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Update on protracted bacterial bronchitis in children



Xiao-bo Zhang, Xiao Wu and Guang-min Nong*

Abstract

Background: Chronic cough is a common symptom in children and protracted bacterial bronchitis (PBB) is one of the causes of chronic cough. However, the understanding of this disease remains limited. The present study aims to update PBB in children.

Methods: The clinical data of children with PBB from 2014 to 2018 were retrospectively analyzed, and PBB clinical features of published studies were summarized. Electronic databases were searched in May 2019. Clinical studies were included in the present study. Reviews were undertaken in duplicate.

Results: Totally 712 cases were analyzed in this study, including 52 cases in our center and 660 cases from 14 studies. In the 52 cases, 88.5% of patients with PBB were less than 6 years old and all of them complained of wet cough. Three cases were confirmed with laryngomalacia, and microbiologically-based-PBB were identified in 13 cases (9 *Streptococcus pneumoniae*, 3 *Staphylococcus aureus*, and 1 *Pseudomonas aeruginosa*). Twenty cases were completely remitted after treatment. In the 14 studies, the patients with PBB were typically younger than 3 years old, accompanying wheezing and airway malacia. Co-infection was common in most western cases, *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis* were the top three pathogens. Symptoms were improved in most patients, whereas some cases with comorbidities required prolonged antibiotics treatment.

Conclusions: PBB is common in male infants with chronic wet cough and accompanied by wheezing and airway deformities. Most cases are clinically diagnosed PBB in China and microbiologically-based-PBB is common in western countries. Co-infection could be found, *Streptococcus pneumoniae* and *Haemophilus influenzae* were the most frequent etiology in China and western countries, respectively. Patients with comorbidities may need extended antibiotics treatment for more than 2 weeks.

Keywords: Protracted bacterial bronchitis, Pathogen, Treatment, Children

Introduction

Protracted bacterial bronchitis (PBB) is an old diagnosis and is considered to be the main cause of chronic wet cough in children [1, 2]. The continual cough of PBB may affect exercise tolerance, disturb sleep, and cause significant levels of morbidity, however, the understanding of the disease remains limited [3, 4]. The lack of awareness

in diagnosis and the confusion in antibiotics course for treatment still exist. In order to update on the management of PBB, this study retrospectively analyzed the clinical data of PBB diagnosed in our center, as well as summarized the PBB clinical features of published studies.

Methods

Patients

Patients diagnosed with PBB and underwent follow-up (aged <14 years) at the First Affiliated Hospital of Guangxi

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Medical University between January 2014 and December 2018 were enrolled in this study.

Inclusion and exclusion criteria

Diagnostic criteria for PPB [5]: (1) clinically-based-PBB: chronic wet cough >4 weeks; without pointers caused by specific disease; cough improved after 2 weeks of treatment with antibiotics. (2) microbiologically-based-PBB: chronic wet cough >4 weeks with evidence of lower respiratory tract infection, positive bacterial culture ($\geq 10^4$ cfu/ml) in sputum or bronchoalveolar lavage fluid (BALF); cough significantly improved after 2 weeks of antibiotic treatment. (3) Exclusion criteria: patients with mycoplasma infection, infiltrate on chest X-ray or CT, immunodeficiency, congenital heart disease, and other basic diseases.

Clinical data collection

Demographic characteristics (gender, age of onset, premature birth or not), clinical manifestations (phase and duration of wet or dry cough, wheezing or not, accompanying symptoms, etc.), physical examination findings, auxiliary examination (blood routine examination, CRP, immune function, bronchoscopy, cell classification of alveolar lavage fluid, etiology, chest X-ray or computed tomography), treatment history, and follow-up information were collected for all enrolled patients. Follow-up information included response to antibiotics, duration of cough, complications, and prognosis which were collected by telephone interview or outpatient consulting every 2 weeks, for a total of 4 weeks.

Information sources of review

We completed a systematic search of databases (CNKI, Wan Fang, Medline, Embase, and Pubmed) in May 2019. Clinical studies with detail data (including diagnostic criteria, demographic characteristics, clinical features, auxiliary examination, treatment, and follow-up information) were included in the present study. Reviews were undertaken in duplicate. We summarized the main observation indexes, including gender, age, course of the disease, pathogenic bacteria, complications, therapeutic drugs, course of antibiotics, and treatment effect.

Statistical analysis

Descriptive analysis was used for this study. Categorical data were expressed as numbers (percentages).

Results

Demographic data of patients with PBB

A total of 52 children of PBB were enrolled in our center, 33 males and 19 females. Fifteen patients were <1 year, 16 patients were between 1 and 3 years of age, 15 patients were 3–6 years old, 6 patients were 6–14 years

