Frequency of pleural effusion in acute bronchiolitis and its effect on prognosis

Frequenza di versamento pleurico nella bronchiolite acuta e suoi effetti sulla prognosi

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ABSTRACT

Aim: **To analyze the frequency of pleural effusion and the effect on prognosis in children with acute bronchiolitis.**

Methods: **A total of 69 infants aged 1-24 months with acute bronchiolitis were studied between September 2009 and December 2010. All patients'age, sex, breastfeeding duration, exposure to smoking, history of using vitamin D, symptoms duration, physical examination and laboratory findings were recorded. Bronchiolitis score and predisposing factors that influence the disease process were determined. Thorax ultrasonography was carried out in all patients, who were evaluated on the 3rd and 7th day of the treatment.**

Results: **Mean age of patients (43 boys, 26 girls) was 11.97 ± 0.69 months (median 11 months). Breastfeeding duration was 8.26 ± 0.56 months (median 8 months). According to bronchiolitis score, 52 patients (75.4%) had mild and moderate bronchiolitis and 17 (24.6%) had severe bronchiolitis; 34 patients (49.2%) had pleural effusion. There was no relation between pleural effusion and symptoms. Frequency of pleural effusion was significantly higher in patients with risk factors.**

Conclusions: **This study demonstrated that most of the acute bronchiolitis cases in the infants studied were accompanied by pleural effusion. Pleural effusion in acute bronchiolitis had no effects on prognosis.**

Keywords: **Acute bronchiolitis, children, pleural effusion.**

SOMMARIO

Scopo: **Valutare la frequenza di versamento pleurico nei bambini affetti da bronchiolite acuta e l'effetto di questa complicanza sulla prognosi.**

Metodi: **Sono stati studiati in tutto 69 bambini piccoli di età compresa tra 1 e 24 mesi con bronchiolite acuta tra settembre 2009 e dicembre 2010. Età, sesso, durata dell'allattamento, esposizione a fumo, anamnesi di supplementazione di vitamina D, durata dei sintomi, esame obiettivo e dati di laboratorio sono stati raccolti per tutti i pazienti. Sono stati valutati lo score di bronchiolite ed i fattori predisponenti che influenzano il decorso della patologia. È stata effettuata un'ecografia toracica in tutti i pazienti ed una vista di controllo programmata alla 3ª e 7ª giornata di trattamento.**

Risulati: **L'età media dei pazienti (43 M e 26 F) era 11,97 ± 0,69 mesi (mediana 11 mesi). La durata dell'allattamento era 8,26 ± 0,56 mesi (mediana 8 mesi). Sulla base dello score di bronchiolite 52 pazienti (75,4%) avevano una bronchiolite di grado lieve e moderato, 17 (24,6%) grave; 34 pazienti (49,2%) presentavano un versamento pleurico. Non vi era relazione tra versamento pleurico e sintomatologia. La frequenza di versamento pleurico era significativamente più elevata nei pazienti con fattori di rischio.**

Conclusioni: **Questo studio dimostra che la maggior parte dei casi di bronchiolite acuta nei bambini piccoli studiati presentava versamento pleurico, ma questo non aveva un effetto negativo sulla prognosi.**

Parole chiave: **Bronchiolite acuta, pediatria, versamento pleurico.**

INTRODUCTION

Acute bronchiolitis is the most common lower respiratory tract disorder and is especially seen in children younger than 2 years old [1]. The relative narrowness of children's upper and lower respiratory tracts compared to adults', the looseness of their respiratory mucosa, the higher number of mucosa glands and the higher metabolic rate and oxygen consumption in children are factors facilitating de-

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velopment of infection. The pleural cavity is surrounded by parietal and visceral pleura. A small amount of liquid secreted by parietal pleura (0.25 ml/kg) is found in-between these two pleura surfaces [2]. The most common cause of pleural effusion in children is infection (50-70% of pleural effusions are parapneumonic effusions), congestive heart failure (5-15%) and malignancy [3]. Thorax ultrasonography (USG) gives information about the amount of pleural liquid, echogenicity and the thickness of the pleural leaf [4]. Data on the frequency of pleural effusion in viral infections of the lung are not available in the literature. This study aimed to determine the frequency of pleural effusion in children with acute bronchiolitis in the 0-2 year age group and to investigate the effects of pleural effusion on the recovery period and process.

