833
Family History of asthma/atopy	0.121	0.379

Multivariable linear regression analysis; the effects of the independent variables were adjusted for each other. tPEF/tE: Time to peak expiratory flow to total expiratory time.

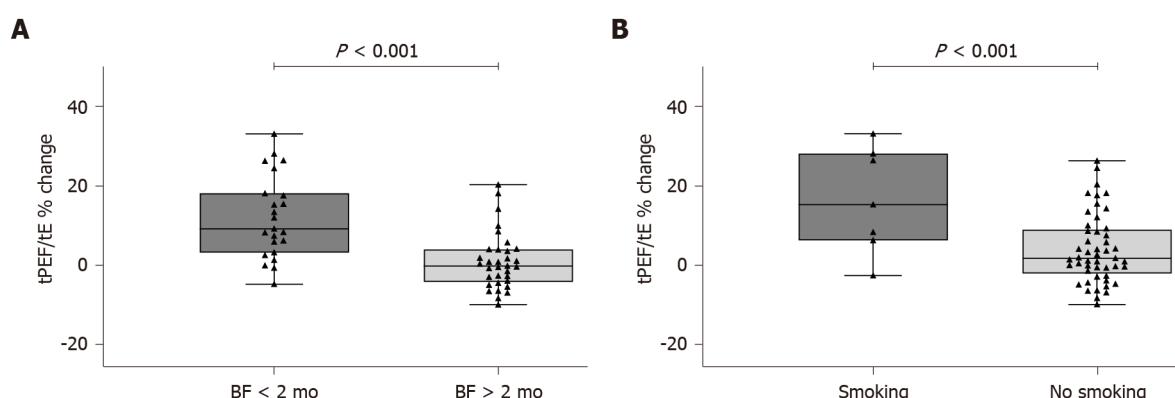


Figure 1 Percent change in time to peak expiratory flow to total expiratory time after bronchodilation in relation to breastfeeding and smoking exposure. A: Breastfeeding; B: Smoking exposure. BF: Breastfeeding; tPEF/tE: Time to peak expiratory flow to total expiratory time.

in those with asthma group[20]. However, in a novel birth cohort of 377 healthy term infants, a link between breastfeeding duration and obstructive or restrictive lung function was not shown[22]. Similarly, in a birth cohort of 620 infants, lung function was assessed at 12 and 18 years of age; duration of breastfeeding did not greatly influence lung function in children with a positive family history for allergic diseases [23]. Thus, whether breastfeeding protects against allergic disease in childhood remains a subject of debate, although exclusive breastfeeding for a duration of 6 mo is the keystone for the promotion of allergy health.

The evaluation of pulmonary function by TBFV analysis has certain benefits in infants in whom forced respiratory flows cannot be performed. Several studies have examined the application of TBFV measurements in a variety of lung disorders and have shown that a reduction in tPEF/tE ratio is suggestive of airway obstruction[11,12,15,24-26]. Zedan *et al*[25] reported that wheezing infants with a positive family history of asthma or who had never been breastfed, displayed significantly lower tPEF/tE compared with healthy controls. Similarly, children and infants with wheezing disorders have a reduced tPEF/tE ratio compared with control subgroups[27,28]. Moreover, studies of infants with chronic lung disease showed impaired lung

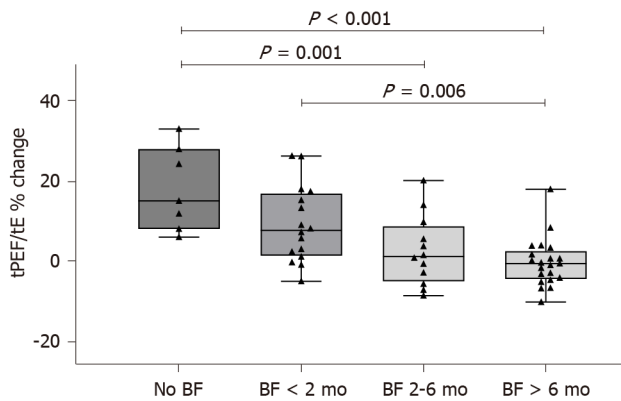


Figure 2 Percent change in time to peak expiratory flow to total expiratory time after bronchodilation in relation to the duration of breastfeeding. BF: Breastfeeding; tPEF/tE: Time to peak expiratory flow to total expiratory time.

compliance and reduced resistance during the first 12 mo of life[29].