Table 1 Clinical characteristics of PBB in the 52 Chinese patients

Characteristics	PBB
Gender, M(F)	33 (19)
Age	
<1y	15 (28.8%)
1-3y	16 (30.8%)
3-6y	15 (28.8%)
6-14y	6 (11.5%)
Course	
>4 week	19 (36.5%)
4-12 week	14 (26.9%)
>12 week	19 (36.5%)
Symptoms	
Wet cough	52 (100%)
Purulent sputum	13 (25%)
Cough both day and night	22 (42.3%)
Wheezing	15 (28.8%)
Fever	11 (21.2%)
Nasal symptoms	19 (36.5%)
Physical examination	
Lung moist rales	30 (57.7%)
Lung wheezing rales	3 (5.8%)
Microbiological findings	13 (25%)
Positive bacterial cultures of Sputum	11 (21.2%)
Spn	8 (15.4%)
Sa	2 (3.8%)
Pae	1 (1.9%)
Positive bacterial cultures of BALF	2 (3.8%)
Spn	1 (1.9%)
Sa	1 (1.9%)
Comorbidities	
Rhinitis	7 (13.5%)
Sinusitis	5 (9.6%)
Laryngomalacia	3 (5.8%)
Airway stenosis	1 (1.9%)
Treatment	
Antibiotic	
Amo	6 (11.5%)
Cep (oral)	15 (28.8%)
Cep (intravenous)	26 (50%)
Azi	5 (9.6%)
Duration	3d-2w
Effects	
Remission	20 (38.5%)
Improve	24 (46.2%)
No improvement	8 (15.3%)
Complication	0

Values are expressed as n (%). M: male; F: female. Spn: *Streptococcus pneumoniae*; Sa: *Staphylococcus aureus*; Pae: *Pseudomonas aeruginosa*. Amo: Amoxicillin-clavulanate; Cep: cephalosporin antibiotics; Azi: Azithromycin.

old. Most of the patients were younger than 6 years old (88.5%) (Table 1).

Clinical characteristics of patients with PBB

Nineteen patients had a duration of cough more than 4 weeks, 14 patients had 4–12 weeks, and more than 12 weeks in 19 patients. The longest duration was 28 weeks. All of the children presented wet cough, including 13 patients with purulent sputum, and 22 patients were coughing both day and night. Fifteen cases accompanied by wheezing, 11 patients accompanied by mild to moderate

fever, and 19 patients had nasal symptoms, including nasal congestion, runny nose, and sneezing. Seven patients accompanied by rhinitis and 5 patients had sinusitis. Physical examination revealed that 30 patients had crackles, 3 patients accompanied by crackles and wheezes (Table 1).

Laboratory characteristics of patients with PBB

Blood routine examination revealed that 14 cases had increased leucocyte and 9 cases with increased neutrophils. All cases had normal CRP, T cell subset, immune globulin, and NK cell. No patient showed a positive result

Table 2 Clinical characteristics of PBB in China

Author	Li [6]	Li [7]	Chen [8]	Shi [9]	Gao [10]	Chi [11]	Shun [12]
Year	2018	2017	2016	2016	2016	2015	2014
Number	50	30	31	31	20	28	28
M(F)	36 (14)	18 (12)	18 (13)	17 (14)	–	26 (2)	17 (11)
Age	3.2y (5 m-14y)	14.5 m (7-49 m)	–	<3y	2 m-14y	8.5 m	6-75 m
Course	2 m	9.7w (5.7–7.1w)	2 m	4-11w	>4w	4.2w	>4w
Antibiotic used	–	20	11	–	–	–	21
Bronchoscopy	50	30	31	31	0	28	8
Bacteria							
Spn	14 (28%)	12 (40%)	6 (19.4%)	16 (51.6%)	2 (10%)	5 (17.9%)	8 (28.6%)
Hi	5 (10%)	10 (33.3%)	7 (22.6%)	3 (9.7%)	3 (15%)	3 (10.7%)	10 (35.7%)
Mcat	4 (8%)	7 (23.3%)	3 (9.7%)	–	–	–	6 (21.4%)
Sa	4 (8%)	–	2 (6.5%)	–	–	–	–
Kpn	–	–	–	2 (6.5%)	–	–	–
Eco	–	–	–	1 (3.2%)	–	1 (3.6%)	–
Pae	–	–	–	3 (9.7%)	–	–	–
Eae	–	–	–	–	–	1 (3.6%)	–
Comorbidities							
Wheeze	30 (60%)	22 (73.3%)	17 (54.8%)	25 (80.6%)	20 (100%)	21 (75%)	–
Rhinitis	–	–	1 (3.2%)	–	–	–	–
Sinusitis	14 (28%)	16 (53.3%)	9 (29%)	–	–	–	–
Airway stenosis	6 (12%)	5 (6%)	5 (16.1%)	2 (6.4%)	–	–	–
Tracheobronchial malacia	5 (10%)	5 (6%)	4 (12.9%)	3 (9.6%)	–	11 (39.2%)	4 (14.2%)
Treatment							
Antibiotic	Amo /Cep /Azi	–	Amo	Amo /Cep /Azi/Car/Tei/Lin	Amo	Amo /Cep	Amo /Cep /Azi
Duration	2-4w	–	>2w	4-6w	2w	17.3 + 3.2d	2w
Follow up	1y	1y	2 m-2y	0.5y	–	2w	–
Effects							
Remission	33	–	23	–	–	–	28
Improve	15	20	8	31	20	28	–
Relapse	–	2	–	–	–	–	–
Complication	–	1*	–	–	–	–	–

Values are expressed as n (%). M: male; F: female. Spn: *Streptococcus pneumoniae*; Hi: *Haemophilus influenzae*; Mcat: *Moraxella catarrhalis*; Sa: *Staphylococcus aureus*; Kpn: *Klebsiella pneumoniae*; Eco: *Escherichia coli*; Pae: *Pseudomonas aeruginosa*; Eae: *Enterobacter aerogenes*. Amo: Amoxicillin-clavulanate; Cep: cephalosporin antibiotics; Azi: Azithromycin; Car: Carbapenems; Tei: Teicoplanin; Lin: linezolid. * bronchiectasia.