MATERIAL AND METHODS

A total of 81 patients diagnosed with acute bronchiolitis during the period September 2009 to December 2010 were admitted to the study. The diagnosis was made based on history and physical examination [1]. Enrolment criteria were: infants aged 1-24 months with a first lower respiratory infection associated with at least one of the following: history of cough and rhinitis, wheezing, crackles, tachypnea, use of accessory muscles and/or nasal flaring, low oxygen saturation (SaO_2), cyanosis with/without fever. Twelve patients were excluded from the study because they failed to present for the control visits scheduled for the 3rd and 7th days of treatment. The parents were interviewed concerning age, gender, breastfeeding duration, smoking at home and their use of Vitamin D. Risk factors such as premature birth, bronchopulmonary dysplasia, congenital heart disease, immunodeficiency, which may affect the acute bronchiolitis process, were determined [1]. The duration of complaints and physical examination findings were recorded. The oxygen saturation of each patient was measured. Fever, coughing, rhinorrhea, cyanosis, apnea, tachypnea, use of accessory respiratory muscles, nasal flaring, wheeze, presence of rale and/or rhonchus, hepatosplenomegaly, and oxygen saturation were recorded. The Respiratory Distress Assessment Instrument (RDAI) was used to assess the severity of the disease [5]. RDAI score ≤ 8 indicates mild and moderate forms, whereas ≥ 9 severe forms (Table I).

Chest radiography was taken in all cases on admission, and parahilar peribronchial infiltrates, hyperexpansion, segmental or lobar atelectasis, and hilar adenopathy as a finding of acute bronchiolitis were assessed [6]. The patients were called in for control on the 3rd and 7th days of the treatment. We assumed recovery to have occurred with a return to normal of the physical examination findings, and with the remission of respiratory distress and toxic appearence. We excluded wheezing and chest radiography as criteria of recovery, because wheezing can persist in some infants for a week or longer [7] and also chest radiography may improve later.

All patients were observed by the same radiologist on admission for thoracic USG. The radiologist was blinded to the study. Patients who developed complications were given appropriate treatment. The thoracic USG was performed by a VX9-4 multi-frequency probe (Siemens Sonoline Antares). In the thoracic USG, a finding of < 5 mm pleural fluid thickness was taken as normal. Pleural fluid thickness of 5 mm or more was accepted as effusion [8].

Ethical Committee Approval

Approval for the study was obtained from the Fatih University, Faculty of Medicine Ethical Committee on June 13, 2009. In addition, written consent of the parents of the participants was collected.

STATISTICAL ANALYSIS

SPSS for Windows 11.5 was used for the statistical analysis of data. The Mann-Whitney U test was adopted for the assessment of variables between two groups; chi-square and Fisher Exact tests were used for categorical variables. In order to investigate the relationship between USG and bronchiolitis score, the chi-square test was used. The data obtained were defined as number and percentage for categorical data; arithmetic mean, standard deviation and median for the variables were defined by measurements. The value of $p < 0.05$ was accepted as statistically significant.

RESULTS

The mean age of the 69 cases was 11.97 ± 0.69 months (median 11 months). Twenty-six of the cases were girls (37.6%) while 43 were boys (62.3%). Twenty-five (36.2%) of the patients were admitted to the hospital in winter, 23 (33.3%) in the spring, 16 (23.1%) in the fall and 5 (7.2%) in the summer months. The period of their breastfeeding was 8.26 ± 0.56 months (median 8 months). Twenty-one patients (30.4%) had been treated in the neonatal intensive care unit due to prematurity, and 2 of these had been previously diagnosed with congenital heart diseases. Since echocardiographic examination was not repeated in our hospital, we had no data about pulmonary hypertension. Pleural effusion and use of antibiotics were significantly higher in these 21 patients (Tables II and III).