Qi *et al*[30] found that wheezing infants had reduced lung function compared with those who were not wheezing, and that tPEF/tE was negatively associated with later poor respiratory outcomes; the deficit in tPEF/tE ratio remained after clinical improvement. However, a study in school-age children with asthma[24] showed no difference in tidal breathing parameters compared with control groups.

In accordance with our main findings, in a preliminary Norwegian study of infants with acute bronchiolitis, the tPEF/tE was reduced but improved after the administration of inhaled adrenaline[31]. By contrast, in another study in infants with bronchiolitis, the researchers did not find any significant differences in tPEF/tE after the administration of nebulized albuterol[32]. In a recent cross-sectional study, tPEF/tE was inversely related to the length of hospital stay and disease severity in infants with bronchiolitis[33], and was also significantly reduced in children exposed to parental smoking[33]. In another study of preschool wheezers, family history of asthma, breastfeeding duration less than 3 mo, and passive smoking, were all significant risk factors for bronchial hyperresponsiveness, defined as tPEF/tE increase > 20% following salbutamol administration[34].

Our study had a number of limitations. First, it was a single-center study with a small sample size; thus the findings cannot be generalized to all populations. Second, a control group was not included in the study design; consequently we could not compare our results with a subgroup of healthy peers. Third, the study design did not include some relevant confounding factors that could affect lung function, such as air pollution.

CONCLUSION

Infants who recovered from acute bronchiolitis and had a shorter duration of breastfeeding or were exposed to cigarette smoke, had TBFV measurements indicative of obstructive lung disease. Tidal breathing is undeniably a complex process, but its measurement during infancy appears promising. To understand the mechanisms by which acute bronchiolitis may affect lung function in infancy and beyond, additional large-scale research is required.

ARTICLE HIGHLIGHTS

Research background

Bronchiolitis is a common viral infection of lower airways and a major cause of morbidity and mortality globally, especially among infants with concomitant medical conditions. The positive effects of breastfeeding are uncontested in infant's health in the short- and long-term.

Research motivation

There are sufficient data suggesting the advantageous effects of breastfeeding on pulmonary function, but less information regarding the influence of breastfeeding on lung function in infants with acute bronchiolitis.

Research objectives

To assess the effects of breastfeeding on tidal breathing flow-volume (TBFV) measurements of infants who recovered from acute bronchiolitis.

Research methods

TBFV analysis was conducted in 56 infants with bronchiolitis prior to hospital discharge. The ratio of time to peak expiratory flow to total expiratory time (tPEF/tE) at baseline and after the administration of 400 mcg salbutamol was assessed using a MasterScreen pediatric respiratory system (Jaeger/CareFusion, Hoechberg, Germany). All infants were tested according to European Respiratory Society/American Thoracic Society guidelines in the middle of natural sleep following feeding. Multivariate regression analysis was used to investigate the outcome of breastfeeding in terms of gender, history of prematurity, and family history of atopy. All analyses were conducted in IBM SPSS version 25.

Research results

There were no differences in baseline TBFV measurements between breastfeeding groups; however, children who breastfed less than 2 mo had a greater tPEF/tE change after bronchodilation ($12\% \pm 10.4\%$ vs $0.9\% \pm 7.1\%$; $P < 0.001$). Additionally, a distinct dose-response relationship between tPEF/tE reversibility and duration of breastfeeding was shown ($P < 0.001$). In multivariable regression analysis, infants who breastfed less (beta -0.335, $P = 0.010$) or were exposed to cigarette smoke (beta 0.353, $P = 0.007$) exhibited a higher tPEF/tE change after bronchodilation, irrelevant of sex, prematurity, and family history of asthma or atopy.

Research conclusions

Infants who recovered from acute bronchiolitis and had a shorter duration of breastfeeding or were exposed to cigarette smoke, had TBFV analyses indicative of obstructive lung disease, independently of other confounding factors. Tidal breathing is undoubtedly a complicated procedure, but its measurement during infancy is promising.

Research perspectives

Additional large-scale studies are required to determine the mechanisms by which acute bronchiolitis may affect lung function in early infancy as well as later in life.

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