Table 3 Clinical characteristics of PBB in the western countries

Author	Pritchard MG [13]	Wurzel DF [14]	Narang R [15]	Chang AB [16]	Kompare M [17]	Donnelly D [18]	Marchant JM [1]
Year	2015	2014	2014	2012	2012	2007	2006
Research	R	P	R	P	R	R	P
Number	44	104	50	50	70	81	43
M(F)	–	72 (32)	–	36 (14)	50 (20)	40 (41)	–
Age	2.7y (1.5–4.0)	19 m (12–30 m)	2.9y (1.7–4.4)	4.5y	3 m	3.9y (5 m–14y)	2.6y
Course	11 m (9–14.7 m)	28w (6–57w)	11 m (8–14 m)	>4w	1–60 m 5 m	>1 m	>3w
Antibiotic used	–	–	–	–	–	9	–
Bronchoscopy	44	104	50	50	70	19	43
Pathogen							
Hi	27 (61.3%)	75 (72.1%)	25 (50%)	5 (10%)	39 (55%)	65 (80%)	20 (46.5%)
Mcat	22 (50%)	45 (43.3%)	14 (28%)	4 (8%)	41 (58.6%)	–	11 (25.5%)
Spn	10 (22.7%)	41 (39.4%)	8 (16%)	19 (38%)	26 (37.1)	30 (37%)	15 (34.9%)
Sa	8 (18.1%)	–	11 (22%)	4 (8%)	–	–	–
Adv	–	22 (21.1%)	–	–	–	–	2 (4.6%)
RSV	–	5 (4.8%)	–	–	–	–	–
PIV	–	–	–	–	–	–	1 (2.3%)
Comorbidities							
Wheeze	–	63 (60.5%)	–	30 (60%)	–	39 (48.1%)	–
Sinusitis	–	–	–	14 (28%)	–	–	–
Airway stenosis	–	–	–	6 (12%)	–	–	–
Tracheobronchial malacia	–	71 (68.2%)	–	5 (10%)	52 (74.2%)	–	–
Treatment							
Antibiotics	Amo /Cla	Amo	Amo /Cla	Amo /Cep /Azi	Amo	Amo	Amo
Duration	6–8w	2w	6w	2–4w	2–4w	4–6w	2w
Follow-up	1–4y	–	–	1y	–	–	1y
Effects							
Remission	–	–	–	–	–	52	–
Improve	33	104	–	50	61	–	43
Relapse	25	–	–	–	43	–	–
Complication	–	–	–	–	–	–	–

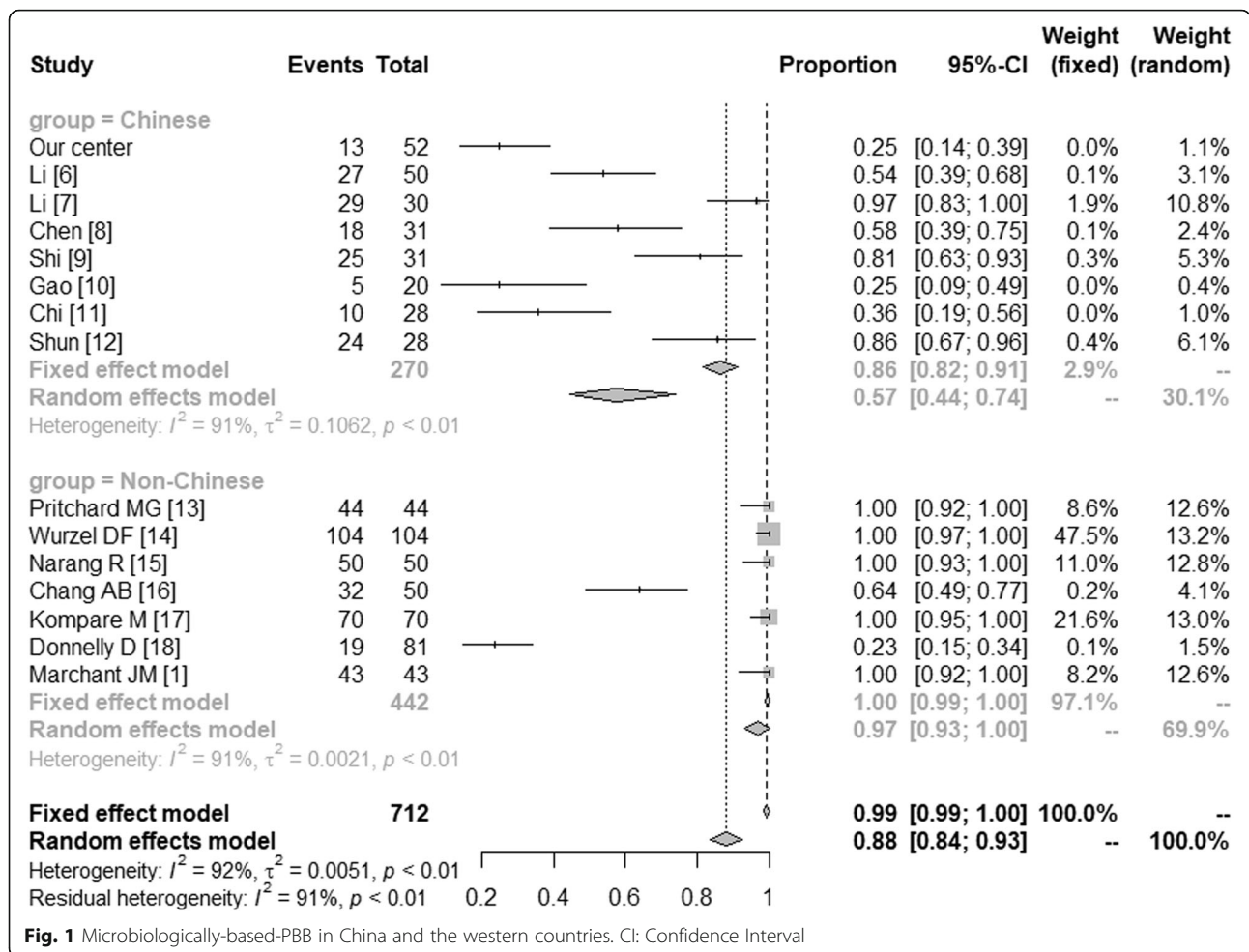
Values are expressed as n (%). R: retrospective research, P: prospective research. M: male; F: female. Hi: *Haemophilus influenzae*; Mcat, *Moraxella catarrhalis*; Spn: *Streptococcus pneumoniae*; Sa: *Staphylococcus aureus*; Adv:adenovirus; RSV:respiratory syncytial virus; PIV:parainfluenza virus. Amo:Amoxicillin-clavulanate; Cla: Clarithromycin; Cep: cephalosporin antibiotics; Azi: Azithromycin.