Fifty-two patients (75.3%) who participated in the study were evaluated as mild-moderate bronchiolitis according to their scoring; 17 patients (24.6%) were diagnosed with severe bronchiolitis and were hospitalized. The age was lower in severe bronchiolitis. Presence of risk factors [1], use of accessory respiratory muscles (retractions), tachypnea, nasal flaring, hepatomegaly, rales, and use of antibiotics were significantly higher in patients with severe disease ($p < 0.001$) (Table V). Also recovery time was significantly longer in this group.

In our study, chest radiography was taken on admission. Hyperexpansion was seen in the chest radiography of 28 patients (40.5%). Hilar adenopathy was

TABLE I: RESPIRATORY DISTRESS ASSESSMENT INSTRUMENT*

	N of points					
Variable	**0**	**1**	**2**	**3**	**4**	**Maximum points**
Wheezing						
Expiratory	None	End	1-2 (1/2nd expiration)	3-4 (3/4th expiration)	All	4
Inspiratory	None	Part	All	NA	NA	2
Location	None	Segmental ≤ 2-4th lung fields	Diffuse ≥ 3-4th lung fields	NA	NA	2
Retractions						
Supraclavicular	None	Mild	Moderate	Marked	NA	3
Intercostal	None	Mild	Moderate	Marked	NA	3
Subcostal	None	Mild	Moderate	Marked	NA	3

Definition of abbreviation: NA, not applicable.

*Within each variable the subscores are summed to give a total score.

The maximum total score for wheezing is 8, and for retraction is 9.

seen in only 5 cases. None of patients had infiltrations on admission. Thirty-one patients (44.9%) had persisting fever and respiratory symptoms despite treatment; chest radiography, repeated during the control visit, revealed parahilar peribronchial infiltrates.

In almost half of the patients, pleural effusion was detected in the thoracic USG. No significant relationship was found between the USG results and patient and disease characteristics except for the presence of a risk factor. Frequency of pleural effusion was significantly higher in patients with risk factors (Table II). No relationship was observed between bronchiolitis score and USG results

TABLE II: RELATIONSHIPS BETWEEN ULTRASONOGRAPHY (USG) AND PATIENT AND DISEASE CHARACTERISTICS

Factor	USG				P
	Normal (n = 35)		**Pathologic (n = 34)**		
	N	**%**	**N**	**%**	
Age (months)	11.8 ± 5.6 (Median = 11)		12.08 ± 5.9 (Median = 11.5)		0.780
Sex (Male/Female)	22/13		21/13		0.56
Use of mother's milk (months)	9.1 ± 5.1 (Median = 11)		7.3 ± 3.8 (Median = 6.5)		0.15
Smoking in the house	16	45.7	18	52.8	0.36
Use of vitamin D	35	100.0	31	91.2	0.11
Risk factor	4	11.4	17	50	0.01
Duration of symptoms (days)	4.5 ± 2.8 (Median = 4)		4.2 ± 3.4 (Median = 3)		0.41
Fever	13	37.1	18	52.9	0.23
Cough	35	100.0	31	91.2	0.11
Rhinitis	31	88.6	24	70.6	0.078
Wheezing	35	100	33	97.1	0.493
Rale	29	82.9	30	88.2	0.734
Rhonchus	34	97.1	33	97.1	1.000
Use of accessory respiratory muscles	13	37.1	14	41.2	0.808
Tachypnea	16	45.7	14	41.2	0.809
Nasal flaring	11	31.4	11	32.4	1.000
Antibiotic treatment (n)	22	62.9	22	64.7	1.000
Recovery period (days)	4.6 ± 2.1 (Median = 4)		5.3 ± 2.7 (Median = 5)		0.20

TABLE III: RELATIONSHIPS BETWEEN ANTIBIOTIC USE AND DISEASE CHARACTERISTICS

Factor	Use of Antibiotics				P
	Yes (n = 44)		No (n = 25)		
	N	%	N	%	
Presence of risk factor	18	40.9	3	12	0.015
Duration of symptoms (day)	5.3 ± 0.53 (Median = 4.5)		2.7 ± 0.21 (Median = 3.0)		0.001
Fever	21	47.7	10	40	0.610
Cough	43	97.7	23	92.0	0.296
Rhinitis	37	84.1	18	72.0	0.350
Wheezing	44	100	24	96	0.362
Rale	40	90.9	19	76.0	0.152
Rhonchus	42	95.5	25	100	0.531
Use of accessory respiratory muscles	23	52.3	4	16	0.004
Tachypnea	24	54.2	6	24	0.022
Nasal flaring	0	45.5	2	8.0	0.001
Recovery period (day)	5.9 ± 0.38 (Median = 5.0)		3.3 ± 0.16 (Median = 3.0)		0.001

(p = 0.52) (Table IV).

