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# Prevalence of Gastroesophageal Reflux of Wheezers in Infancy and Early Childhood

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## Abstract

**Background:** Gastroesophageal reflux (GER) has largely been recognized as a physiological phenomenon in infancy and early childhood and the relationship of severe, recurrent wheezing to gastroesophageal reflux disease (GERD) has been well described. However it has remained unclear how many mildly wheezy infants are complicated by GER.

**Objective:** This study investigated the prevalence of GERD among wheezers in infancy and early childhood in Japan. Subjects and Method: We evaluated esophageal pH monitoring in wheezy children under 2 years old.

Results: A positive pH index was found in 9.4% of all subjects.

**Conclusion:** Although the prevalence of GERD among severe wheezers was higher in previous reports, our study concluded that the prevalence of GERD among wheezers was lower in younger children.

Keywords: Gastroesophageal reflux; Infant; pH index; Wheezer

## Introduction

**Research Article** 

In some severe recurrent wheezers who do not respond to asthma medication including inhaled corticosteroids, wheezing is caused by gastroesophageal reflux (GER) [1-2]. However, physiological GER is largely recognized in younger children [3] and gastroesophageal reflux disease (GERD) manifests various symptoms other than wheezing [4]. It remains unclear how GER is associated with wheezing. Additionally, it has not yet been determined whether recurrent wheezers in infancy later develop asthma. Therefore, we evaluated the prevalence of GER among infantile wheezers by 24-hour esophageal pH monitoring (EpHM).

## Object

This study investigated the prevalence of GERD among general wheezers in infancy and early childhood in Japan.

#### Subjects and Methods

The subjects were included in this study prospectively. 32 patients were admitted to Yokohama City Minato Red Cross Hospital because of wheezy exacerbation. The mean months of age in this patient group was  $12.7\pm5.2$  (range: 3 to 24). Past patient and family medical histories, laboratory data including serum IgE, peripheral eosinophils counts, specific-IgE (ImmunoCAP, Phadia AB, Sweden) including air-borne antigens: mites, house dust and Japanese cedar, and food-antigens: egg-white, cow's milk and wheat, and rapid Respiratory Syncytial virus antigen test of nasal swab were analyzed (Check RSV, SA Scientific Inc., USA). 11 of 32 patients (34.4%) were positive sensitization to food antigens. 8 patients (25.0%) had treated as diagnosed asthma taking controller medication at admission, all had taken leukotriene receptor antagonist (4mg/day) and 3 patients had budesonide inhalation suspension (0.5mg/day) together.

All patients were treated with systemic administration of corticosteroids (soluble prednisolone 0.5mg/kg×4/day) and inhaled

beta stimulant (salbutamol 0.1ml q 4-8hrs) for 4 or 5 days after admission. Twenty-four-hour esophageal pH monitoring (EpHM) was performed on the 6th or 7th hospitalized day after completion of acute treatment when the respiratory state had stabilized and wheeze, tachypnea and desaturation had disappeared (PH 101 ZS, Chemical Instruments CO., LTD., Japan). The ratio of the duration of pH less than 4.0 within the 24-hour monitoring period was expressed as the pH index. A positive pH index was defined as a ratio of 4% or higher [6]. In addition to pH index, we also calculated the numbers of reflux episodes while awake as defined by a number of episodes showing pH < 4.0, based on the previous report by Yoshida et al. [7].

#### Results

Among these 32 patients, 3 patients (9.4%) were found to have GER based on EpHM. The mean pH index based on the ratio of time under pH 4.0 was 1.36 (SD; 1.82) %. The mean numbers of reflux episodes while awake was 2.9 (SD; 3.4) /hr.

## Discussion

Although it has been demonstrated that GER causes severe recurrent wheeze in infancy and early childhood, there are limited data on the prevalence of GER among wheezers in younger children,

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N	32	
age (m/o)	12.7 (5.2)	
sex, male	23 (71.9%)	
birth at gestational age (week)	37.0 (3.04)	
weight of birth (g)	2781.5 (589.9)	
first episode of wheeze (m/o)	6.5 (3.8)	
serum IgE (IU/mI)	192.0 (515.9)	
peripheral eosinophils count (µL)	500.2 (440.9)	
positive sensitization to aeroantigens	11 (34.4%)	
positive sensitization to food antigens	17 (53.1%)	
complete breast-fed	13 (40.6%)	
daycare attendance	18 (56.3%)	
having siblings	16 (50.0%)	
having pets	8 (25.0%)	
exposure of smoker	15 (46.9%)	
atopic dermatitis	6 (18.8%)	
food allergy	8 (25.0%)	
parental bronchial asthma	9 (28.1%)	
febrile state of admission	20 (62.5%)	
RSV infection at admission	6 (18.8%)	
previous asthma controller medication	8 (25.0%)	
leukotriene receptor antagonist (4mg/day)	8 (25.0%)	
budesonide inhalation suspension (0.5mg/day)	3 (9.4%)	

Data are expressed as number (ratio) or mean (SD).

Table 1: Clinical characteristics of subjects.

pH index >= 4%	3/32 (9.4%)
pH index (%)	1.36 (1.82)
numbers of reflux episodes at awake (/hr)	2.9 (3.4)

† EpHM; esophageal pH monitoring

Data are expressed as number (ratio) or mean (SD).

Table 2: Results of EpHM †

Author (year), location	Age, y	Study design	Sample size N	Prevalence of Reflux n/N (%)
Gorenstein et al (2003), Israel [8]	Mean (SD): 1.4 (2.8)	Retrospective	153	64/153 (41.8)
Teixeira et al (2007), Brazil [9]	Mean: 2.6	Prospective	69	47/69 (68.1)
Present study Japan	Mean (SD): 1.1 (0.4)	Prospective	32	3/32 (9.4)

 Table 3: Pediatric studies that examined GERD in indivisuals with asthma in early childhood.

especially infants. Our data demonstrated that the prevalence of GER among wheezers in younger children was only 3 of 32 patients (9.4%).

In a study of 47 severe, recurrent wheezers ranging from 5 to 58 months old, Saglani and colleagues reported that GER was the predominant cause [2]. In that study, the frequency of GER was 23% among their subjects, that of asthma was 41% and 11 of 19 patients with definite asthma also had GER, as defined by abnormal pH. In a study limited to younger children, Gorenstein and colleagues reported that the prevalence of GERD was 41.8% among 153 asthmatic children aged 1.4 (SD; 2.8) years old [8]. Teixeira and colleagues indicated that

This article was originally published in a special issue, Lung Disorders/ Injury handled by Editor(s). Dr. Yutong Zhao, University of Pittsburgh, USA the prevalence of GERD was 68.1% in 69 patients with a mean age of 2.6 years old [9].

There is a difference in the prevalence of GERD among asthmatic children between the present study and previous reports. Demographic differences may be reflected in the results of our study. Brand and colleagues proposed phenotypes of wheezing disorders in pre-school children as episodic wheeze and multiple-triggered wheeze based on temporal pattern [10]. Although the previous study included more severe multiple-triggered wheezers, our study included not only multiple-triggered wheezers but also episodic wheezers.

Although the prevalence of GERD among severe wheezers was higher in previous reports, our study concluded that the prevalence of GERD among general wheezers is lower in younger children.

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