when blood samples were collected for respiratory virus detection (respiratory syncytial virus, adenovirus, and parainfluenza virus type 1, 2, 3). A total of 14 patients underwent bronchoscopy, and all cases revealed mucosal congestion; 12 cases had thin secretions, 2 cases having purulent secretions. Laryngomalacia was identified in 3 cases, 1 case with tracheal stenosis. Positive bacterial cultures were confirmed in 25% of cases (13/52 cases). *Streptococcus pneumoniae* (Spn) was found in nine cases, *Staphylococcus aureus* (Sa) in three cases, and *Pseudomonas aeruginosa* (Pae) in one case. Among them, one

case of Sa and one case of Spn were found in BALF. Forty-five children received a chest X-ray examination, 27 cases showed increased lung markings. The chest CT of five cases was normal (Table 1).

Treatment and follow-up

All patients received antibiotics treatment for 3–7 days before our treatment, however, symptoms received no improvement or repeated after the withdrawal. In all enrolled patients, 6 patients were treated with oral amoxicillin-clavulanate (Amo) and 15 patients received oral



cephalosporin antibiotics. Moreover, 26 patients received intravenous cephalosporin, and 5 children were administered with Azithromycin (Azi) because they were allergic to penicillin and cephalosporins. All enrolled patients underwent outpatient follow-up every 2 weeks for a total of 4 weeks. Cough in the 24 hospitalized children was improved significantly when discharged from hospital after treatment for 3 to 7 days. Among the 28 outpatients, 20 cases received a resolution of cough after 2 weeks of treatment, while 8 cases still had a cough, including 5 cases with irregular medication and 3 cases accompanied by rhinitis (Table 1).

Article review

Fourteen studies were identified (7 studies in China and 7 studies in the western countries, $N = 660$). We further analyzed the data to confirm whether the clinical feature is similar or not in the east and the west. All of the studies in China were retrospective designs, which showed a high proportion of male and most of them were younger than 3 years old. Fifty two patients performed antibiotic treatment before sputum culture and 178 cases (178/218, 81.7%) underwent

airway bronchoscopy. The proportion of positive pathogen culture was 63.3% (138/218 cases), other cases were diagnosed as clinically-based-PBB. The detected bacteria were Spn (63/138 cases, 45.7%), *Haemophilus influenzae* (Hi) (41/138 cases, 29.7%), *Moraxella catarrhalis* (Mcat) (20/138 cases, 14.5%), Sa (6/138 cases, 4.4%), Pae (3/138 cases, 2.2%), *Klebsiella pneumoniae* (2 cases, 1.4%), *Escherichia coli* (2 cases, 1.4%) and *Enterobacter aerogenes* (1 case, 0.7%). Furthermore, PBB was often accompanied by wheezing and was partially associated with sinusitis, airway stenosis, and tracheobronchomalacia. Most cases improved and some relapsed after treatment with Amo (Table 2).