Vitamin D use was found to be quite high (95.6%). In 34 patients (49.2%), smoking in the home was present. No relationship was found between smoking at home and disorder characteristics (p = 0.834). During the follow up of patients, use of antibiotics was necessary in 44 patients (63.7%). When the relationship between antibiotic use and patient characteristics was examined, presence of risk factors, the duration of symptoms, occurrence of tachypnea or nasal flaring and recovery period were found to be significantly higher in antibiotics users (p = 0.015, p = 0.001, p = 0.022, p = 0.001, p = 0.001 respectively). The remaining characteristics were not significant (Table III).

DISCUSSION

In this study, it has been shown that pleural effusion accompanied 49.2% of the acute bronchiolitis cases. According to our knowledge, this is the first study to investigate the frequency of pleural effusion for acute bronchiolitis patients in the pediatric age group. Whereas pleural effusion may be asymptomatic, according to the amount of effusion it may also cause cough, dyspnea, retractions, tachypnea, orthopnea, the use of accessory respiratory muscles, and/or cyanosis [2]. These symptoms that overlap with the findings of acute bronchiolitis may result in the disruption of clinical treatment and longer recovery periods. There is insufficient information available about how pleural effusion takes place in acute bronchiolitis. However increased capillary permeability related with bronchial inflammation might be the cause of effusion. Nakayama et al. have shown that the increase of interleukin (IL)-1 beta and IL-6 in viral infections is related to pericardial effusion [9]. Similar inflammatory processes may explain pleural effusion in children with acute bronchiolitis. Also increased intrapleural negative pressure and the increased pulmonary capillary pressure due to increased cardiac load may have a role [2]. In this study, even though it was not statistically significant, we found in the pleural effusion group that the recovery period was longer, accompanied by higher risk factors, and fever, tachypnea and nasal flaring was more frequently seen.

Clinical risk factors for hospitalization in the acute bronchiolitis process include premature birth, bronchopulmonary dysplasia, congenital heart diseases, and immunodeficiency [1]. In our study, 21 patients had been treated in the neonatal intensive care unit due to prematurity and of these 2 were diagnosed with congenital heart diseases. Also, frequency of pleural effusion was significantly higher in the 21 patients with risk factors. Similarly in this study, the recovery time, frequency of severe disease, and use of antibiotics were significantly higher in patients with risk factors. As expected, use of accessory respiratory muscles, tachypnea, nasal flaring, and hepatomegaly were significantly higher

TABLE IV: RELATIONSHIP BETWEEN BRONCHIOLITIS SCORE AND ULTRASONOGRAPHY (USG)

	Bronchiolitis score		
	Mild-moderate	Severe	Total
USG finding			
Positive	26 (76.5%)	8 (23.5%)	34 (100%)
Negative	26 (74.3%)	9 (25.7%)	35 (100%)
Total	52 (75.4%)	17 (24.6%)	59 (100%)

χ^2 = 0.044, p = 0.52.

TABLE V: COMPARISON OF FREQUENCIES OF CLINICAL SIGNS/SYMPTOMS BETWEEN MILD-MODERATE AND SEVERE CASES

	Mild-moderate N (%)	Severe N (%)	p
Fever	23 (44.2)	8 (47)	0.52
Cough	49 (94.2)	17 (100)	0.42
Rhinitis	39 (75)	16 (94.1)	0.08
Wheezing	51 (98)	17 (100)	0.75
Rale	42 (80.7)	17 (100)	0.047
Rhonchus	50 (96.1)	17 (100)	0.56
Retractions	10 (19.2)	17 (100)	0.000
Tachypnea	13 (25)	17 (100)	0.000
Nasal flaring	5 (9.6)	17 (100)	0.000
Hepatomegaly	4 (7.6)	17 (100)	0.000

in patients with severe disease. Pulmonary hypertension and hemodynamic instability caused by infection can facilitate the formation of pleural effusion in patients with congenital heart disease. Incomplete development of the airway, damage to the airway, and airway hyperreactivity underlie the increased morbidity of respiratory syncytial virus infection in prematurely born infants and may explain the development of pleural effusion [10].

Acute bronchiolitis is usually a self-confining disorder and acute inflammations may be observed in the respiratory tract, eustachian tube and middle ear. Hypoxemia, respiratory failure, apnea and bacterial superinfection are among the complications related to bronchiolitis. Less frequently, myocarditis, inappropriate antidiuretic hormone excretion, and bronchiolitis obliterans due to over formation of granulation tissue during regeneration of bronchioles may be experienced. In children with bronchiolitis, the existence of fever, young age and secondary bacterial infections may be considered as indications for antibiotic use [11,12]. Such bacterial infections should be treated in the same manner as they would be treated in the absence of bronchiolitis [1].

In children with bronchiolitis, the prevalence of otitis media may range between 16% and 50% [13,14]. In a study by Andrade et al. acute otitis media was detected in 62% of the 42 patients with bronchiolitis [15]. In this study, the secondary infection frequency was determined to be 63.7%; in the follow up, acute otitis media was detected in 13 patients (29.5%). Patients with acute otitis media were treated with amoxicillin (40 to 80 mg/kg per day divided into two doses) [16].

Current evidence does not support routine radiography in children with bronchiolitis and is insufficient to demonstrate that chest radiograph abnormalities correlate well with disease severity [1]. One study showed that parahilar peribronchial infiltrates, hyperexpansion, segmental or lobar atelectasis, and hilar adenopathy were the most common roentgenographic findings in acute bronchiolitis. Respiratory syncytial virus infection was associated with more abnormal chest roentgenograms than any of the other viruses. Hilar adenopathy was more common in adenovirus infection. Young infants had significantly more abnormal roentgenographic findings (more hyperexpansion and parahilar peribronchial infiltration) than older children [6]. In another study, 25% of the hospitalized bronchiolitis patients had radiological findings, such as atelectasis and infiltration [17]. In this study, chest radiography was performed on admission. We found that hyperexpansion was the most common radiological finding in acute bronchiolitis. Because none of the patients had infiltration on admission, we assumed the infiltration as a complication of acute bronchiolitis. In this study, febrile or hypoxemic infants of 1-4 months of age with lower respiratory tract infection were hospitalized. In afebrile infants 1-4 months of age with lower respiratory tract infection, the most likely bacterial pathogen is *C. Trachomatis*. Thus azithromycin (20 mg/kg once daily for 3 days) or erythromycin (50 mg/kg per day every 6 hours for 14 days) therapy was given to afebrile infants aged 1-4 months. *Streptococcus pneumoniae* is the most frequent cause of "typical" bacterial pneumonia in children of all ages. In children younger than 5 years who are thought to have bacterial lower respiratory tract infection based on clinical presentation, physical findings and supportive laboratory data, if obtained, but who do not require inpatient therapy, amoxicillin is usually considered the drug of choice. For this reason, amoxicillin therapy (90-100 mg/kg per day by mouth in 3 divided doses for 7 to 10 days) was given to febrile infants from 4 months to 2 years of age. In this age group, in children who failed to improve after 24 to 48 hours of amoxicillin therapy, a macrolide was added [18]. When the relationship between antibiotic use and patient characteristics was examined, presence of risk factors, tachypnea, nasal flaring and recovery period were found to be significantly higher in those who used antibiotics. This significance may be related to severity of disease.

The limitations of this study are that viral serology was not carried out and that we had a small number of acute bronchiolitis patients.

In conclusion, this study demonstrated that a high ratio of pleural effusion accompanies acute bronchiolitis cases. Studies that analyze the effect on pleural effusion in acute bronchiolitis in more detail are required.

CONFLICT OF INTEREST STATEMENT: None of the authors has any conflict of interest to declare in relation to the subject matter of this manuscript.

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