Children with PBB in the western countries were also common in male, most patients were younger than 6 years old. Nine patients performed antibiotic treatment before culture and 380 cases (380/442, 86%) underwent airway bronchoscopy. Co-infection could be found in the 442 cases of PBB, some patients were caused by multiple pathogenic species and some cases were co-infected by bacteria and viruses. The main pathogens were: Hi (191/471 cases, 40.5%), Mcat (137/471 cases, 29.1%), Spn (119/471 cases, 25.3%), and Sa (24/471 cases, 5.1%). Most patients accompanied by wheezing and

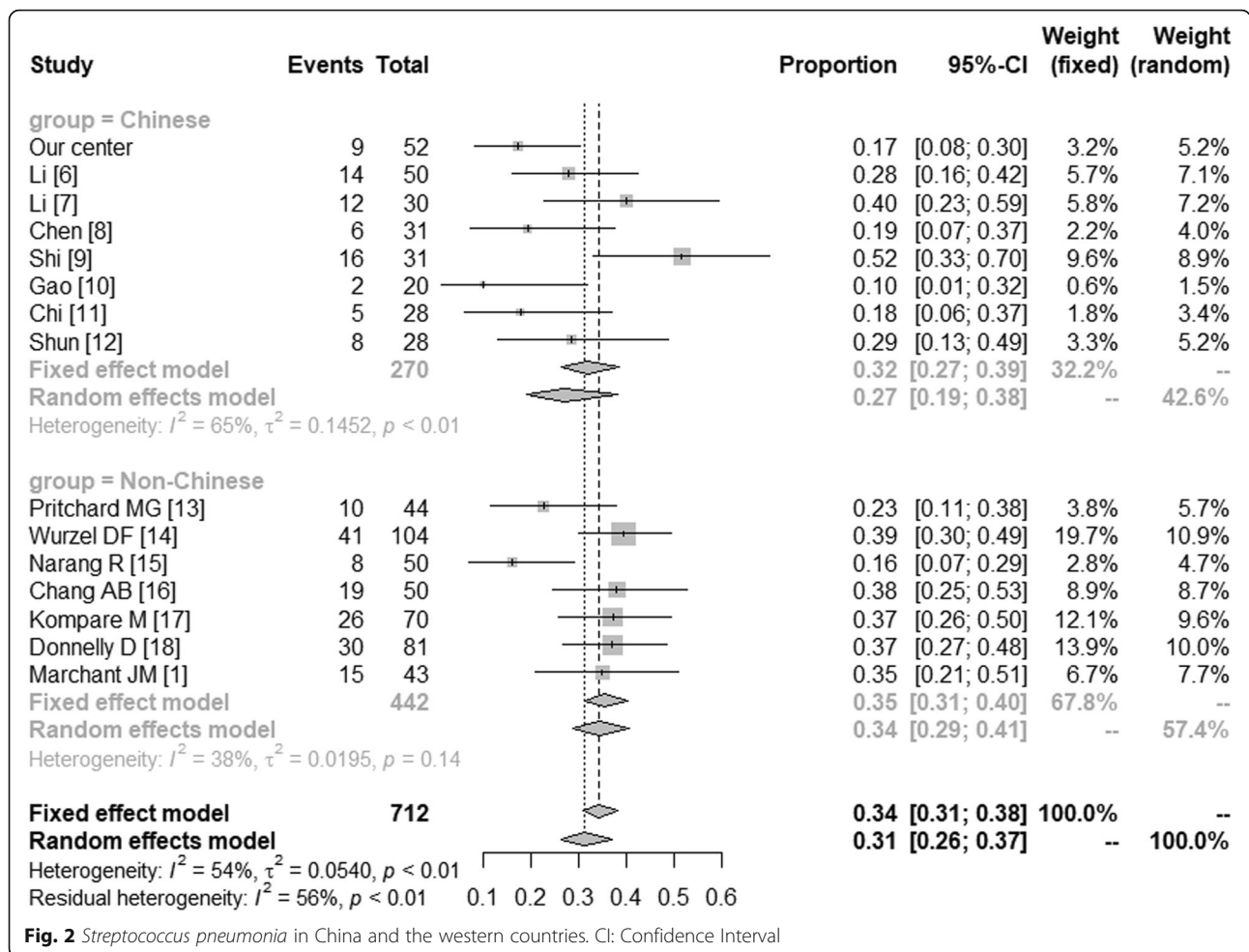


Fig. 2 Streptococcus pneumoniae in China and the western countries. CI: Confidence Interval

tracheobronchomalacia. Antibiotic treatment for 2 weeks revealed improvement in most cases, however, 68 relapsed cases (most of the patients with tracheobronchial malacia) needed to extend the course of antibiotic treatment (Table 3).

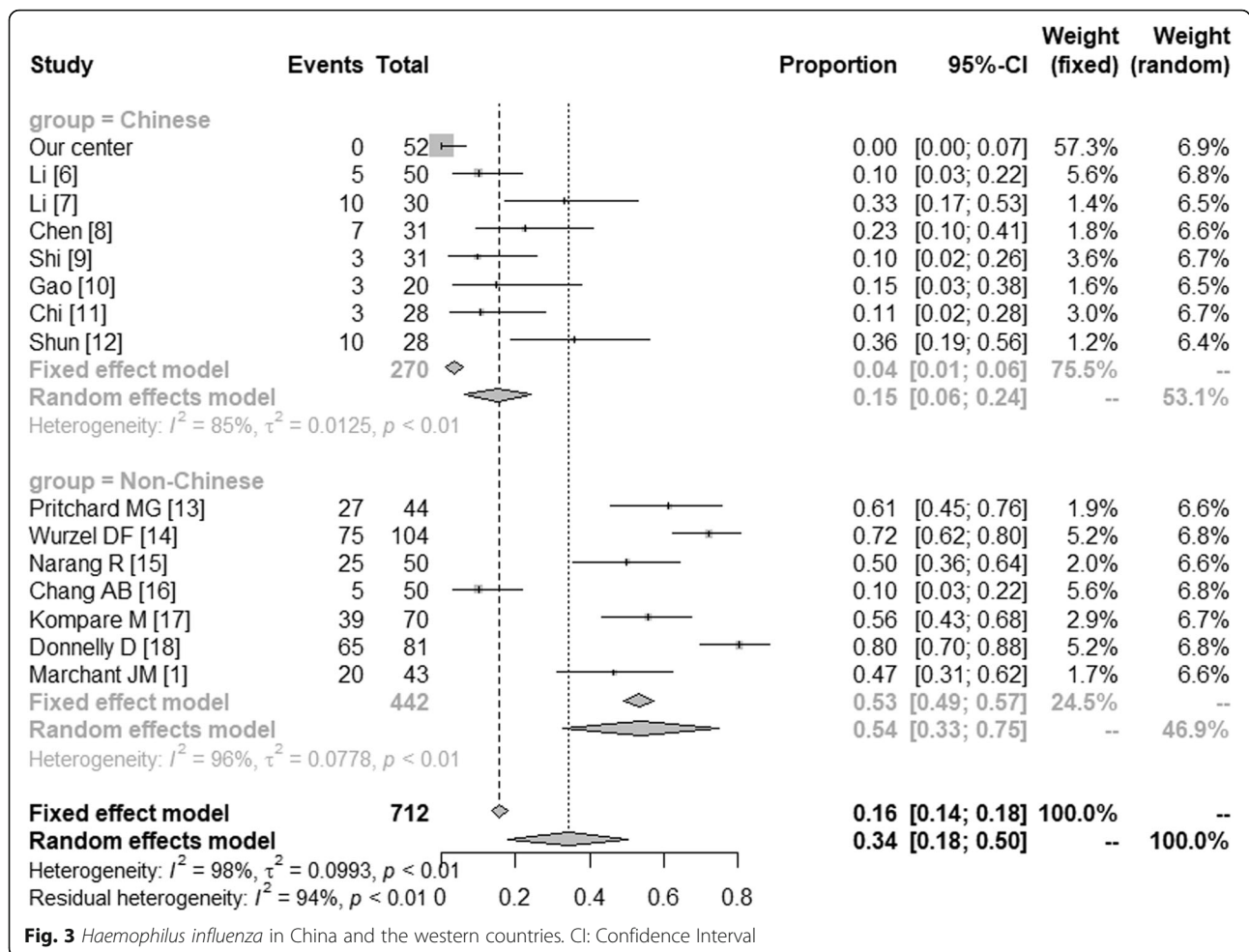
The microbiologically-based-PBB and the main pathogens in China and in the western countries were further compared by meta-analysis. The microbiologically-based-PBB in China (Proportion = 0.57 [0.44; 0.74]) and in the western countries (Proportion = 0.97 [0.93; 1.00]) were shown in Fig. 1. In Fig. 2, we have compared the *Streptococcus pneumoniae* in Chinese (Proportion = 0.27 [0.19; 0.38]) and non-Chinese (Proportion = 0.34 [0.29; 0.41]). The *Haemophilus influenzae* in China (Proportion = 0.15 [0.06; 0.24]) and in the western countries (Proportion = 0.54 [0.33; 0.75]) were shown in Fig. 3. And Fig. 4 illustrated the *Moraxella catarrhalis* in Chinese (Proportion = 0.04 [0.00; 0.08]) and non-Chinese cases (Proportion = 0.30 [0.11; 0.49]).

Discussion

PBB is also known as persistent endobronchial infection and chronic bronchitis of childhood [4]. It was the most

frequent etiologies in children with chronic cough [19], however, it has remained largely unrecognized [20]. To make an accurate diagnosis and a therapeutic approach to this common disease in children is needed [21]. This study analyzed the clinical characteristics of PBB in our center and in the published clinical studies, in order to deepen the understanding of PBB and provide a partial basis for the management of PBB.

The confirmed diagnosis of PBB depended on positive bacterial cultures of sputum or BALF [5]. Most of the cases were clinically diagnosed PBB and only 25% of patients were diagnosed as microbiologically-based-PBB among the 52 children enrolled in our study. Studies published in China showed that microbiologically-based-PBB was 63.3%. In other words, there were more than 30% of PBB cases were diagnosed as clinically-based-PBB. However, the number of microbiologically-based-PBB was higher in western countries than that in China. The lower rate of the positive pathogen may be related to the small number of cases who underwent bronchoscopy because it is impractical to conduct bronchoscopy for every child with chronic wet cough [5]. Young

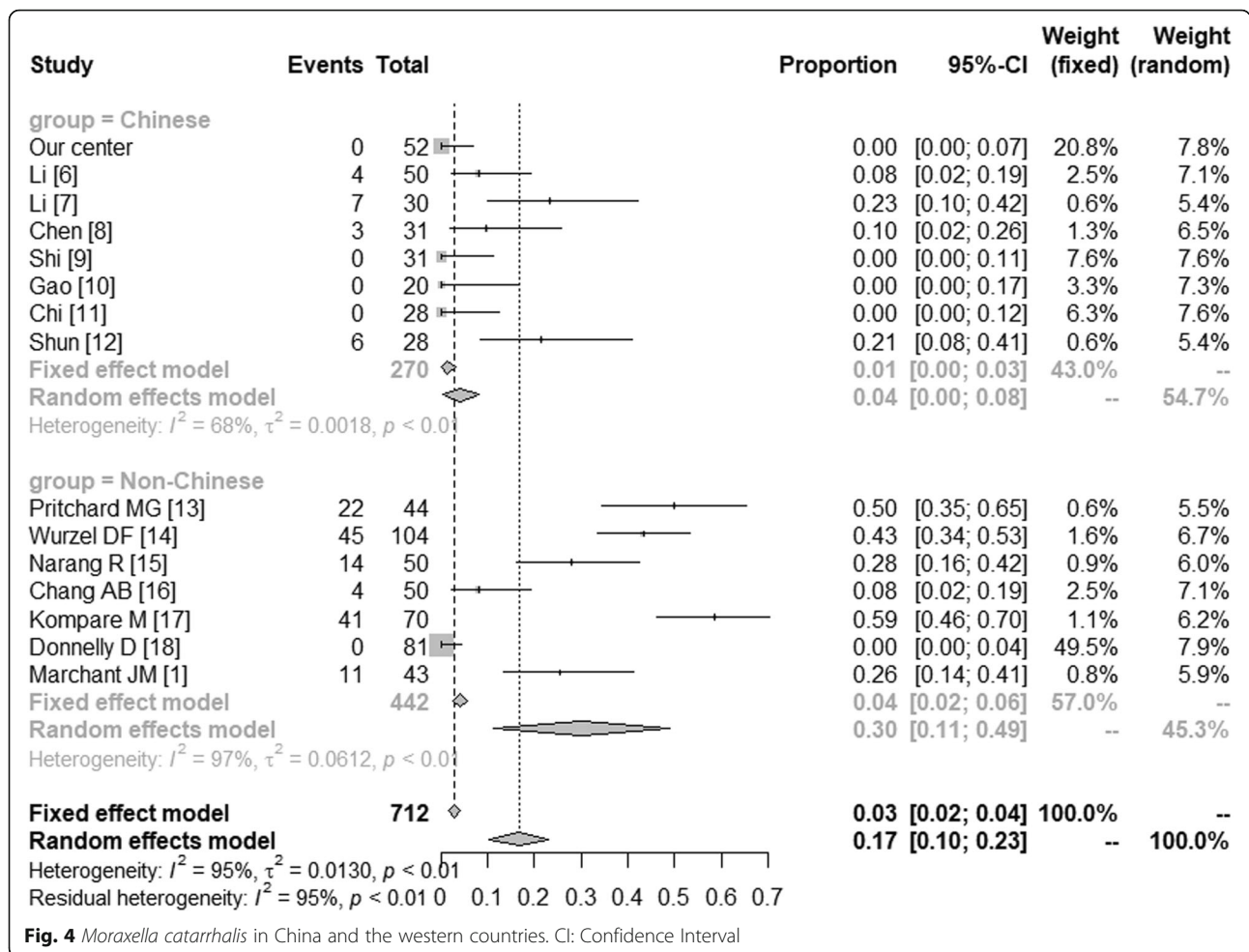


children usually couldn't expectorate efficient sputum for culture and the effect of antibiotic therapy before enrollment may also contribute to the negative culture. A study reported that the culture results of bronchial aspirates were the same with BALF in some of the cases [22]. Therefore, bronchial aspirates may replace BALF in patients who couldn't tolerate a lavage or expectorate sufficient sputum for reliable culture.

For the pathogen analysis, the most common pathogens in our center were Spn (17.3%) and Sa (5.8%), and the top five pathogens were Spn, Hi, Mcat, Sa, and Pae in the published Chinese research. The data from the western countries revealed that the main pathogenic bacteria were Hi, Mcat, Spn, and Sa. The top three pathogens were the same in the east and west, and Spn and Hi were the most frequent etiology in China and the western countries, respectively. This result may be caused by the inconsistent distribution of pathogenic bacteria and the choice of antibiotics in different countries and regions. Co-infection could be found in the identified studies, some patients were caused by multiple bacteria and several cases were co-infected by bacteria

and viruses [1, 14]. Consistent with the findings, microbiota dysbiosis can be found in the BALF of patients with PBB [23] and the inflammation may not be driven by single bacteria [24]. Viruses also can be detected in BALF of patients with PBB, however, there was no evidence to prove that PBB was virus-induced [25].

Studies showed that PBB occurred mainly in younger than 3 years old males [26]. In China, the youngest patient was 2 months old (median age was 8.5 months) and the duration of cough varied from 4 weeks to 2 months [11]. The onset age of patients with PBB in other countries was 3 months old (average age was 6 years old) and the longest duration was 60 months [14, 16, 17]. Our result was consistent with previous studies, most patients were less than 6 years old males, and the longest duration was 28 weeks, suggesting infants and preschool children with a chronic wet cough should be alert to be PBB. Some patients with PBB presented with wheezing, and some may co-exist with asthma [5]. The prospective studies [14, 16] found that approximately 60% of children with PBB were accompanied by wheezing, whereas a study reported wheezing could be observed in all



children with PBB [10]. Consistent with those findings, wheezing was the most common symptom in children with PBB in our study. PBB with chronic cough and wheezing was likely to misdiagnosis as asthma [13]. These children can be distinguished from asthma which was characterized by a dry cough and effective corticosteroid treatment [4, 27]. However, some children with unsatisfactory effects after antibiotic therapy should pay attention to the diagnosis of asthma because some PBB were finally diagnosed as asthma. In addition, the prolonged chronic wet cough of PBB may be associated with airway deformities which led to the dysfunction of cilia, mucus retention, and secondary infection. There were 3 cases of laryngomalacia and 1 case of airway stenosis in our data. Tracheobronchomalacia and airway stenosis was observed in patients with PBB in China. Wurzel [14] reported that 68.3% of PBB accompanied by tracheobronchomalacia (71/104 cases) and 74% (52/70 cases) of children were combined with airway malacia [17], suggesting that airway deformities were also common in patients with PBB in the western countries.

Amo was preferred for the treatment of PBB since it was sensitive to the common pathogens [5]. Studies showed that the improvement of cough symptoms required antibiotic treatment at least 10–14 days. Most children received a resolution of cough after amoxicillin-clavulanate treatments for 2–4 weeks, while cough relapsed again in some cases with tracheobronchial malacia [17]. Data in China found that most children treated with antibiotics received a resolution of cough, while certain patients with comorbidities (rhinitis, sinusitis) and poor compliance exhibited recurrent symptoms and unsatisfactory effects [7]. A retrospective study involving 81 children with PBB showed that cough relapsed in a large proportion of patients who received 2 weeks of antibiotic treatment and 13% of them needed a longer course of treatment [18]. The inflammation of PBB related to NLRP3/IL-1 β [28] and biofilm formation which was considered to be a reason for a longer period of antibiotic treatment [4]. Gross et al [29] suggested the duration of initial antibiotic treatment was associated with recurrent PBB because 6 weeks of antibiotics

treatment reduced the recurrent PBB than 2 weeks of treatment. Given cough was improved significantly in all patients who treated in hospital in our center, while 8 in 28 outpatients still had a cough. We proposed whether the patients' compliance in the different settings of treatment will affect the resolution of the symptoms. Therefore, 2 weeks of Amo treatment was considered to be reasonable, however, further investigations (such as comorbidities, bronchoscopy, culture of BALF, and patients' compliance) should be undertaken and the duration of treatment should be extended if symptoms persisted or relapsed [29, 30]. The vaccine may benefit to the management of PBB for it can decrease the respiratory symptoms and antibiotics course [31].

Studies suggested that PBB, chronic suppurative lung and bronchiectasis were in a dynamic development process. PBB was considered to be the early stage of chronic suppurative lung disease and it shared some similarities with early bronchiectasis [32]. PBB and bronchiectasis had similar gene expressions related to macrophage function and resolution of inflammation [33]. Although cause and effect were unproven, some repeated PBB may result in progress to bronchiectasis [4]. Li [7] reported a patient with PBB who developed to be bronchiectasis after a 1-year follow-up. A study revealed 13 children with PBB were diagnosed with bronchiectasis after 2 years follow-up in a prospective cohort study with 161 patients; Hi infection and recurrent PBB were the major risks for bronchiectasis [34]. Therefore, the possibility of bronchiectasis should be paid attention to patients with Hi infection and repeated PBB.

This study has the limitation that the sample size of our center was relatively small. The second limitation is the possibility of bias may exist because of the retrospective design. In addition, the follow-up was relatively short which may be difficult to reflect the outcome of PBB. Nevertheless, the combined analysis of the published data from the east and west limits this potential bias.

Conclusions

In conclusion, PBB is common in male infants with chronic wet cough and may be accompanied by wheezing and airway deformities. Most cases are clinically diagnosed PBB in China and microbiologically-based-PBB is common in western countries. Co-infection could be found, and Spn, Hi, Mcat are the main pathogens. Spn and Hi were the most frequent etiology in China and western countries, respectively. Patients with comorbidities may need extended antibiotics treatment for more than 2 weeks.

Abbreviations

Adv: Adenovirus; Amo: Amoxicillin-clavulanate; Azi: Azithromycin; BALF: Bronchoalveolar lavage fluid; Car: Carbapenems; Cep: Cephalosporin antibiotics; CI: Confidence Interval; Cla: Clarithromycin; Eae: *Enterobacter aerogenes*; Eco: *Escherichia coli*; F: Female; Hi: *Haemophilus influenzae*;

Kpn: *Klebsiella pneumoniae*; Lin: Linezolid; M: Male; Mcat: *Moraxella catarrhalis*; Pae: *Pseudomonas aeruginosa*; PBB: Protracted bacterial bronchitis; PIV: Parainfluenza virus; RSV: Respiratory syncytial virus; Sa: *Staphylococcus aureus*; Spn: *Streptococcus pneumoniae*; Tei: Teicoplanin

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Not applicable.

Authors' contributions

Xiaobo Zhang collected and analyzed the data, as well as prepared the manuscript; Xiao Wu collected the data and provided an interpretation of data; Guangmin Nong contributed to the conception of this study and overall supervision. The author(s) read and approved the final manuscript.

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Availability of data and materials

All data in this study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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